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Using Transjugular Intrahepatic Portosystemic Shunts for Complications of Cirrhosis

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Introduction

Cirrhosis is a leading cause of morbidity and mortality and often arises during development of portal hypertension and its related complications. Portal decompression is therefore an important therapeutic objective. Historically, portal decompression was achieved by surgical diversion of blood from the portal vein to the systemic circulation. These major operations were associated with considerable mortality and morbidity, which decreased their utilization. About 25 years ago, a radiologic method for portal decompression, via a transjugular route, was developed to create a track between the intrahepatic portion of the portal vein and the hepatic vein, which was then kept patent using a metal stent. The transjugular intrahepatic portosystemic shunts (TIPS) revived interest in the use of portal decompression for treatment of portal hypertensive complications of cirrhosis. Over the last decade, the metal stents have been coated with materials to prevent occlusion of the lumen by in-growth of tissue from the surrounding liver. We review the clinical utility of TIPS and coated stents for the treatment of portal hypertension.

History of TIPS

Rosch and colleagues first described the creation of a track between the hepatic and portal vein using serial dilators via a cutaneous approach [1]. Subsequently, cryoprobes were used to extend the duration of patency of such tracks [2]. In 1981, Colapinto and colleagues created the first intrahepatic portosystemic shunt in a patient using balloon angioplasty [3]. The ability

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to keep the track open by placing an expandable metal stent was a major technical breakthrough in the development of TIPS [4]. The long-term efficacy of these shunts was however limited by the ingrowth of tissue from the surrounding liver. Due to concerns of stent dysfunction, polytetrafluoroethylene (PTFE) coated stents were introduced [5]. The use of PTFE covered stents are currently preferred over bare stents [6].

TIPS Procedure

Optimal outcomes following TIPS depend on a careful selection of the patient, technically proficient placement of the shunt and also the peri-procedural care of the patient. These are briefly reviewed below:

Patient preparation

The initial pre-procedural work up of a patient prior to TIPS placement depends on the clinical circumstances under which the shunt is to be placed. Regardless of whether the shunt is placed electively or emergently, a thorough medical assessment should always be performed to assess procedural risks [7]. Specifically, subjects with a prior history of encephalopathy should have the encephalopathy treated and their mental status optimized before elective TIPS placement [8]. It is also generally recommended that a large volume paracentesis be performed if tense ascites is present. This allows the liver to drop down and makes it easier for the angiographic catheter to get to the portal vein from the hepatic vein. If there is any suggestion of cardiopulmonary disease, a cardiac assessment is also warranted because of the potential for development of pulmonary edema following TIPS. A Doppler ultrasound exam to document patency of the portal vein should also be performed. The liver function should be assessed prior to the procedure with a bilirubin and INR; subjects with a high bilirubin are at risk of developing progressive liver failure after TIPS and may not be well served by this procedure especially when placed under elective circumstances [7]. Finally, antibiotic prophylaxis to cover bacteria resident in skin and in the intestine is often used and is a standard of practice although in a single clinical trial, routine antibiotic prophylaxis was not found to decrease peri-procedural infection [9, 10]. There is no role for the routine use of fresh frozen plasma or platelet transfusions in all cases undergoing TIPS.

The TIPS procedure

Using aseptic technique, a cutaneous access to the right jugular vein is obtained. Using this access, a catheter is passed via the right atrium in to the inferior vena cava and then the right hepatic vein [11]. The Colapinto needle is extruded and a track created between the hepatic and intrahepatic portion of the portal vein. This is secured by passage of a guidewire in to the portal vein. Balloon angioplasty is performed over the wire to dilate the track and then a stent is positioned across the track. The stent is then deployed and dilated up to achieve a diameter of about 10 mm Hg and to bring the pressure gradient between the portal vein and hepatic vein to less than 12 mm Hg [12].

Post-procedural management

The principal complication in the immediate perioperative period is hemorrhage. This is usually not clinically significant. However, occasionally hemoperitoneum from extrahepatic puncture of the portal vein and a large intrahepatic hematoma can develop. Vital signs are carefully monitored for several hours after the procedure. Shunt patency is assessed by use of Doppler sonography usually in the first four weeks and then at six months to a year; with currently available covered stents, the overall risk of shunt stenosis is approximately 24 % at 2 years [13]. The gold standard to evaluate shunt patency is angiography, however, due to cost and invasive nature, it is reserved for patients with stent occlusion on ultrasound or clinical signs of recurrent portal hypertension.

The use of TIPS in specific clinical conditions

The principal physiologic consequence of TIPS is the shunting of blood from the hypertensive portal vein to the hepatic vein thereby decompressing the portal vein. It is therefore used primarily to treat conditions that are directly related to portal hypertension. Variceal hemorrhage and ascites are two major complications of cirrhosis that are due to portal hypertension and TIPS plays a key role in the management of these complications.

