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Review Article

The use of transjugular intrahepatic portosystemic stent shunt (TIPS) in the management of portal hypertensive bleeding

Gin-Ho Lo^{a,b,*}

^a Department of Medical Research, Digestive Center, E-Da Hospital, Kaohsiung, Taiwan, ROC ^b I-Shou University, Kaohsiung, Taiwan, ROC

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Abstract

Acute esophageal variceal hemorrhage is a terrible complication of portal hypertension and. rebleeding is very common in survivors of acute variceal bleeding. Traditional medical management options include the use of vasoconstrictor, balloon tamponade, and endoscopic therapy. Though endoscopic therapy has achieved successful hemostasis in the majority of acute variceal bleeding episodes, the outcome is usually dismal when such therapy fails. Transjugular intrahepatic portosystemic stent shunt (TIPS) was invented to decompress portal hypertension, but is now widely used in Western countries to treat patients with refractory variceal hemorrhage or refractory ascites. By contrast, TIPS has not been commonly used in Asia. In this article, I have reviewed the role of TIPS in the management of portal hypertensive bleeding, which will hopefully be useful for clinicians facing variceal bleeding that is not amenable to endoscopic therapies. Copyright © 2014 Elsevier Taiwan LLC and the Chinese Medical Association. All rights reserved.

Keywords: esophageal varices; gastric varices; TIPS

1. Introduction

Acute esophageal variceal hemorrhage (AEVH) is a devastating complication of portal hypertension. The natural history of AEVH shows that its associated mortality may be as high as 40%, with a high incidence of early rebleeding, i.e., in about 30-50% of survivors.^{1,2} Fortunately, because of the advancement of medical and endoscopic therapies, the mortality rate has been reduced to approximately 15% in recent years. The factors responsible for AEVH are not well delineated. Portal pressure, variceal pressure, and the tension of the esophageal variceal wall are factors that have been demonstrated to be associated with AEVH. Hepatic venous pressure

E-mail address: ghlo@kimo.com (G.-H. Lo).

gradient (HVPG) > 12 mmHg is noted to be requisite in those patients with variceal rupture.³ Poor hepatic reserve and an abundance of red color signs on the large varices are also important factors predictive of AEVH.⁴

A few treatment options are available for the management of AEVH. Vasoconstrictors and endoscopic therapy are most frequently used to control AEVH. Up to 20-30% of these procedures may fail.^{1,5–8} Among various factors, HVPG > 20 mmHG measured early after admission has been documented to be an important prognostic factor predictive of treatment failure.⁹ To relieve portal pressure, beta blockers such as propranolol, nadolol, or carvedilol have been adopted to prevent variceal rebleeding.^{1,10–12} However, during acute bleeding, these drugs are not useful in hemostasis and are contraindicated in patients with unstable vital signs. By contrast, TIPS is used to alleviate portal hypertension, and could lead to cessation of torrential variceal bleeding as well as prevention of further rebleeding. We undertake a review of the development and application of TIPS on the therapy of

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^{*} Corresponding author. Dr. Gin-Ho Lo, Department of Medical Research, Digestive Center, E-DA Hospital, 1, Yi-Da Road, Kaohsiung County 824, Taiwan, ROC.

variceal bleeding, anticipating that this technique may be widely used to rescue patients with intractable variceal bleeding.

2. Development of TIPS

In 1969, Rosch and coworkers¹³ first introduced the concept of TIPS through the use of animal studies. In 1982, Colapinto et al¹⁴ were the first to apply TIPS to six patients with advanced cirrhosis and portal hypertension and lifethreatening esophageal variceal bleeding. The varices were obliterated angiographically, and an intrahepatic portosystemic shunt was created by inflating the 9-12 mm diameter angioplasty balloon of a Gruntzig dilatation catheter in the needle tract between the portal and hepatic veins. Consequently, the portal venous pressure was reduced by 20%. Although three patients survived the initial hemorrhage, all six patients died within 6 months despite the patency of the shunts that were examined at postmortem.¹⁴ Subsequently, Palmaz et al¹⁵ substantially advanced the field when they designed an expandable shunt, which became the basis of the current standard TIPS procedure to maintain long-term patency. TIPS was introduced into clinical practice in 1988.¹⁶ However, Ring and associates¹⁷ modified the technique by eliminating the transhepatic catheter and implanting a flexible Wallstent, which transformed TIPS into a 1-2-hour procedure with a high success rate and a low complication rate.¹⁸ Currently, TIPS is usually initiated through puncture of the right internal jugular vein, via the superior vena cava, into the right hepatic vein. Transhepatic portography was initially applied to recognize the portal vein for puncture at an early stage of development for TIPS. This approach has gradually been replaced by ultrasound-guided localization. Under fluoroscopic control, the major branch of the right portal vein could be punctured, avoiding the risk of bleeding evoked by percutaneous puncture of the portal vein. Thereafter, the Wallstent is usually dilated to 8-10 mm. If the varices are still filling rapidly, they may then be catheterized and embolized. It has been observed that 10% of patients may require overdilatation of a stent using a 12-mm balloon.¹⁹

After insertion of a stent, stenosis and occlusion may develop gradually, which in turn lead to reversal of portal hypertension. A dysfunction rate up to 80% was noted in the bare stents. Stents covered with polytetrafluoroethylene (PTFE) was demonstrated to improve shunt patency by avoiding the pseudointimal hyperplasia. Primary patency could be improved from 36% with bare stents to 76% with covered stents, with a significant reduction of hepatic encephalopathy and similar survival rates.²⁰

The first indication for TIPS was acute variceal hemorrhage that was not amenable to endoscopic and pharmacological therapy. Subsequently, TIPS was also used in the prevention of gastroesophageal variceal rebleeding, ectopic variceal bleeding, portal hypertensive gastropathy bleeding, and refractory ascites. To date, there have been a multitude of studies published related to TIPS.^{21,22} Most of these studies used bare stents, unless a variation was mentioned specifically. This

review focuses on the application of TIPS in the treatment of portal hypertensive bleeding.

