Transjugular Intrahepatic Portosystemic Shunt before and after Liver Transplantation

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Abstract

The transjugular intrahepatic portosystemic shunt (TIPS) has long been referred to as a procedure performed as “a bridge to transplantation” since, like many other portosystemic shunts, it decompresses the portal circulation and stabilizes patients but does not definitively treat portal hypertension. One of the major advantages of TIPS over surgically placed portosystemic shunts in the transplant era is that the TIPS is intrahepatic and is removed in situ with the native liver, and usually does not need additional surgery (unlike takedown/ligation of surgical shunts). There are several studies that evaluate TIPS before transplantation—not as a bridge/temporizing measure, but as a prelude to the transplant to decompress the portal circulation and reduce portosystemic engorgement and collaterals and thus, in theory, reduce intraoperative bleeding during liver transplantation. However, these studies, mostly in the transplant literature, have been equivocal from an intraoperative and posttransplant clinical outcome standpoint. TIPS creation in liver transplant recipients is another interesting aspect of TIPS. There has been a debate about whether or not liver transplantation adds additional technical difficulty to the TIPS procedure. Initially, many theories were proposed as to the technical difficulty of TIPS in a transplanted liver. However, recent opinions and published studies demonstrate that whole-graft liver transplantation does not pose a significant technical difficulty to TIPS. Moreover, there are several recent studies evaluating the outcomes of TIPS in liver transplant recipients, showing that outcomes are less favorable when compared with TIPS in nontransplanted patients. This article discusses the results of TIPS as a preoperative prelude to liver transplantation. In addition, it discusses the technical and clinical outcomes of TIPS in liver transplant recipients.

Keywords

- TIPS
- portal hypertension
- liver transplantation

Objectives: Upon completion of this article, the reader will be able to describe the clinical indications, technical success, and complications arising from performing TIPS in the liver transplant population.

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Transjugular intrahepatic portosystemic shunt (TIPS) has long been used as “a bridge to transplantation” since, like many other portosystemic shunts, it decompresses the portal circulation and temporizes patients but does not definitively treat portal hypertension. One of the major advantages of

TIPS over surgically placed portosystemic shunts in the transplant era is that the TIPS is intrahepatic and is removed in situ with the native liver during transplantation, and usually does not need additional surgery (e.g., takedown/ligation of surgical shunts).¹ There are several studies that actually evaluate TIPS before transplantation, not as a bridge/temporizing measure but as a prelude to the transplant to decompress the portal circulation and reduce portosystemic engorgement and collaterals. This, in theory, may reduce intraoperative bleeding during liver transplantation.¹⁻²⁰

In addition, TIPS creation in liver transplant recipients is another interesting aspect of TIPS. There has been a debate whether or not liver transplantation adds additional technical difficulty to the TIPS procedure; there are several recent studies evaluating the outcomes of TIPS in liver transplant recipients.²¹⁻²⁷

TIPS as a Preoperative Prelude to Liver Transplantation

Bundled pricing/reimbursements for liver transplant surgeries have been the result of predictability (reproducible expenses) in hospital resource utilization.²⁸ Careful selection of liver transplant candidates and optimizing those at higher risk have been found to reduce hospital resource utilization and improve outcomes.²⁸⁻³⁰ In theory, pretransplant TIPS may reduce portosystemic collaterals and portal venous engorgement, which would reduce the risk of intraoperative bleeding and thus reduce the amount of transfused blood products. In addition to cost, intraoperative blood product transfusion during liver transplant operation is believed by many to be associated with worse clinical outcomes and reduced hospital resources.^{1,28} However, reduction of intraoperative transfusion of blood products has not shown consistent improved outcomes.¹⁻²⁰