Variceal hemorrhage

In-hospital mortality of variceal bleeding has decreased to approximately 15% over the last decade, which is still clinically significant [14]. The use of TIPS is likely to have played a key role in this improvement compared to prior literature. However, to use this procedure and obtain optimal outcomes, the role of TIPS must be considered in the context of where in the natural history of variceal hemorrhage it is used.

Primary Prophylaxis

There are no trials that have formally evaluated the value of TIPS for prophylactic portal decompression to keep the HVPG < 10 mm Hg and thus prevent varices and therefore variceal hemorrhage. On the other hand, the side effects of TIPS are well established [15]. Therefore, there is no role for TIPS for the prevention of varices or for primary prophylaxis of variceal hemorrhage. It has also been shown that TIPS performed prior to liver transplant or other intraabominal surgery does not reduce operative time or intra-operative blood loss [16]. Therefore the use of TIPS for these indications cannot be justified based on the available evidence.

Active hemorrhage

Once bleeding occurs, spontaneous hemostasis occurs in only 50% of subjects compared to over 90% of cases with non-variceal sources of upper gastrointestinal bleeding [17]. Those with a HVPG > 20 mm Hg who bleed are more likely to bleed severely and fail initial medical and endoscopic treatment. Patients are often bacteremic at the time of admission with bleeding and the use of prophylactic broad spectrum antibiotics directed towards intestinal flora has been shown to improve survival in the period around active hemorrhage [19]. Actively spurting varices, severe anemia and hypotension at the time of admission are also markers identifying subjects less likely to respond to medical therapy. In those where bleeding cannot be quickly controlled, the mortality is high [20]. Development of aspiration pneumonia, transfusion of more than 5 units of packed red cells, hypotension and the need for artificial ventilator support are risk factors for mortality [20].

The initial goals of management of active hemorrhage include hemodynamic resuscitation, prevention and treatment of complications and achievement of hemostasis. The principles and practice of hemodynamic resuscitation and management of complications have been reviewed in depth elsewhere and the reader is referred to several excellent reviews for a more detailed discussion of these topics [21]. The first-line approach for control of bleeding includes a combination of pharmacologic treatment and endoscopic variceal ligation (EVL) with rubber bands. This combination is superior to the use of pharmacologic or endoscopic treatment alone [21]. Endoscopic sclerotherapy may be performed when the bleeding is too severe to allow adequate visualization for band ligation but is rarely needed. Active esophageal variceal hemorrhage can be controlled in about 80% of subjects using such an approach. There are however cases where bleeding cannot be controlled and active bleeding continues or recurs following a brief period of cessation. Over transfusion is a risk factor for such early rebleeding and should be avoided; the target hemoglobin is in the 8–9 gm/dl range in such patients [22].

The failure to control bleeding is usually clinically obvious with large amounts of red blood in the nasogastric tube, hypotension, tachycardia and the need to continually transfuse to maintain the hemoglobin in the target range. This identifies a subset of patients at great risk of dying from their variceal hemorrhage [23]. When this occurs in septic subjects who are already hyperbilirubinemic, the mortality is particularly high [24]. The development of pneumonia and multiorgan failure are ominous and often pre-terminal events regardless of the outcome of bleeding.

Prior to the availability of TIPS, subjects who failed first-line therapy were managed by surgical approaches to control bleeding. Emergency surgery is a viable option for salvage therapy of variceal hemorrhage especially if the liver function is normal. However, in high risk patients, mortality from emergency portocaval surgery is high at 88% [17]. The ability to quickly decompress the portal vein with TIPS without the risks of major abdominal surgery has led to the use of TIPS for such cases. TIPS can be correctly placed and the portal vein decompressed in over 90% of subjects with severe refractory variceal hemorrhage [25]. In an early study, subjects deemed to be high risk for surgical portocaval shunting (i.e. those with aspiration pneumonia, severe liver failure (bilirubin >6mg/dl, and prothrombin time >5 seconds than control), tense ascites, severe cardiac, pulmonary or renal disease, or coma were managed by initial control of bleeding with balloon tamponade followed by TIPS within hours [26]. The airway was protected by intubation prior to balloon tamponade. Only 2/30 patients rebled due to variceal bleed. The 6 week survival rate was 60%, with aspiration pneumonia as the most common precipitant of multi-organ failure in those patients that died. Analysis of the subgroup of TIPS patients that did not develop aspiration pneumonia, revealed a 6 week survival of 90%. This study demonstrated that patients that have a high-risk of operative mortality can successfully be managed with a TIPS [26]. These data have been corroborated by several other studies [27–29].