3. TIPS for refractory esophageal variceal bleeding

The first indication for TIPS is refractory variceal bleeding, which is generally regarded as those variceal episodes that are not readily controlled by combination of vasoconstrictors and endoscopic therapy. In 1992, LaBerge et al²³ performed TIPS in 24 patients in whom endoscopic injection sclerotherapy (EIS) failed to control variceal bleeding. Hemostasis was achieved in the 12 patients with active bleeding, and the mortality rate at 1 month was 20%. In another series consisting of 59 patients, including 23 patients with active bleeding, bleeding control failed in two patients. The rebleeding rate was up to 31% and the mortality rate was 35% during the index hospitalization. Overall, serious complications were encountered in eight patients (14%).²⁴

In 1996, Sanyal et al²⁵ enrolled 30 patients with actively bleeding esophageal varices or contiguous gastric varices despite sclerotherapy for rescue TIPS insertion. TIPS was successfully placed in 29 patients and hemostasis was achieved in all 29 patients. The 6-week survival rate was 60%.²⁵ Banares and associates²⁶ used salvage TIPS for variceal bleeding uncontrolled by medical and endoscopic therapy in 56 decompensated cirrhosis patients. Hemostasis was achieved in 95% of these cases. Eight patients (15%) had recurrent bleeding at 1 month after TIPS, and seven died during the 1st week after the procedure. The mortality rate at 30 days was 28%.²⁶ A similar study from Azoulay et al,²⁷ who performed salvage TIPS within 3 hours after endoscopy, showed that hemostasis was achieved in 90% of cases and 10% had persistent bleeding. Early rebleeding was 7% and mortality at 30 days was 29%. The actuarial survival following salvage TIPS was 51.7% at 1 year.²⁷ Other similar studies showed that TIPS can be helpful for patients with acute variceal bleeding in whom medical and endoscopic therapy has failed.²⁸⁻³⁰ However, an appreciably high 1 month mortality rate up to 35% may be encountered.

4. Early use of TIPS in acute variceal bleeding with a high risk of treatment failure

HVPG > 20 mmHg has been noted to be an important factor predicting treatment failure in patients with acute variceal bleeding. Monescillo et al³¹ randomized 116 cirrhotic patients with acute variceal bleeding who had HVPG \geq 20 mmHg to receive TIPS within 24 hours of admission or be categorized in the non-TIPS group. The results showed that early TIPS had a reduced treatment failure as compared to the non-TIPS group (12% vs. 50%). The inhospital and 1-year mortality rates were also significantly reduced in the early-TIPS group (11% and 31%, respectively).³¹ However, a single session of sclerotherapy was applied in patients randomized to the non-TIPS group, which has been shown to be inferior to banding ligation in the control of active variceal hemorrhage.⁵ Moreover, aside from in Europe, HVPG measurement is not routinely performed in most hospitals.

However, patients with Child-Pugh Class B or C with persistent bleeding revealed through endoscopy were regarded as high risk for treatment failure. Garcia-Pagan et al³² performed a controlled study to compare TIPS and pharmacotherapy combined with endoscopic variceal ligation (EVL) in these 63 high risk acute variceal bleeding patients. Among the early TIPS group, a PTFE-covered stent was inserted within 72 hours of admission.³² After a median follow-up of 16 months, rebleeding or failure to control bleeding occurred in 45% of patients in the pharmacotherapy-EVL group as compared with 3% in the early TIPS group (p = 0.0001). The 1-year actuarial survival was 61% in the pharmacotherapy-EVL group versus 86% in the early-TIPS group (p < 0.001). Additionally, serious adverse events were similar between the two treatment groups. Surprisingly, the incidence of hepatic encephalopathy was higher in the pharmacotherapy-EVL group than the early TIPS group (29% vs. 15%). Thus, early TIPS was suggested for patients with cirrhosis who had acute variceal bleeding and high risk for treatment failure.

Is early TIPS really more effective than pharmacotherapy-EVL in the control of acute variceal hemorrhage? The outcomes of patients in the control arm of this study were noted to be worse than previous studies³³; thus, overestimation of the actual benefits of TIPS over standard therapy has been questioned.³⁴ Furthermore, 296 patients with varied reasons or who met the exclusion criteria had been excluded from that controlled trial. This may imply that a small proportion of patients with acute esophageal variceal bleeding may actually require early use of TIPS. As shown in the study by Augustin et al,³⁴ the combination of vasoconstrictor, antibiotics, and EVL after acute esophageal variceal bleeding is associated with very low mortality. Only Child-Pugh Class C patients with baseline creatinine level higher than 1.0 mg/dL carried a high mortality rate up to 46% as compared with 8% if creatinine level was less than 1.0 mg/dL. Our previous study revealed that patients with active variceal bleeding treated with emergency EVL could achieve a 97% successful hemostasis and 30-day mortality was 19%.⁵ Based on these studies, the selection of patients suitable for early TIPS appears to require further investigation. If the incidence of hepatic encephalopathy was indeed reduced in patients receiving early TIPS compared with those in the pharmacotherapy-EVL group, early TIPS should be considered in those patients with a high risk of treatment failure.

5. TIPS versus surgical shunt for acute esophageal variceal bleeding

Surgical shunt, devascularization, and esophageal transaction had been widely adopted in the past to control variceal bleeding. Currently, surgical measures to decompress portal hypertensive bleeding have been largely discarded by most cardiovascular surgeons except those who strongly advocate the approach.^{35,36} Orloff et al³⁷ performed a controlled study to compare emergency portacaval shunt (EPCS) and TIPS in patients with cirrhosis "all comers" with acute esophageal variceal bleeding. A total of 154 patients were enrolled, and EPCS or TIPS was initiated within 24 hours of variceal bleeding. The patients' follow-up duration was primarily in the 5-10 year range. TIPS was successful in controlling variceal bleeding for 30 days in 80% of patients, but long-term control of variceal bleeding was achieved in only 22%. By contrast, EPCS controlled variceal bleeding immediately and permanently in 97% of patients (p < 0.001). Encephalopathy occurred with a threefold greater frequency following TIPS than after EPCS (61% vs. 21). The survival rate was significantly greater following EPCS than after TIPS (p < 0.001). This study suggested that in unselected patients with cirrhosis and acute esophageal variceal bleeding, EPCS could be a firstline emergency therapy. However, it is difficult to achieve such favorable outcomes by use of EPCS in other institutions. Contrary to the report of early TIPS by Garcia-Pagan et al,³² the outcomes of early-TIPS by Orloff³⁷ were apparently not as favorable and it is difficult to explain the discrepancy.