► **Table 1** demonstrates a limited meta-analysis performed by Saad et al of hospital resource utilization including packed red blood cells in the transplant population.¹ The table demonstrates that from a hospital resource standpoint, there is no significant difference between orthotopic liver transplantations with prior TIPS and orthotopic liver transplants without a prior TIPS (► **Table 1**).¹ Interestingly, orthotopic liver transplants with surgical portosystemic shunts required rather than fewer hospital resources (including blood transfusion). This is because surgical portosystemic shunts need to

be reversed (be taken down), which adds to the transplant procedure time, complexity, and increased hospital resources (► **Table 1**). Commonly, these shunts are adhered, and the surgical anatomy and surgical dissection are difficult. This is the foundation of the assertion that one of the major advantages of TIPS in the transplant era is that it is removed in situ with the native liver, with little additional technical complexity to the transplant surgery. However, TIPS has occasionally been considered as a complicating factor in some liver transplant surgeries mostly by having the stent extend extrahepatically in the hepatic venous outflow inferior vena cava or in the main portal vein or mesenteric vein.^{1,9,31-38} The exact incidence of adding difficulty to transplantation surgery is unknown but is thought to be relatively uncommon, and reports of these difficulties are usually overstated.¹ Moreover, even studies reporting technical surgical difficulty during the transplant surgery due to an indwelling TIPS attest that the technical difficulties encountered are not insurmountable.^{1,9,31-38}

The study by Saad et al was the only study that compared adult right lobe living-related liver transplants with or without prior TIPS (TIPS performed intentionally with 48-72 hours before transplant surgery).¹ This case-controlled retrospective study also showed no significant value in performing TIPS before living-related liver transplantation. However, the authors did conclude that TIPS may reduce the risk of poor outcomes in high risk (high acute physiology and chronic health evaluation [APACHE-II] scores and coagulopathic patients) patients.¹

TIPS in Liver Transplant Recipients

Liver transplant recipients currently are living longer, and as a result hepatic grafts are more likely to fail (simply due to increased longevity) or hepatitis C may recur leading to recurrent portal hypertension.^{21,22} These two etiologies are the leading causes of recurrent portal hypertension in liver transplant recipients undergoing TIPS, but may vary between institutions and even countries. In three recent studies in the United States from four different institutions (one study included two institutions) including 79 liver transplant recipients, in 50 patients (63%, $n = 50/79$) the need for TIPS in the liver transplant was due to hepatitis C recurrence, and in 14 patients (18%, $n = 14/79$) was due to primary graft failure.^{22,24,25} A single study from the United Kingdom involving two institutions demonstrated that only 14% ($n = 3/22$) of

Table 1 Hospital resource utilization for adult orthotopic liver transplantations

Resource	OLT no TIPS	OLT + TIPS	OLT + SPSS
pRBC transfusion (L)	3.8 ($n = 4,018$)	3.4 ($n = 136$)	6.2 ($n = 163$)
Operating time (h)	6.6 ($n = 1,317$)	7.4 ($n = 138$)	10.1 ($n = 163$)
ICU stay	4.9 ($n = 1,234$)	5.0 ($n = 71$)	6.8 ($n = 138$)
Total hospital stay (d)	21.9 ($n = 1,270$)	26.3 ($n = 136$)	27.9 ($n = 253$)

Abbreviations: d, days; h, operating hours; ICU, intensive care unit; L, liters; OLT, adult orthotopic liver transplant; pRBC, packed red blood cells; SPSS, surgical portosystemic shunt; TIPS, transjugular intrahepatic portosystemic shunt.

Source: Modified from Saad et al.¹

patients had recurrent portal hypertension due to hepatitis C recurrence.²⁶

In the United States, TIPS is performed in 1 to 4% of liver transplant recipient patients.^{22,24,25} In three studies involving four institutions in the United States, a total of 81 liver transplant recipients underwent a TIPS procedure out of a total of 3,785 liver transplant recipients (2.1%, $n = 81/3,785$).^{22,24,25} Conversely, 5.5% of TIPS procedures performed at two of these institutions were found to be in transplant recipients.²² There are two issues for discussion regarding TIPS in liver transplant recipients: technical considerations and the outcome of TIPS in this particular population.