In a study of subjects with refractory bleeding, the 30 day mortality following TIPS placement was 28% and survival was significantly lower in patients of Child-Pugh Class C, at 48% versus 90% for Childs A or C (P <.001) [30]. Subjects who have developed multi-organ failure or have severe hyperbilirubinemia and high model for end-stage liver disease (MELD) scores are likely to die even after successful achievement of hemostasis. It is therefore important to identify when first-line therapy has failed quickly and move to portal decompression with TIPS before complications such as sepsis, acute on chronic liver failure and multi-organ failure set it.

Prevention of rebleeding from varices

Survivors of an episode of variceal hemorrhage are at high risk of rebleeding if left alone [31]. The risk factors for recurrent hemorrhage include increasing age and severity of liver failure [23, 32]. The first-line treatment for prevention of rebleeding from esophageal varices is the combined use of EVL and non-selective beta blockers [21]. Numerous clinical trials have evaluated the utility of TIPS versus endoscopic therapy for the prevention of recurrent bleeding and are summarize in Table 1. The results of a meta-analysis on TIPS compared to endoscopic therapy for secondary prophylaxis of variceal hemorrhage are displayed in Figure 1 [33]. In general, most studies used bare stents and the endoscopic therapy used was sclerotherapy in many trials. The routine use of covered stents for TIPS and the use of EVL rather than sclerotherapy should be kept in mind while placing this literature in perspective.

In general, TIPS is superior to endoscopic treatment for the prevention of rebleeding. This does not however translate in to a survival advantage. TIPS is also associated with an increased risk of hepatic encephalopathy which occurs in about a third of subjects. Bare stents are further limited by the ingrowth of a pseudointima from the surrounding liver and the occlusion of the shunt from hyperplasia of this pseudointima [34, 35]. These considerations

relegated TIPS to the role of salvage therapy for refractory variceal hemorrhage and especially as a bridge to transplant [26, 28].

Several recent developments have led to the reassessment of the role of TIPS. First, the problem of shunt stenosis has been largely obviated by the availability of coated stents which are associated with a much improved patency rate (about 76% at 2 years) [36]. Also, in a landmark study, Monescillo et al performed hepatic vein catheterization within 12 hours of admission for variceal hemorrhage and randomized subjects with a HVPG > 20 mm Hg to either endoscopic treatment and beta blockers or TIPS [37]. Subjects receiving TIPS had significantly less bleeding and improved survival. A recent multi-center study also evaluated an early TIPS approach for long-term control of bleeding [38]. This trial also confirmed that TIPS performed within 72 hours of admission confers a survival advantage compared to EVL and pharmacologic treatment with beta blockers and nitrates (in 12/31 subjects). The results of this study are illustrated in Figure 2. While these are very encouraging and lead us to re-evaluate the role of TIPS in the long-term management of variceal bleeding, there are several findings that should give pause. First, the 6 week failure rate with EVL was 35%; this is a high failure rate and more than that expected within this time frame for subjects with a Child Pugh score < 13. The use of nitrates (which has been largely abandoned in routine practice) and its potential role in the failure rate of the EVL plus pharmacologic treatment arm prevents easy generalizability of these data. Finally, this study excluded subjects with a Child Pugh score > 13 and the data are principally applicable for those with lower CPT scores. Despite these caveats, there is now a growing trend towards early assessment of hepatic venous pressure gradients after initial control of bleeding and the use of TIPS within 72 hours especially if the liver function is relatively preserved.

TIPS has also been compared to surgical shunts to manage rebleeding esophageal varices. A meta-analysis revealed that the 30-day and 1 year survival was equivalent for TIPS and surgical shunts, however at 2 years, surgical shunt patients had greater survival with an Odds Ratio (OR) 2.5 (95% CI 1.2–5.2) [39]. Shunt failure was significantly reduced in surgical shunts versus TIPS [39]. However, with the advent of covered stents, this is less of an issue.

Recurrence of GI bleeding after TIPS placement

In most instances, TIPS is an effective way to control bleeding varices. There are however occasions when bleeding can recur. When bleeding continues despite adequate portal decompression, one may consider embolization of the left gastric vein [40]. On the other hand, if bleeding recurs a few days following TIPS placement, one must consider several possibilities. Immediately after TIPS placement, the stent continues to expand radially and shorten along its long axis. Therefore, if the stent does not protrude in to the portal vein by a few millimeters, the stent can retract in to the parenchymal tract causing it to collapse [34]. Another possibility is acute thrombosis of the shunt. This can be evaluated by a variety of imaging modalities. In some cases, recurrent bleeding may represent hemobilia due to a vascular-biliary fistula [15]. Finally, we have seen instances where subjects with elevated right heart pressures post-TIPS can reflect these pressures via the open shunt in to the portal system preventing adequate decompression. These possibilities should be considered when clinically significant bleeding recurs after a successful TIPS placement.