6. Controlled studies of TIPS versus endoscopic therapy for prevention of esophageal variceal rebleeding

Prior to the introduction of TIPS, beta blockers and endoscopic therapy have been widely used to prevent esophageal variceal rebleeding.^{10,38–40} Many studies have been undertaken to compare the relative effectiveness and safety between TIPS and endoscopic therapy or beta blockers. The recurrent bleeding rates associated with TIPS ranged from 10% to 24%, whereas it was approximately 26-57% among patients receiving endoscopic therapy. Hepatic encephalopathy was generally more common in patients treated with TIPS. Moreover, TIPS is associated with high rates of shunt stenosis and occlusion, 41-45 potentially because of the use of bare stents. A meta-analysis including 11 trials with 811 patients revealed that variceal rebleeding was significantly more frequent with endoscopic therapy (47%) compared with TIPS (19%). However, the use of TIPS did not improve survival.⁴⁶ Thus, TIPS is not considered to be the first-line choice in the prevention of esophageal variceal rebleeding.

Among the trials included in the analysis,⁴⁵ most studies adopted EIS as endoscopic therapy. Only three studies used EVL.⁴⁶⁻⁴⁸ Moreover, the rebleeding rates associated with EVL in these studies ranged from 42% to 59%, percentages that were remarkably higher than those in other studies demonstrating the superiority of EVL over sclerotherapy.^{49,50} EVL plus beta blocker is now regarded as the therapy of choice to prevent esophageal variceal bleeding.^{1,51} Interestingly, only two studies have compared EVL plus propranolol versus TIPS in the prevention of variceal rebleeding.^{42,52} The rebleeding rate was 30% in the combination group, compared with 19% in the TIPS group, without a statistically significant difference. Hepatic encephalopathy was found significantly more often in the TIPS group (40%) than in the combination group (20%). Based on these studies, it can be concluded that TIPS cannot be recommended as the first-choice treatment for prevention of variceal rebleeding.

7. TIPS versus drug therapy for prevention of esophageal variceal rebleeding

Drug therapy using a combination of beta blocker and isosorbide-5-mononitrate has been shown to be superior to or comparable to EVL in the prevention of esophageal variceal rebleeding.^{53–55} Until now, only one study had compared TIPS and drug therapy for prevention of esophageal variceal rebleeding.⁵⁶ The study enrolled 91 patients and showed that rebleeding occurred in 13% of TIPS-treated patients versus 39% of drug-treated patients. Encephalopathy was more frequent in TIPS than in drug-treated patients and the identified cost of therapy was double for TIPS-treated patients. However, the 2-year survival probability between the two treatments was identical. Thus, TIPS is suggested not to be used as a first-line treatment.

8. TIPS versus surgical shunt for prevention of esophageal variceal rebleeding

TIPS was created as a substitute for a surgical shunt in the treatment of portal hypertension. Consequently, it is probable that fewer shunt operations have occurred worldwide now that TIPS has become more widely available. However, controlled studies comparing between TIPS and shunt operation are also rarely reported. A controlled trial in 2006 comparing distal splenorenal shunt (DSRS) and TIPS in patients in whom medical therapy failed showed that the rebleeding rate was 5.5% in the DSRS group and 10.5% in the TIPS group, not a significant difference.⁵⁷ Also, the incidence of hepatic encephalopathy and survival were similar between both therapies. It appears that patients with esophageal variceal bleeding in whom medical therapy failed and with good liver reserve can be treated with either TIPS or shunt surgery.

9. TIPS for gastric variceal hemorrhage

It is well recognized that the general incidence of gastric variceal bleeding is significantly lower than that of esophageal variceal bleeding. However, rupture of gastric varices usually results in more severe hemorrhage and a higher mortality rate than esophageal varices.^{1,2} The optimal method to halt bleeding gastric varices is still an unresolved issue. A variety of methods including EIS, thrombin injection, EVL, use of detachable snares, endoscopic obturation using tissue adhesives (glue), TIPS, balloon-occluded retrograde transvenous obliteration (BRTO), and surgery have been used for the management of bleeding gastric varices with some success.^{58,59} Endoscopic obturation with cyanoacrylate (histoacryl or glue) has increasingly garnered support among medical practitioners worldwide, except for in the United States.⁵⁹

Many studies have demonstrated that TIPS is feasible for patients with gastric variceal hemorrhage. Two studies from England and France used TIPS to prevent rupture of gastric varices in patients with refractory bleeding.^{60,61} Hemostasis was achieved in 90–96% of patients. The follow-up period

was 7 months and 1 year, respectively. Rebleeding rates were similar between the two studies, i.e., 29% and 31%, respectively. These results suggested that TIPS could be used in patients with cirrhosis and refractory gastric variceal bleeding and were effective in achieving hemostasis as well as preventing rebleeding. The other studies also revealed that the use of TIPS in the management of gastric varices was as effective as its use in bleeding esophageal varices.^{62,63}

10. TIPS versus glue injection for gastric variceal hemorrhage

A retrospective analysis from the United Kingdom showed that the rebleeding rates within 30 days were significantly lower in TIPS patients than in patients using glue (15% vs. 30%, p = 0.005).⁶⁴ However, during the 6-month follow-up, rebleeding rates were 20% and 35%, respectively. TIPS as a therapy was significantly more expensive than glue therapy, though survival rates did not differ between the two groups. The other retrospective study from the United States showed that glue injection was similar to TIPS in controlling gastric variceal bleeding as well as preventing variceal rebleeding and survival.⁶⁵ However, the TIPS group had a higher rate of long-term morbidity requiring hospitalization (41% with a TIPS vs. 1.6% in the glue group, p < 0.0001).

We performed a prospective, randomized controlled trial comparing TIPS and glue therapy.⁶⁶ Our study enrolled 72 patients with acute gastric variceal hemorrhage that was initially controlled with vasoconstrictor and enodscopic therapy. After a median follow-up of 33 months, gastric variceal rebleeding was significantly lower in the TIPS group than in the glue group (11% vs. 38%, p = 0.01). Survival and complications were similar in both groups. Based on our trial, we suggested that TIPS could be the first choice in patients presenting with acute gastric variceal hemorrhage.