Technical Aspects

Since the early years of the dissemination of the clinical practice of TIPS in the United States, there has been a debate whether liver transplant anatomy adds to the technical difficulty of the posttransplant TIPS procedure.^{20,23,39,40} It has been emphasized that knowledge of portal and hepatic venous anatomy and surgical anastomoses is paramount before undertaking the TIPS procedure.

Piggyback Anastomosis

Richard et al raised the anatomic concern for piggyback anastomoses posing technical difficulty to the TIPS procedure.³⁹ Saad et al discussed the piggyback anastomosis and also supported the assertions that it may pose added technical difficulty, but only if the anastomosis is significantly angulated downward.²² Both studies were anecdotal and not substantiated with sufficient data due to very small sample sizes.^{22,39} Another concern about the piggyback anastomosis is that it is partly extrahepatic, and operators must be cognizant about avoiding extrahepatic punctures.²² If conventional TIPS cannot be achieved (or if there is concern for extrahepatic puncture), an unconventional TIPS approach such as the gun-site technique may be used.²² Capacious caval stumps and hepatic venous outflow stenoses may pose additional technical challenges during the TIPS procedure.^{22,39}

Split Grafts, Especially Left Lobe Grafts

Anecdotally, split grafts (especially undersized grafts such as left lobe grafts in growing children) may pose additional technical difficulties. This is because the orientation of the hepatic veins and portal veins may not be conventional because, as the grafts hypertrophy, they concurrently rotate. Moreover, almost all interventional radiologists are accustomed to performing the TIPS from a right or, to a lesser extent, middle hepatic vein approach while targeting the right portal vein; they are not generally accustomed to left hepatic vein to left portal vein TIPS creation. Real-time ultrasound guidance may be useful in these cases, or again the gun-site technique may be used.⁴⁰

Comparative Analysis of Technical Outcomes between TIPS in Hepatic Grafts and TIPS in Native Livers

A comparative technical analysis between TIPS in transplants and TIPS in native livers has been published.²² These authors made the comparison in two different institutions

that approached "difficult TIPS" in two different ways. One institution in the study approached an initial technical TIPS failure (transplant or native liver) by reattempting the conventional TIPS procedure another day with a different (usually more experienced) operator. The other institution switched from a conventional TIPS approach, defined as a single right transjugular approach, to an unconventional TIPS approach. Unconventional approaches included unconventional accesses or additional/augmenting accesses, which included femoral venous access, transhepatic venous access, gun-site technique, and left paraumbilical vein access.²² In both institutions, there was no significant difference in technical success on all attempts (conventional and/or unconventional), and there was no statistical significance in outcomes by converting to unconventional approaches.²² The overall first attempt technical success and ultimate technical success (multiple and/or unconventional approaches included) in both institutions for transplant livers versus native livers was 87 versus 92% for first attempts and 97 versus 97% for ultimate technical success.²² The authors did, however, state that the majority of these transplants were whole liver grafts, and not overly angulated piggyback anastomoses, and that if there were more split grafts or angulated piggyback anastomoses, the results may not have been so favorable.²²