Ascites

Another major complication of cirrhosis is ascites. It affects over 60% of subjects with cirrhosis and results from hemodynamic changes triggered by sinusoidal portal hypertension which causes a decrease in effective circulating volume and activates sodium and water retention [41]. In the initial stages of ascites, the fluid can be easily managed with sodium

restriction and diuretics. However, a proportion of subjects is unresponsive to diuretics or cannot tolerate effective doses of diuretics due to the development of side effects. This is also referred to as refractory ascites [42]. Refractory ascites occurs in approximately 10% of patients with cirrhosis [43]. Progressive refractoriness to diuretics is a prelude to the onset of renal dysfunction and development of hepatorenal syndrome a dreaded complication of cirrhosis associated with a high mortality. Ascites with a low protein concentration in a subject with advanced liver failure and hyponatremia is at high risk of becoming infected resulting in spontaneous bacterial peritonitis. Spontaneous bacterial peritonitis can drive the progression from medically manageable ascites to refractory ascites and hepatorenal syndrome.

TIPS have been used principally for subjects with refractory ascites. The literature is however confounded by the small sample size in several studies, the failure to use albumin during large volume paracentesis, the widely varying serum albumin levels across trials and the exclusion of subjects with clinically significant hyperbilirubinemia in some but not other trials [44–48]. Regardless of these limitations, several facts stand out. TIPS is very effective in causing clinical resolution of ascites over a period of several weeks. This is mainly associated with a natriuresis which is caused by decreased proximal tubular sodium reabsorption as measured by lithium clearance [49]. It is also very effective and superior to repeated large volume paracentesis and diuretics for the maintenance of an ascites-free state. It is however noteworthy that most subjects need to continue sodium restriction and the majority of subjects require some diuretic dosing on an ongoing basis to maintain an ascites-free state.

The potential impact of TIPS on survival in subjects with refractory ascites remains controversial. The results of several randomized controlled trials are summarized in Table 2. Three large multicenter trials which were rigorously performed failed to demonstrate a survival advantage [45, 46, 48]. However, two studies showed an improvement in survival [44, 47]. One of these studies included subjects with more preserved liver function and is not truly comparable to the other studies [44]. In the other study, subjects with recurrent ascites despite paracentesis requiring additional taps (recidivant ascites) were included whereas in the earlier trials only subjects with truly refractory ascites were included [47]. Based on these data, it is the position of these authors that in subjects with rigorously documented refractory ascites, TIPS can be claimed to improve survival. It is however possible that if TIPS is performed when ascites recurs rapidly but does not fully meet criteria for refractory ascites, it may be beneficial. This possibility is currently under evaluation in a large multi-center clinical trial. Meta-analyses of these trials have been performed and come to divergent conclusions; it is our position that the heterogeneity across studies limits interpretation of these meta-analyses [50–54]. The results of one meta-analysis are outlined in Figure 3 [50].

Other indications and contraindications for TIPS

TIPS has been used for a number of portal hypertensive complications. There are several anecdotal series of the use of TIPS for the treatment of type 1 hepatorenal syndrome [55, 56]. The quality and strength of the evidence from these studies is suspect due to the small numbers of subjects, lack of randomization and retrospective nature of these data. It is also important to remember that the MELD score was originally developed to predict outcomes after TIPS and is driven largely by the serum creatinine [57]. At this time, the use of TIPS in such cases should be considered second line and experimental. In most centers, if used, it is used as a last ditch effort when all other means such as vasoconstrictor therapy has failed and liver transplant is not an option. In those who are transplant candidates, renal replacement therapy should be used to bridge them to transplant if they fail vasoconstrictor

therapy. The use of TIPS to prevent recurrence of hepatorenal syndrome after an initial response to vasoconstrictors remains experimental.

TIPS has also been used to control recurrent bleeding from portal gastropathy. There are instances where chronic bleeding from portal gastropathy requires repeated transfusions. TIPS have been found in one study to reduce transfusion requirement [58]. At this author's institution, the experience has been mixed with some subjects showing a beneficial response while others have not shown any response. It is also this authors anecdotal experience that subjects with NASH and portal gastropathy are more likely to have troublesome bleeding and that such cases are more likely to have elevated right heart pressures. TIPS has been used for management of gastric varices. One RCT comparing TIPS and cyanoacrylate for secondary prophylaxis demonstrated a significant reduction in rebleeding with TIPS with no difference in survival and one study demonstrated effective use of TIPS as salvage therapy in bleeding gastric varices [59, 60]. It was demonstrated that TIPS can effectively stop bleeding from ectopic varices and may be used particularly in cases with stomal variceal hemorrhage in subjects with an enterostomy and portal hypertension [61].