11. TIPS versus BRTO for gastric variceal hemorrhage

BRTO is widely used by Japanese gastroenterologists to treat fundal varices. This method uses a catheter through the femoral vein, inferior vena cava, and left renal vein to occlude feeding vessels of gastric varices; a large volume (40–50 mL) of a sclerosant, ethanolamine, is injected shortly afterward. BRTO is generally shown to be accompanied by satisfactory outcomes and mild adverse effects. However, BRTO is performed by radiologists and requires the presence of a gastrorenal shunt. Therefore, BRTO has not been adopted by gastroenterologists worldwide except for in Japan and Korea.

Two retrospective studies have compared TIPS and BRTO in the treatment of gastric variceal hemorrhage. One study from Korea included only 21 patients with active gastric variceal bleeding and showed that BRTO could achieve hemostasis and preventing rebleeding as effectively as TIPS.⁶⁷ The other study from Japan included 77 patients in the BRTO group and 27 patients in the TIPS group.⁶⁸ The cumulative gastric variceal rebleeding rate at 1 year was 2% in the BRTO group and 20% in the TIPS group. The survival rate was significantly more improved in Child-Pugh Class A patients receiving BRTO than in those receiving TIPS. The survival rate among Child-Pugh Class B and C was similar between both therapies.

12. Use of TIPS in Taiwan and Asia

Though TIPS is well accepted in Western countries as a treatment for portal hypertension, very few doctors in Taiwan are willing to use it to handle variceal hemorrhage. The handicap may be related to technique difficulty, fear of complications such as hepatic encephalopathy or restenosis, or possibly easier and successful control of variceal hemorrhage by current endoscopic therapies. The most important factor affecting the use of stents may be the lack of reimbursement by the National Health Insurance Administration of Taiwan. The first report regarding use of TIPS to address variceal bleeding in Taiwan showed that 15 of 16 TIPS were technically successful.⁶⁹ Unfortunately, two patients died from hypovolemic shock and acute respiratory distress, respectively. Among the six patients with active variceal bleeding, five (83%) achieved hemostasis. Recurrent variceal bleeding occurred in four patients (33%). Hepatic encephalopathy was encountered in three patients (25%). However, Tzeng et al⁷⁰ reviewed data from 107 patients receiving emergency TIPS treatment for refractory variceal bleeding. Control of bleeding was achieved in 61 of 73 patients (83%). However, rebleeding developed in 50% of these patients by the 12th month of follow-up and 23 patients (31%) died within 30 days of undergoing the TIPS procedure. The poor outcome related to these TIPS results may be because of application of TIPS as a rescue therapy as well as inexperience with the technique. Subsequently, with the improvement of technique, the use of TIPS to prevent gastric variceal rebleeding showed a favorable outcome.⁶⁵ Based on published studies, it appears that TIPS is also not popular in other Asian countries. In fact, BRTO is more popular than TIPS in Japan and Korea.^{67,68} This may explain why TIPS is rarely used in these countries for the management of variceal hemorrhage. In China, a retrospective analysis showed that early TIPS is more effective than endoscopic treatment in preventing variceal rebleeding and improving survival, without increase the occurrence of hepatic encephalopathy. In the other prospective study,⁷¹ TIPS combined with coronary vein embolization was shown to increase shunt patency and decrease rebleeding to 5.7%, compared with 20% in patients receiving TIPS alone.⁷²

13. Discussion

The widespread use of TIPS in the treatment of portal hypertension has been ongoing for more than 2 decades. The TIPS device was created to substitute for the existing shunt operation. The use of TIPS is advantageous because it obviates the risk of mortality associated with surgical intervention. Moreover, the use of TIPS instead of a surgical shunt could theoretically decrease the disadvantages inherent in the process of liver transplantation. However, a variety of complications may be encountered.^{22,23} These complications may be classified as technical, shunting-induced, and systemic (Table 1). The occurrence of technical complications is primarily related to operator technique. Variations in patients' anatomy can be important factors leading to dismal outcomes. Complications such as cardiac arrhythmia and hemoperitoneum may increase mortality rates, but can be reduced through practice of the technique. Regional complications such as shunt stenosis and occlusion are related to pseudointimal hypertrophy.¹⁸ However, covered stents have been documented to reduce the frequency of such complications. Furthermore, postprocedure monitoring with Doppler ultrasound every 6 months is advisable.⁷³ The flow velocity in the stent is expected to be between 80 cm/second and 160 cm/ second shortly after TIPS.⁷⁴ In case of shunt dysfunction, the necessity of revision should be based on the clinical situation at hand. The use of low-molecular-weight heparin in the immediate postprocedure environment is believed to reduce the risk of acute pulmonary embolism and the likelihood of thrombosis.¹⁹ Recurrence of variceal bleeding episodes are usually attributed to stenosis of the stents, and TIPS angiography and pressure measurement are often required.⁶⁶ TIPS may be regarded as a side-to-side shunt and thus the development of hepatic encephalopathy and hepatic failure after placement of a stent may be unavoidable. In our own experience, prophylactic use of lactulose 20-30 mL per day could prevent the occurrence of hepatic encephalopathy. On very

Table 1

Com	plications	of	transiugular	intrahepatic	portosystemic	stent shunt.
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Types	Complications	Incidence (%)
Technical complications		
-	Transcapsular puncture	33
	Biliary fistula, hemobilia	<5
	Hemoperitoneum	1-2
	Cardiac arrhythmias	<1
	Complete heart block	<1
	Fistula	Rare
	Nontarget organ (gallbladder, colon, kidney) rupture	Rare
Thrombotic-embolic	-	
complications		
	Shunt stenosis, occlusion	18-78
	Extensive thrombosis	3-15
	Pulmonary emboli	Rare
	Disseminated intravascular coagulation	Rare
Direct shunting-induced complications		
	Heart failure	Rare
	Acute pulmonary edema	Rare
	Hepatic encephalopathy	20-40
	Hepatic failure	5
	Severe hyperbilirubinemia	5
Systemic complications		
	Bacteremia, sepsis	2-10
	Fever not related to infection	1-5
	Hemolytic anemia	10-15
	Contrast-induced transient kidney failure	Rare

rare occasions, associated complications such as severe jaundice or hepatic encephalopathy may require occlusion of TIPS to prevent hepatic failure or control encephalopathy. Smaller diameter stents such as those less than 10 mm may elicit a lower risk of hepatic encephalopathy and hepatic failure. However, the effect of portal pressure decompression to less than 12 mmHg may be reduced with a small-diameter stent. The use of prophylactic antibiotics has not been shown to reduce the incidence of infection rates.⁶⁹ Some scholars still advocate the use of prophylactic antibiotics to decrease bacterial infections. A detailed discussion of TIPS complications and its management is presented in the study by Gaba et al.⁷⁵ Though many complications have been associated with the use of TIPS, most of these adverse events can be managed or lessened by supportive therapies. The TIPS procedure is estimated to be associated with a mortality of 1-2%. The use of a covered stent is documented to be able to reduce TIPS dysfunction and the incidence of hepatic encephalopathy.²⁰