Clinical Outcome

In recent years, with larger case numbers and longer follow-up, several studies have evaluated the clinical effectiveness of TIPS in liver transplant recipients (► **Table 2** demonstrates the studies that had 10 or more patients). Most recent studies report that TIPS appears to be less clinically effective in liver transplant recipients compared with nontransplanted patients.^{21,22,24,26,41} Moreover, TIPS in liver transplant recipients for ascites is likely to have a poor clinical response. The varying results in the literature is due to amalgamation of ascites patients with variceal bleeding patients, varying definitions of clinical success for ascites response, and varying degrees of retransplant thresholds.²² Most authors agree that transplant-free survival is poor, and Model for End-Stage Liver Disease (MELD) thresholds that predict poor survival are lower than those for patients with native livers (< 15–17 MELD indicative of poor prognosis and high mortality within 3–6 months without retransplantation).^{22,25,26} Two studies used a MELD of 15 as a threshold, and both demonstrated a significant survival difference with an average survival for a pre-TIPS MELD > 15 of 3 months and a pre-TIPS MELD < 15 of 49 months. One study used a MELD of 17 as a threshold, and demonstrated a significant transplant-free graft survival difference (1-year graft survival of 54 vs. 8% for pre-TIPS MELD < 17 vs. pre-TIPS MELD ≥ 17, respectively).²² Moreover, these authors compared the grafts that survived 3 months versus those that survived more than 3 months, and MELD score was a statistically significant predictor (14 ± 4.9 vs. 18.6 ± 4.5 months, respectively [$p = 0.002$]).²²

Two case-controlled studies compared the transplant TIPS group with nontransplant patients undergoing TIPS.^{24,26} Kim

Table 2 TIPS in liver transplant recipients

Study	n	Primary indications		Months from LT	Clinical success		Retransplant rate ^b	> 1-year survival
		Ascites	Variceal bleeding		Ascites ^a	Variceal bleeding		
Finkenstedt 2009	10	7 (70%)	1 (10%)	15	43%	100%	20%	20%
Amesur et al 1999	12	6 (50%)	6 (50%)	69	67%	67%	42%	64%
Kim et al 2008	14	8 (57%)	6 (43%)	46	57%	50%	0%	14%
Choi et al 2009	18	16 (89%)	2 (11%)	31	50%	100%	33%	–
Saad et al 2010 ^c	19	19 (100%)	0 (0%)	40	16%	–	21%	–
Feyssa et al 2011	26	26 (100%)	0 (0%)	17	58%	–	8%	50%
King et al 2011	22	14 (64%)	8 (36%)	45	78%	75%	0%	32%
Saad et al 2013	39	35 (90%)	4 (10%)	29	31%	100%	28%	22%
Total ^d	141	112 (79%)	29 (21%)	34	51%	74%	0–33%	14–64%

Abbreviations: LT, liver transplant; TIPS, transjugular intrahepatic portosystemic shunt.

^aClinical response is subject to definitions.

^bThis value should not be taken objectively, as retransplant rate is subject to graft availability, recipient stability, and the aggressiveness of the transplant service.

^cExcluded from the total analysis since the same patients were included in 2013 study.

^dThe total, if not given in a range, is a weighted mean (weighted to the number of cases in each study series).

et al showed a higher infectious complication rate in the posttransplant group, as well as a high hepatic encephalopathy rate (> 80%) and a poor 1-year transplant-free survival of 14%.²⁴ The high encephalopathy rate was suggested by an earlier study by Lerut et al to be due to the neurotoxic effect of calcineurin inhibitors that are not metabolized by the first pass metabolism of the liver (because it is bypassed by the TIPS); these authors documented high levels of the calcineurin inhibitors.²⁰ Conversely, King et al in another case-controlled study showed no difference in hepatic encephalopathy between transplant and nontransplant patients after undergoing TIPS.²⁶ However, the clinical success rate for TIPS was significantly lower for transplanted patients compared with nontransplant patients (93 vs. 77%, respectively).²⁶

Conclusion

In conclusion, TIPS as a prelude to liver transplantation in an attempt to decompress the portal circulation appears to have no effect on blood product and hospital resource utilization. Whole-graft liver transplantation does not pose significant technical difficulty on the TIPS procedure; however, split grafts and angulated piggyback anastomoses may pose additional technical difficulty for the TIPS procedure. Liver transplant recipients undergoing TIPS do not survive as long as their counterparts who have not been transplanted (graft survival is poor after TIPS), and a MELD score of less than 15 to 17 is a prognostic indicator of poor graft survival post-TIPS. Liver transplant recipients with ascites may not respond clinically as well as nontransplant patients do, although this finding is subject to graft survival and definitions of clinical success.

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