There are several reports of an effective resolution of refractory hepatic hydrothorax following TIPS [62–66]. All of the caveats about worsening liver failure should be kept in mind in this population who are quite sick to start with.

TIPS has also been used to effectively manage Budd Chiari syndrome [67–70]. In such cases, the hepatic vein cannot be entered and a direct vena cava to portal vein puncture is required. It effectively decompresses the hepatic parenchyma in such cases and can bring liver function back to normal. Budd Chiari syndrome is often associated with a hypercoagulable state and a work up for this is mandatory; TIPS placement is associated with an increased risk of thrombosis in such cases and most centers use anticoagulation routinely for at least six months even in the absence of demonstrable hypercoagulable state. In those with a hypercoagulable state and Budd Chiari syndrome, lifelong anticoagulation is recommended [71]. In those with chronic Budd Chiari syndrome, hypertrophy of the caudate lobe can compress the inferior vena cava; in such cases, additional stenting of the vena cava may be required to decompress the intrahepatic vena cava especially if symptomatic.

TIPS has been used in the management of portal vein thrombosis. A recent long-term follow up study on non-tumor related portal vein thrombosis treated with TIPS revealed thrombus resolution in 57% of patients, however many of these patients had non-occlusive thrombus, and TIPS was used as the primary indication in only 4 out of 70 patients[72]. There are case reports of TIPS placement and direct fibrinolysis of the thrombus followed by systemic anticoagulation [73]. These are high risk procedures and associated with considerable morbidity and are not considered routine standard of care procedures. In chronic extrahepatic portal vein obstruction with cavernous transformation, several reports indicate that TIPS can be placed in to one of the collaterals [74, 75]. However, whether this translates into clinical benefit remains an open question.

Another potential application of TIPS is the treatment of veno-occlusive disease. There are case reports and small series of subjects who received TIPS for veno-occlusive disease developing after bone marrow transplant [76–78]. The use of TIPS for this indication must be individualized given the relative paucity of data for this and the medically complex condition of a subject who has recently received a bone marrow transplant.

Although TIPS has been used in the management of the complications of portal hypertension, care must be taken when selecting appropriate patients to undergo a TIPS. The absolute and relative contraindications to a TIPS are outlined in Table 3 [6]. The presence of active encephalopathy is a relative contraindication for TIPS when being considered in an

elective setting. TIPS should not be considered for the treatment of hepato-pulmonary syndrome or porto-pulmonary syndrome. In the latter condition, the increased venous return to the right heart in the face of a fixed resistance in the pulmonary bed may precipitate severe right heart failure. For similar reasons, severe tricuspid regurgitation and congestive heart failure are contraindications to TIPS, as the TIPS can precipitate pulmonary edema in these conditions [79]. Subjects with polycystic liver disease are at high risk of bleeding if these are punctured during a TIPS and the procedure should not be performed in such cases [6]. The presence of a hepatocellular cancer especially with portal vein thrombosis is also considered a contraindication unless there is an isolated tumor far away from the track of the shunt. TIPS may be used to treat complications of cirrhosis, however, careful patient selection is important.

Complications of TIPS

There are three broad categories of complications of TIPS. These include those that are related to the technique, those related to portosystemic shunting and unique complications. These complications are summarized in Table 4.

Technical complications are mainly related to the puncture of structures that were not meant to be punctured and those related to malfunction or maldeployment of the stent. Figure 4 illustrates the development of a fistula between the TIPS stent and biliary system [15].

Hepatic encephalopathy is the most important medical complication after TIPS. It presents typically with acute worsening of mental status within 2–3 weeks of shunt placement [8]. Increasing age, liver dysfunction and shunt diameter are key risk factors for the development of encephalopathy after TIPS placement [80, 81]. Importantly, studies with bare stents found an increased risk of encephalopathy after TIPS placement for ascites [44, 45, 47, 48]. Subsequently, other studies found that the rates of encephalopathy were lower with coated stents compared to bare stents [36, 82]. A recent meta-analysis further corroborates this [83]. However, there are several issues that limit the robustness of these conclusions: (1) the trials were not designed to test this endpoint, (2) the methodology to evaluate encephalopathy was highly variable across studies and even from one study arm to the other in different studies, and (3) the data did not correct for background encephalopathy and liver function. These data are also somewhat counter-intuitive because one would expect greater shunt patency with coated stents and thus more portosystemic shunting and encephalopathy. These data however raise the intriguing possibility that better portal decompression reduces bowel edema and bacterial translocation thereby reducing the systemic inflammatory state associated with cirrhosis which has been implicated in the genesis of encephalopathy. This remains to be proven.