The contraindications are shown in Table 2. Older age, pre-TIPS encephalopathy, Model for End-Stage Liver Disease (MELD) score higher than 18 and serum bilirubin greater than 3 mg/dL are the most significant predictors of outcome and may be regarded as relative contraindications.^{74,76} The indications of TIPS are summarized in Table 3. Currently, esophageal variceal bleeding can usually be managed with a combination of pharmacologic therapy, EVL, and control of gastric variceal bleeding by glue injection. Because of the associated potential complications, however, TIPS has been recommended as a rescue tool for treatment failure in acute variceal bleeding or failure in prevention of variceal rebleeding by a combination of pharmacologic and endoscopic therapy. Early TIPS may be required for patients with a high risk of treatment failure (i.e., Child-Pugh Class B with active bleeding upon endoscopy or Child-Pugh Class C). TIPS may also be advised for patients with concomitant prominent esophageal and gastric varices, because many endoscopic sessions may be required for these patients to achieve variceal obliteration. For patients with prominent gastroesophageal varices, with or without a history of bleeding, and the presence of massive ascites, TIPS may also be a good option to "treat two complications by one method". TIPS has also been shown to be effective for patients with ectopic variceal bleeding or portal hypertensive gastropathy bleeding, but not in gastric antral vascular ectasia.  $^{77-79}$  However, patients with contraindications (Table 2) should not be considered for TIPS. Patients

Table 2

Contraindications to transjugular intrahepatic portosystemic stent shunt.

Right heart failure Pulmonary hypertension Severe encephalopathy

Polycystic liver disease

Hepatocellular carcinoma or cholangiocarcinoma Portal vein thrombosis

Hepatic veins obstruction

Severe renal dysfunction

Systemic infection

#### Table 3

Indications for TIPS for portal hypertensive bleeding.

- Early TIPS for Child-Pugh Class B patients with active esophageal variceal bleeding at endoscopy or Child-Pugh Class C
- Refractory acute esophageal variceal bleeding by combination with endoscopic and pharmacologic therapy
- Recurrent esophageal variceal bleeding despite combination therapy with banding ligation and beta-blockers

Esophageal varices bleeding with concomitant gastric varices Gastric variceal bleeding, esophageal and fundal varices (GOV2) Recurrent gastric variceal bleeding despite endoscopic therapy Portal hypertensive gastropathy bleeding Ectopic variceal bleeding

Prophylaxis of first variceal bleeding in patients with refractory ascites

TIPS = transjugular intrahepatic portosystemic stent shunt.

presenting with acute variceal bleeding associated with hepatocellular carcinoma generally have a dismal prognosis.⁸ We have encountered one case of advanced hepatocellular carcinoma with intractable variceal bleeding by EVL and balloon tamponade that was finally rescued by TIPS; the patient survived for more than 2 years. In addition, it has been demonstrated that TIPS may influence first-line treatment of hepatocellular carcinoma, resulting in impaired overall survival.⁸⁰ Patients with acute variceal bleeding and poor liver reserve as shown by Child-Pugh score greater than 12, Acute Physiology and Chronic Health Evaluation II score greater than 18 points, and serum bilirubin greater than 6 mg/dL have a dismal outcome after TIPS.⁸¹ Thereafter, liver transplantation should be considered if possible.

In conclusion, TIPS has been widely used in the treatment of acute variceal bleeding and prevention of variceal rebleeding. The use of TIPS is beneficial for troublesome cases with variceal bleeding, but should be based on the procedural expertise that exists at each hospital.

#### References

- Garcia-Tsao G, Sanyal AJ, Grace ND, Carev W. Prevention and management of gastroesophageal varices and variceal hemorrhage in cirrhosis. *Hepatology* 2007;46:922–38.
- Carbonell N, Pauwels A, Serfaty L, Fourdan O, Lévy VG, Poupon R. Improved survival after variceal bleeding in patients with cirrhosis over the past two decades. *Hepatology* 2004;40:652–9.
- Bosch J, Abraldes JG, Groszmann R. Current management of portal hypertension. J Hepatol 2003;38:s54–68.
- Beppu K, Inokuchi K, Koyanagi N, Nakayama S, Sakata H, Kitano S, et al. Prediction of variceal hemorrhage by esophageal endoscopy. *Gastrointest Endosc* 1981;27:213–8.
- Lo GH, Lai KH, Cheng JS, Lin CK, Huang JS, Hsu PI, et al. Emergency banding ligation versus sclerotherapy for the control of active bleeding from esophageal varices. *Hepatology* 1997;25:1101–4.
- Lo GH, Chen WC, Chen MH, Tsai WL, Chan HH, Cheng LC, et al. The characteristics and the prognosis for patients presenting with actively bleeding esophageal varices at endoscopy. *Gastrointest Endosc* 2004;60: 714–20.
- Chen WC, Lo GH, Tsai WL, Hsu PI, Lin CK, Lai KH. Emergency endoscopic variceal ligation versus somatostatin for esophageal variceal bleeding. J Chin Med Assoc 2006;69:60–7.
- Lo GH. Management of acute esophageal variceal hemorrhage. *Kaohsiung J Med Sci* 2010;26:55–67.

- Moitinho E, Escorsell A, Bandi JC, Salmeron JH, Garcia-Paqan JC, Rodes J, et al. Prognostic value of early measurements of portal pressure in acute variceal bleeding. *Gastroenterology* 1999;117:626–31.
- Lebrec D, Poynard T, Hillon P, Benhamou J-P. Propranolol for prevention of recurrent gastrointestinal bleeding in patients with cirrhosis: a controlled study. N Engl J Med 1981;305:1371–4.
- Lo GH, Chen WC, Wang HM, Yu HC. Randomized, controlled trial of carvedilol versus nadolol plus isosorbide mononitrate for the prevention of variceal rebleeding. *J Gastroenterol Hepatol* 2012;27:1681–7.
- Lin HC, Yang YY, Hou MC, Huang YT, Lee FY, Lee SD. Acute administration of carvedilol is more effective than propranolol plus isosorbide-5-mononitrate in the reduction of portal pressure in patients with viral cirrhosis. *Am J Gastroenterol* 2004;**99**:1953–8.
- Rosch J, Hanafee WN, Snow H. Transjugular portal venography and radiologic portacaval shunt: an experimental study. *Radiology* 1969;92: 1112-4.
- Colapinto RF, Stronell RD, Gildiner M, Ritchie AC, Langer B, Taylor BR, et al. Formation of intrahepatic portosystemic shunts using a balloon dilatation catheter: preliminary clinical experience. *Am J Roentgenol* 1983;140:709–14.
- Palmaz JC, Sibbit RR, Reuter SR, Garcia F, Tio FO. Expandable intrahepatic portocaval stent shunts. Early experience in the dog. *Am J Roentgenol* 1985;145:821-5.
- Rossle M, Richter GM, Noldge G, Haag K, Wenz W, Gerok W, et al. Performance of an intrahepatic portacaval shunt (PCS) using a catheter technique: a case report. *Hepatology* 1988;8:1348A.
- Ring EJ, Lake JR, Roberts JP, Gordon RL, Laberge JM, Read AE. Using transjugular intrahepatic portosystemic shunts to control variceal bleeding before liver transplantation. *Ann Intern Med* 1992;116:304–9.
- Conn HO. Transjugular intrahepatic portal-systemic shunts: the state of the art. *Hepatology* 1993;17:148–58.
- Kerlan RK, LaBerge JM, Gordon RL, Ring EJ. Transjugular intrahepatic portosystemic shunts: current status. AJR Am J Roentgenol 1995;164: 1059–66.
- 20. Bureau C, Garcia Pagan JC, Layrargues GP, Metivier S, Bellot P, Perreault P, et al. Patency of stents covered with polytetrafluoroethylene in patients treated by transjugular intrahepatic portosystemic shunts: longterm results of a randomized multicentre study. *Liver Int* 2007;27:742–7.
- Burroughs AK, Patch D. Transjugular intrahepatic portosystemic shunt. Semi Liver Dis 1999;19:457-73.
- Boyer TD. Transjugular intrahepatic portosystemic shunt: current status. Gastroenterology 2003;124:1700–10.
- LaBerge JM, Ring EJ, Lake JR, Ferrell LD, Doherty MM, Gordon RL, et al. Transjugular intrahepatic portosystemic shunts: preliminary results in 25 patients. J Vasc Surg 1992;16:258–67.
- Helton WS, Belshaw A, Althaus S, Park S, Coldwell D, Joharsen K. Critical appraisal of the angiographic portacaval shunt (TIPS). *Am J Surg* 1993;165:566–71.
- Sanyal AJ, Freedman AM, Luketic VA, Purdum PP, Shiffman ML, Tisnado J, et al. Transjugular intrahepatic portosystemic shunts for patients with active variceal hemorrhage unresponsive to sclerotherapy. *Gastroenterology* 1996;111:138–46.
- Banares R, Casado M, Rodriguez-Laiz JM, Camunez F, Matilla A, Echenagusta A, et al. Urgent transjugular intrahepatic portosystemic shunts for control of acute variceal bleeding. *Am J Gastroenterol* 1998;93: 75–9.
- Azoulay D, Castaing D, Majno P, Saliba F, Ichai P, Smail A, et al. Salvage transjugular intrahepatic portosystemic shunts for uncontrolled variceal bleeding in patients with decompensated cirrhosis. *J Hepatol* 2001;35: 590-7.
- McCormick PA, Dick R, Panagou EB, Chin JK, Greenslade L, McIntyre N, et al. Emergency transjugular intrahepatic portasystemic stent shunting as salvage treatment for uncontrolled variceal bleeding. *Br J Surg* 1994;81:1324–7.
- Rubin RA, Haskal ZJ, O'Brien CB, Cope C, Brass CA. Transjugular intrahepatic portosystemic shunting: decreased survival for patients with high APACH II scores. Am J Gastroenterol 1995;90:556–63.