There are also unique complications of cirrhosis such as TIPS associated hemolysis and vegetative infections associated with TIPS [15, 84, 85]. TIPS induced hemolysis is rarely seen with coated stents. Vegetative infections associated with TIPS were also mainly reported with bare stents; these can be treated with prolonged antibiotics. We have in a single case removed the stent 2 months after placement using angiographic methods.

Summary

Since its first clinical application three decades ago, TIPS has become a treatment option for portal decompression. TIPS have been successfully used for secondary prophylaxis of variceal hemorrhage and in salvage therapy for acute variceal hemorrhage. TIPS have also been demonstrated to be superior to repeated large volume paracentesis to manage refractory ascites. However, the use of TIPS comes with the risk of hepatic encephalopathy and no survival benefit for refractory ascites. The survival benefit for TIPS as secondary

prophylaxis for variceal hemorrhage is controversial. Future trials should focus on optimizing patient selection to achieve a survival advantage with TIPS.

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Abbreviations

TIPS	Transjugular Intrahepatic Portosystemic Shunt
EVL	Endoscopic Variceal Ligation

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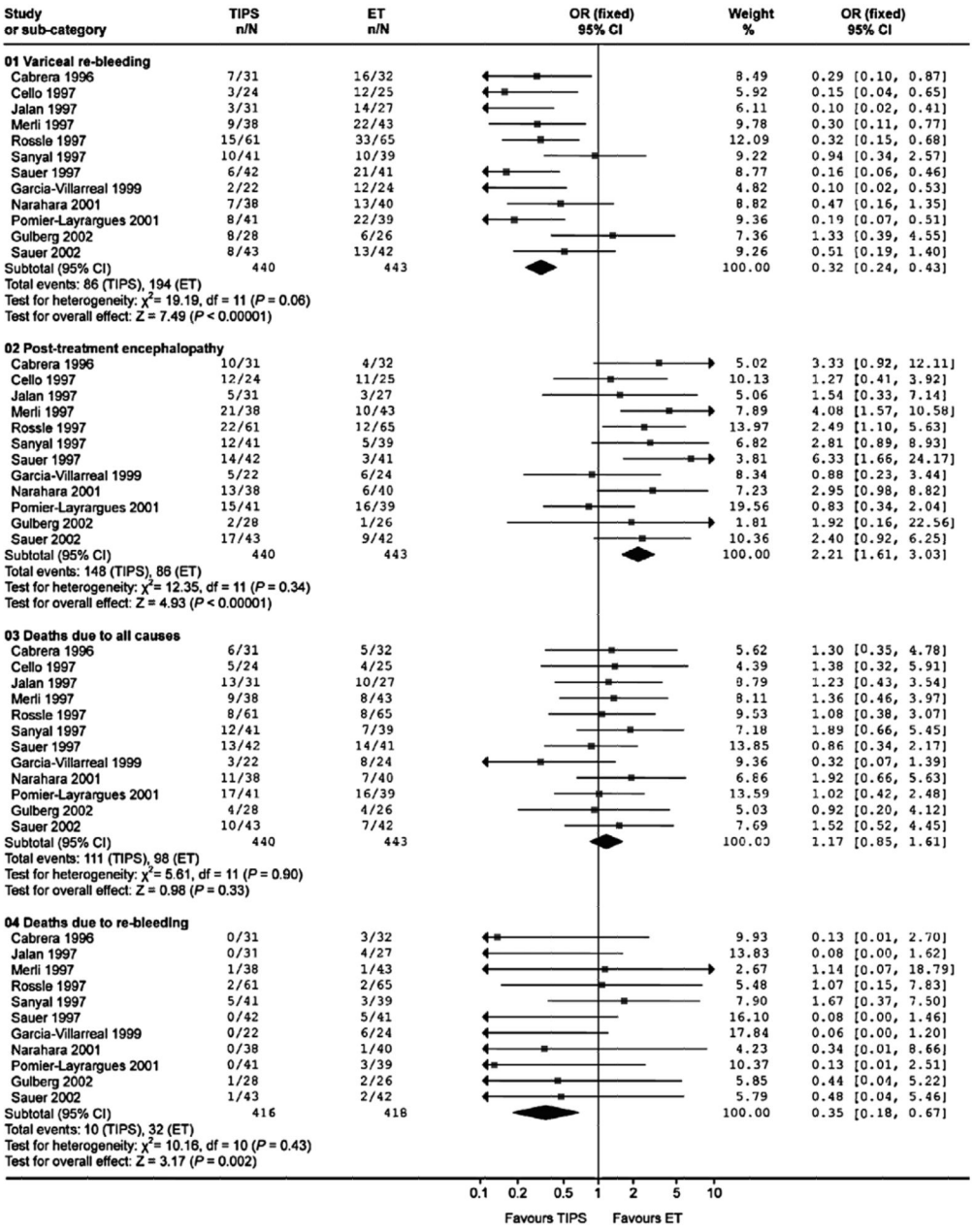

Figure 1.

Forest plot of meta-analysis revealing Odds Ratios for variceal re-bleeding, post-treatment encephalopathy, death due to all causes, and deaths due to re-bleeding comparing TIPS and endoscopic therapy [32].

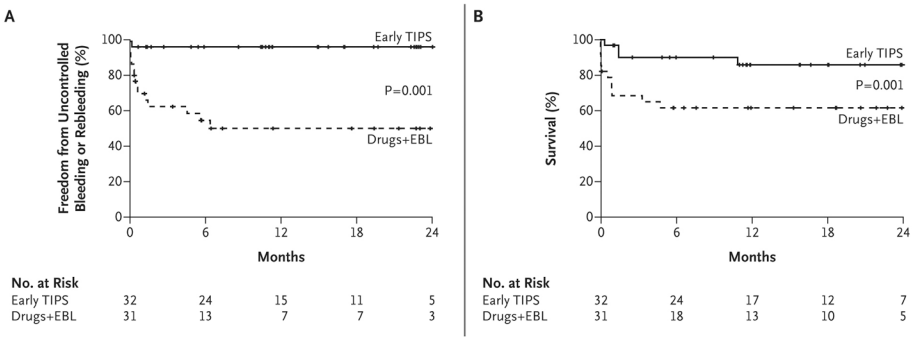

Figure 2.
Panel A: Probability of remaining free from rebleeding or uncontrolled bleeding. Panel B: Survival, according to treatment Group [38].

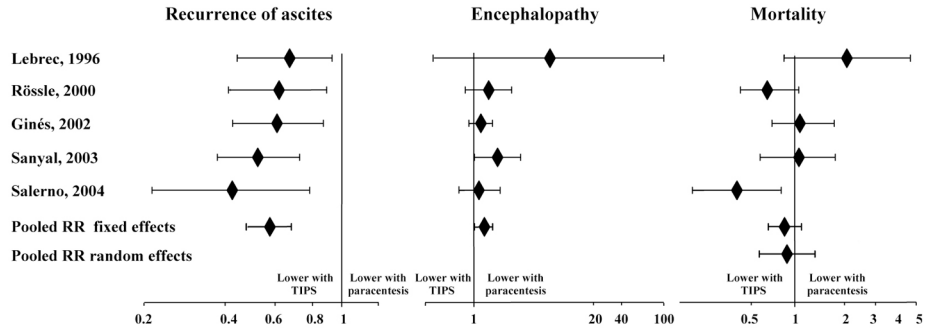

Figure 3.
Relative Risks and 95% CI for recurrence of ascites, encephalopathy and mortality comparing TIPS and repeated paracentesis for refractory ascites [50].