- Patch D, Nikolopoulou V, McCormick A, Dick R, Armonia A, Wannamethee G, et al. Factors related to early mortality after transjugular intrahepatic portosystemic shunt for failed endoscopy in acute variceal bleeding. *J Hepatol* 1998;28:454–60.
- Monescillo A, Martinez-Lagares F, Ruiz-del-Arbol L, Sierra A, Guevara C, Jimenez E, et al. Influence of portal hypertension and its early decompression by TIPS placement on the outcome of variceal bleeding. *Hepatology* 2004;40:793–801.
- Garcia-Pagan JC, Caca K, Bureau C, Laleman W, Appenrodt B, Luca A, et al. Early use of TIPS in patients with cirrhosis and variceal bleeding. N Engl J Med 2010;362:2370–9.
- 33. Abraldes JG, Villanueva C, Banares R, Aracil C, Catalina MV, Garcia-Pagan JC, et al. Hepatic venous pressure gradient and prognosis in patients with acute variceal bleeding treated with pharmacologic and endoscopic therapy. *J Hepatol* 2008;48:229–36.
- 34. Augustin S, Altamirano J, Gonzalez A, Dot J, Abu-Suboh M, Armengo JR, et al. Effectiveness of combined pharmacologic and ligation therapy in high-risk patients with acute esophageal variceal bleeding. *Am J Gastroenterol* 2011;**106**:1787–95.
- 35. Orloff MJ, Orloff MS, Orloff SL, Rambotti M, Girard B. Three decades of experience with emergency portacaval shunt for acutely bleeding esophageal varices in 400 unselected patients with cirrhosis of the liver. J Am Coll Surg 1995;180:257–72.
- Liao GS, Wu MH, Yu JC, Wu HS, Chen TW, Hsieh CB, et al. Transection of the esophagus is optional in the modified Sugiura procedure. *Hepatogastroenterology* 2009;89:133–8.
- Orloff MJ, Vaida F, Haynes KS, Hye RJ, Isenberg JI, Jinich-Brook H. Randomized controlled trial of emergency transjugular intrahepatic portosystemic shunt versus emergency portacaval shunt treatment of acute bleeding esophageal varices in cirrhosis. J Gastrointest Surg 2012;16: 2094–111.
- Garcia-Tsao G, Bosch J. Management of varices and variceal hemorrhage in cirrhosis. N Engl J Med 2010;362:823–32.
- Lo GH. The role of endoscopy in secondary prophylaxis of esophageal varices. *Clin Liver Dis* 2010;14:307–23.
- Lo GH. Prevention of esophageal variceal rebleeding. J Chin Med Assoc 2006;69:553–60.
- 41. Sanyal AJ, Freedman AM, Luketic VA, Purdum 3rd PP, Shiffman ML, Cole PE, et al. Transjugular intrahepatic portosystemic shunts compared with endoscopic sclerotherapy for the prevention of recurrent variceal hemorrhage. A randomized, controlled trial. *Ann Intern Med* 1997;**126**:849–57.
- 42. Cello JP, Ring EJ, Olcott EW, Koch J, Gordon R, Sandhu J, et al. Endoscopic sclerotherapy compared with percutaneous transjugular intrahepatic portosystemic shunts after initial sclerotherapy in patients with acute variceal hemorrhage: A randomized, controlled trial. *Ann Intern Med* 1997;**126**:858–65.
- Rossle M, Deibert P, Haag K, Ochs A, Olschewski M, Siegerstetter V, et al. Randomized trial of transjugular-intrahepatic-portosystemic shunt versus endoscopy plus propranolol for prevention of variceal rebleeding. *Lancet* 1997;**349**:1043–9.
- 44. Sauer P, Theilmann L, Stremmel W, Benz C, Richter GM, Stiehl A. Transjugular intrahepatic portosystemic stent shunt versus sclerotherapy plus propranolol for variceal rebleeding. *Gastroenterology* 1997;113: 1623–31.
- 45. Jalan R, Forrest EH, Stanley AJ, Redhead DN, Forbes J, Dillon JF, et al. A randomized trial comparing transjugular intrahepatic portosystemic stent shunt with variceal band ligation in the prevention of rebleeding from esophageal varices. *Hepatology* 1997;**26**:1115–22.
- 46. Papatheodoridis GV, Goulis J, Leandro G, Patch D, Burroughs AK. Transjugular intrahepatic portosystemic shunt compared with endoscopic treatment for prevention of variceal rebleeding: a meta-analysis. *Hepatology* 1999;**30**:612–22.
- 47. Pomier-Layrargues G, Villeneuve JP, Deschenes M, Bul B, Perreault P, Fenyves D, et al. Transjugular intrahepatic portosystemic shunt (TIPS) versus endoscopic variceal ligation in the prevention of variceal rebleeding in patients with cirrhosis: a randomised trial. *Gut* 2001;48: 390-6.

- 48. Sauer P, Benz C, Theilmann L, Richter G, Stremmel W, Stiehl A. Transjugular intrahepatic portosystemic stent shunt (TIPS) vs. endoscopic banding in the prevention of variceal rebleeding: final results of a randomized study (abstract). *Gastroenterology* 1998;114:A1334.
- Lo GH, Lai KH, Cheng JS, Hwu JH, Chang CF, Chen SM, et al. A prospective, randomized trial of sclerotherapy versus ligation in the management of bleeding esophageal varices. *Hepatology* 1995;22:466–71.
- Hou MC, Lin HC, Kuo BI, Chen CH, Lee FY, Lee SD. Comparison of endoscopic variceal injection sclerotherapy and ligation for the treatment of esophageal variceal hemorrhage: A prospective randomized trial. *Hepatology* 1995;21:1517–22.
- Lo GH, Lai KH, Cheng JS, Chen MH, Huang HC, Hsu PI, et al. Endoscopic variceal ligation plus nadolol and sucralfate compared with ligation alone for the prevention of variceal rebleeding: A prospective, randomized trial. *Hepatology* 2000;**32**:461–5.
- Sauer P, Hansmann J, Richter GM, Stremmel W, Stiehl A. Endoscopic variceal ligation plus propranolol vs. transjugular intrahepatic portosystemic shunt: a long-term randomized trial. *Endoscopy* 2002;34:690–7.
- Villanueva C, Minyana J, Ortiz J, Gallego A, Soriano G, Torras X, et al. Endoscopic ligation compared with combined treatment with nadolol and isosorbide mononitrate to prevent recurrent variceal bleeding. N Engl J Med 2001;345:647–55.
- Lo GH, Chen WC, Chen MH, Hsu PI, Lin CK, Tsai WL, et al. Banding ligation versus nadolol and isosorbide mononitrate for the prevention of esophageal variceal rebleeding. *Gastroenterology* 2002;123:728–34.
- Lo GH, Chen WC, Lin CK, Tsai WL, Chan HH, Chen TA, et al. Improved survival in patients receiving medical therapy as compared with banding ligation for the prevention of esophageal variceal rebleeding. *Hepatology* 2008;48:580–7.
- Escorsell A, Banares R, Garcia-Pagan JC, Gilabert R, Moitinho E, Piqueras B, et al. TIPS versus drug therapy in preventing variceal rebleeding in advanced cirrhosis: A randomized controlled trial. *Hepatology* 2002;**35**:385–92.
- Henderson JM, Boyer TD, Kutner MH, Galloway JR, Rikkers LF, Jeffers LJ, et al. Distal splenorenal shunt versus transjugular intrahepatic portal systemic shunt for variceal bleeding: a randomized trial. *Gastroenterology* 2006;**130**:1643–51.
- Sarin SK, Primignani M, Agarwal SR. Gastric varices. In: de Franchis R, editor. Portal hypertension III. Proceedings of the third Baveno International Consensus Workshop on definitions, methodology and therapeutic strategies. Oxford: Blackwell Science; 2001. pp. 76–96.
- Lo GH, Lai KH, Cheng JS, Chen MH, Chiang HT. A prospective, randomized trial of butyl cyanoacrylate injection versus band ligation in the management of bleeding gastric varices. *Hepatology* 2001;33: 1060-4.
- Chau TN, Patch D, Chan YW, Nagral A, Dick R, Burroughs AK. Salvage transjugular intrahepatic portosystemic shunts: gastric fundal compared with esophageal variceal bleeding. *Gastroenterology* 1998;114:981–7.
- Barange K, Peron JM, Imani K, Otal P, Payen JL, Rousseau H, et al. Transjugular intrahepatic portosystemic shunt in the treatment of refractory bleeding from ruptured gastric varices. *Hepatology* 1999;**30**: 1139–43.
- Rees CJ, Nylander DL, Thompson NP, Rose JD, Record CO, Hudson M. Do gastric and oesophageal varices bleed at different portal pressures and is TIPS an effective treatment? *Liver* 2000;20:253–6.
- 63. Tripathi D, Therapondos G, Jackson E, Redhead DN, Hayes PC. The role of the transjugular intrahepatic portosystemic stent shunt (TIPSS) in the management of bleeding gastric varices: clinical and haemodynamic correlations. *Gut* 2002;**51**:270–4.
- Mahadeva S, Bellamy MC, Kessel D, Davies MH, Millson CE. Costeffectiveness of N-butyl-2-cyanoacrylate (histoacryl) glue injections