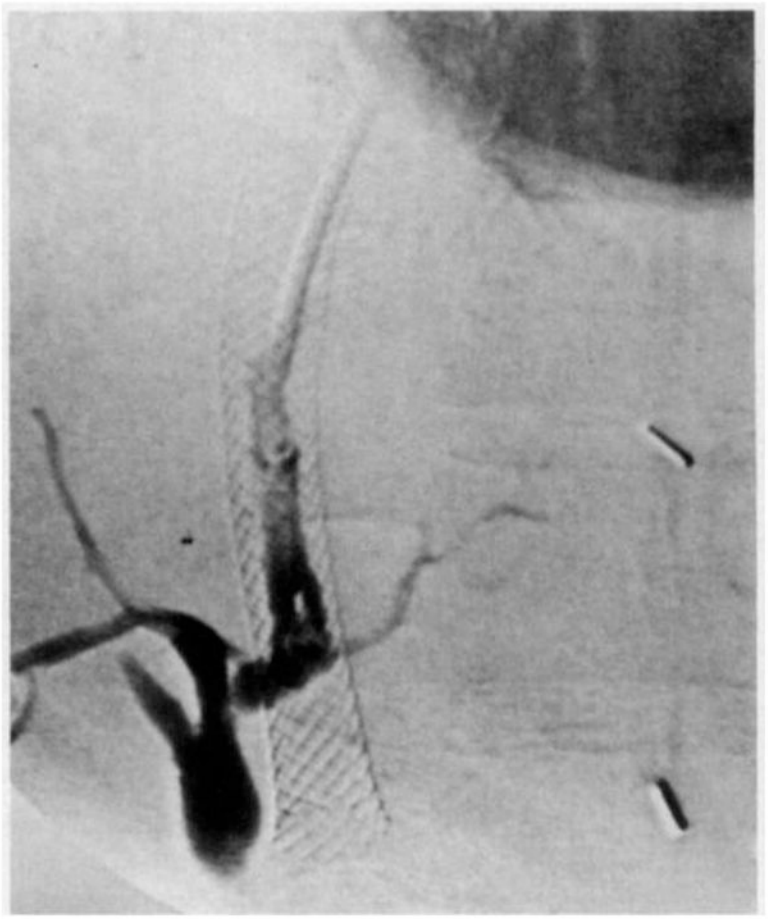

Figure 4.
Fistula between stent and biliary system [15].

Table 1

Randomized control trials for the use of TIPS versus endoscopic therapy as secondary prophylaxis of variceal hemorrhage.

Author, year	Endoscopic	N	Variceal Rebleeding (%)			Hepatic Encephalopathy (%)			Mortality (%)		
			TIPS	ET	*P* value	TIPS	ET	*P* value	TIPS	ET	*P* value
Cabrera, 1996	ES	63	23	52	<.02	33	13	<.05	20	16	NS
Cello, 1997	ES	49	13	48	.012	58	44	.2	42	36	NS
Jalan, 1997	EVL	58	10	52	.0006	36	33	NS	42	20	NS
Sanyal, 1997	ES	80	22	21	NS	29	13	.001	29	18	.03
Sauer, 1997	ES or EVL	83	23	57	.0001	29	13	.041	29	27	NS
Rossle, 1997	ES	46	15	41	<.001	36	18	.011	13	12	NS
Merli, 1998	ES	81	24	51	<.05	55	26	.006	24	19	.50
Garcia-Villareal, 1999	ES	46	9	50	.001	23	25	NS	15	33	<.05
Pomier- Layrargues, 2001	EVL	80	18	66	<.001	47	44	NS	41	41	NS
Sauer, 2002	EVL	85	19	30	NS	41	21	.041	19	17	NS
Gulberg, 2002	EVL	54	33	37	NS	8 #	4 #	--	20	17	NS
Garcia-Pagan, 2010	EVL	63	3	45	.001	25	39	NS	13	38	<.01

ET = Endoscopic therapy, ES = Sclerotherapy, EVL = Endoscopic Variceal Ligation, NS = Not statistically Significant (*P* value not stated), # at one month

Table 2

Randomized controlled trials to compare TIPS and repeated paracentesis in the management of refractory ascites.

Author, year	N	Treatment failure			Encephalopathy			Survival – 1 year		
		TIPS %	Repeated paracentesis	*P* value	TIPS %	Repeated paracentesis %	*P* value	TIPS %	Repeated paracentesis %	*P* value
Lebrec, 1996	25	77	92	--	23	0	--	29	56	<.05 #
Rossle, 2000	60	16	57	--	58	48	NS	69	52	NS
Gines, 2002	70	49	83	.003	77	66	NS *	41	35	NS
Sanyal, 2003	109	42	84	<.001	42	23	NS **	--	--	NS
Salerno, 2004	66	21	57	.012	61	39	NS ***	77	52	.021
Narahara, 2011	60	13	80	<.001	67	17	<.001	80	49	<.005

* severe encephalopathy grade III, IV was significantly higher in TIPS group (*P*=.03)

** higher incidence of moderate to severe HE in TIPS group (*P*=.058)

*** number severe HE episodes per patient higher in TIPS: 0.97 versus 0.36 (*P*=.039)

2-year survival

NS = not statistically significant

Table 3

Absolute and relative contraindications for TIPS procedure [6]

Absolute Contraindications	Relative Contraindications
Congestive Heart Failure	INR > 5
Severe pulmonary hypertension	Platelet < 20000/cm3
Multiple hepatic cysts	Moderate pulmonary hypertension
Uncontrolled systemic infection, or sepsis	Portal vein thrombosis
Unrelieved biliary obstruction	

Table 4

Complications of TIPS

Technical Complications	
(i) Related to access	Capsule puncture
	Intraperitoneal bleed
	Hepatic infarction
	Fistula
	Hemobilia
(ii) Related to the stent	Thrombosis
	Occlusion
	Stent Migration
	Sepsis
Related to portosystemic shunting	Hepatic encephalopathy
	Hemodynamic consequences
	Sepsis
	Intravascular hemolysis
Unique complications	Endotipsitis