versus transjugular intrahepatic portosystemic shunt in the management of acute gastric variceal bleeding. *Am J Gastroenterol* 2003;**98**:2688–93.

- Procaccini NJ, Al-Osaimi AM, Northup P, Argo C, Caldwell SH. Endoscopic cyanoacrylate versus transjugular intrahepatic portosystemic shunt for gastric variceal bleeding : a single-center v.s. analysis. *Gastrointest Endosc* 2009;**70**:881–7.
- 66. Lo GH, Liang HL, Chen WC, Chen MH, Lai KH, Hsu PI, et al. A prospective, randomized controlled trial of transjugular intrahepatic portosystemic shunt versus cyanoacrylate injection in the prevention of gastric variceal rebleeding. *Endoscopy* 2007;**39**:679–85.
- Choi YH, Yoon CJ, Park JH, Chung JW, Kwon JW, Choi GM. Balloonoccluded retrograde transvenous obliteration for gastric variceal bleeding: its feasibility compared with transjugular intrahepatic portosystemic shunt. *Korean J Radiol* 2003;4:109–16.
- Ninoi T, Nakamura K, Kaminou T, Nishida N, Sakai Y, Kitayama T, et al. TIPS versus transcatheter sclerotherapy for gastric varices. *AJR Am J Roentgenol* 2004;**183**:369–76.
- Yang CF, Tzeng WS, Chang JM, Liang HL, Huang JS, Pan HB, et al. Experience with transjugular intrahepatic portosystemic shunts for gastroesophageal variceal bleeding. *J Chin Med Assoc* 1996;57: 204–13.
- Tzeng WS, Wu RH, Lin CY, Chen JJ, Sheu MJ, Koay LB, et al. Prediction of mortality after emergent transjugular intrahepatic portosystemic shunt placement: use of APACHE II, Child- Pugh and MELD scores in Asian patients with refractory variceal hemorrhage. *Korean J Radiol* 2009;10: 481–9.
- 71. Chen S, Li X, Wei B, Tong H, Zhang MG, Huang ZY, et al. Recurrent variceal bleeding and shunt patency: prospective randomized controlled trial of transjugular intrahepatic portosystemic shunt alone or combined with coronary vein embolization. *Radiology* 2013;**268**:900–6.
- Xue H, Zhang M, Pang JX, Yan F, Li YC, Lv LS, et al. Transjugular intrahepatic portosystemic shunt vs endoscopic therapy in preventing variceal rebleeding. *World J Gastroenterol* 2012;18:7341–7.
- Zizka J, Elias P, Krajina A, Michl A, Lojik M, Ryska P, et al. Value of Doppler sonography in revealing transjugular intrahepatic portosystemic shunt malfunction: a 5 year experience in 216 patients. *AJR Am J Radiol* 2000;**175**:141–8.
- 74. Rossle M. TIPS: 25 years later. J Hepatol 2013;59:1081-93.
- Gaba RC, Khiatani VL, Knuttinen MG, Omene BO, Carrillo TC, Bui JT, et al. Comprehensive review of TIPS technical complications and how to avoid them. *AJR Am J Roentgenol* 2011;**196**:675–85.
- Salerno F, Merli M, Cazzangima M, Valeriano V, Rossi P, Lovaria A, et al. MELD score is better than Child-Pugh score in predicting 3-month survival of patients undergoing transjugular intrahepatic portosystemic shunt. *J Hepatol* 2002;**36**:494–500.
- Vangeli M, Patch D, Terreni N, Tibbalis J, Watkinson A, Davies N, et al. Bleeding ectopic varices- treatment with transjugular intrahepatic portosystemic shunt (TIPS) and embolization. *J Hepatol* 2004;41:560–6.
- Kamath PS, Lacerda M, Ahlquist DA, McKusick MA, Andrews JC, Nagomey DA. Gastric mucosal responses to intrahepatic portosystemic shunting in patients with cirrhosis. *Gastroenterology* 2000;118:905–11.
- Saphr L, Villeneuve JP, Dufresne MP, Tasse D, Bui B, Willems B, et al. Gastric antral vascular ectasia in cirrhotic patients: absence of relation with portal hypertension. *Gut* 1999;44:739–42.
- Knuppel E, Bettinger D, Euringer W, Thimme R, Roessle M, Spangenberg HC, et al. Influence of transjugular intrahepatic portosystemic stent on firstline treatment of hepatocellular carcinoma. *Hepatology* 2013;58:2211–2.
- Loffroy R, Estivalet L, Cherblanc V, Favelier S, Pottecher P, Hamza S, et al. Transjugular intrahepatic portosystemic shunt for the management of acute variceal hemorrhage. *World J Gastroenterol* 2013;19:6131–43.