Clinical Science

Outcomes after transjugular intrahepatic portosystemic stent shunt: a “bridge” to nowhere

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Abstract
BACKGROUND: Transjugular intrahepatic portosystemic shunting was first conceived inadvertently by Josef Rosch in 1969. The transjugular intrahepatic portosystemic stent shunt (TIPS) was ultimately introduced in 1989 as a therapeutic option for the management of complicated portal hypertension.1–4

METHODS: Patients undergoing TIPS from 2001 to 2010 at a teaching hospital with a transplant program were studied. The median data are presented.

RESULTS: TIPS was undertaken in 256 patients. TIPS decreased portal vein–inferior vena cava (IVC) gradients from 17 to 5 mm Hg (P < .001). Reinterventions were undertaken in 54 patients (21%). Survival after TIPS was 26 months; liver transplantation was undertaken in 35 (14%) patients.

CONCLUSIONS: TIPS effectively decompresses portal hypertension but leads to frequent reinterventions and short survival. After TIPS, liver transplantation is uncommonly undertaken. TIPS is a “bridge” to transplantation that is seldom “crossed,” and TIPS continues to be plagued by frequent reinterventions. Outcomes after TIPS and the infrequency of transplantation after TIPS make it difficult to recommend on merit.

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Transjugular intrahepatic portosystemic shunting was first conceived inadvertently by Josef Rosch in 1969. The transjugular intrahepatic portosystemic stent shunt (TIPS) was ultimately introduced in 1989 as a therapeutic option for the management of complicated portal hypertension.1–4 Quickly, TIPS became the option of choice, particularly for nonsurgeons to treat variceal bleeding refractory to endoscopic therapy as well as ascites refractory to medical management in patients with portal hypertension.5 TIPS has become a widely used modality for portal decompression over the last 20 years, reducing portal pressures with technical success approximately 90% of the time.6,7

Liver transplantation continues to be the only hope of cure for portal hypertension. However, organ allocation and availability continue to be limiting factors. An inordinate number of patients are on the waiting list relative to organs available for transplantation. Therefore, increasing the survival of patients while on the waiting list for liver transplantation would be highly beneficial.

TIPS continues to be touted as a “bridge” to transplantation.8–11 TIPS does not increase blood transfusion requirements, operating time, or operative mortality during subsequent liver transplantation,3,9 yet no studies have
ever shown TIPS to increase survival or portend a propensity subsequent liver transplantation. Nonetheless, over the past 2 decades, TIPS has become the “first-line” modality of choice for portal decompression for patients with refractory variceal bleeding or ascites caused by cirrhosis and portal hypertension.

TIPS has been plagued by patency issues because of high rates of occlusion and stenosis, requiring frequent surveillance and reinterventions. TIPS has also been plagued by high failure rates. Rebleeding after TIPS occurs in 20% to 30% of patients, and about 45% of patients treated for ascites have recurrent ascites within 1 year. Many believe these numbers have all improved with the application of covered stents. However, many issues plaguing TIPS may be issues beyond stenosis and patency. Still, the emergency insertion of TIPS carries a grim prognosis with a 30-day mortality of about 30%, and long-term outcomes do not seem impressive.

We have been outspoken in our concerns about the abandonment of surgical shunting and the preferential application of TIPS. We have taken issue with “accepted” beliefs that TIPS effectively palliates complicated portal hypertension and promotes the application of liver transplantation. Therefore, this study was undertaken to evaluate outcomes after TIPS in our hospital and the usefulness of TIPS as an effective “bridge” to transplantation. We hypothesized that TIPS was an end therapy associated with poor outcomes and survival and that TIPS did not effectively route patients with cirrhosis toward subsequent liver transplantation.

Materials and Methods

Data management

All patients who underwent TIPS from 2001 to 2010 at a large teaching hospital with an associated transplant program were studied with institutional review board approval. A database was developed to include all patients who underwent TIPS, including patients who underwent subsequent liver transplantation. Patients who underwent TIPS after liver transplantation were excluded from this study. Uncovered stents were used exclusively from January 1, 2001, until covered stents were first used on May 14, 2003. Covered stents were exclusively used after January 7, 2005. The first patient who underwent TIPS with a covered stent and subsequently underwent transplantation underwent TIPS on October 2, 2003.

Data were stored in Microsoft Excel (Microsoft Corp, Redmond, WA) files. Statistical analysis used Graphpad Instat version 3.06 and Graphpad Prism 5 (Graphpad Software Inc, San Diego, CA). Survival curve analysis was also undertaken on Graphpad Prism 5, which permitted the log-rank and Wilcoxon tests on the Kaplan-Meier survival curves. When appropriate, data are presented as median (mean ± standard deviation). Survival data are presented as median predicted survival with a confidence interval (CI) based on Kaplan-Meier survival curve analysis. A P value ≤ .05 was considered significant.

Results

TIPS was performed in 256 patients, 62% men and 38% women, with an age of 56 years (56 ± 10.2 years). TIPS alone (ie, without subsequent liver transplantation) was performed in 221 patients, whereas 35 patients underwent TIPS followed by subsequent liver transplantation. Follow-up was 20 months (30 ± 31.6 months) after TIPS. For those undergoing transplantation, the time between TIPS and transplantation was 3 months (6 ± 10.5 months). Of patients who underwent TIPS alone, 72% were Child class B, whereas those undergoing TIPS before liver transplantation were Child class B in 55% and Child class C in 38% (Table 1). The Model for End-stage Liver Disease (MELD) Score and Child class did not predict subsequent transplantation, but the Child-Pugh score did (Table 1). For patients who were Child class A, 11% underwent subsequent liver transplantation. For patients who were Child class B, 12% underwent liver transplantation, and for patients who were Child class C, 26% underwent subsequent liver transplantation.

For patients who underwent TIPS alone, 72% had alcohol as a contributing factor to their cirrhosis, and 49% had viral hepatitis as a contributing factor; 29% had both alcohol and viral hepatitis as the etiology of cirrhosis (Table 2). For patients who underwent TIPS before liver transplantation, 65% had alcohol as a contributing factor to their cirrhosis, and 69% had viral hepatitis as a contributing factor, with 43% having both alcohol and viral hepatitis as the etiologies of cirrhosis (Table 2). The etiology of cirrhosis did not discriminate between patients who underwent TIPS alone versus patients who underwent TIPS before liver transplantation (Table 2, P = .26).

| Table 1 MELD score, Child-Pugh score, and Child class of patients who underwent TIPS alone or TIPS before orthotopic liver transplantation (OLT) |
|-----------------|------------------|-------------------|
| TIPS alone | TIPS before OLT | P value |
| MELD score | 11 (12 ± 6.1) | 13 (13 ± 5.3) | .36 |
| Child-Pugh score | 8 (8 ± 1.4) | 9 (9 ± 1.6) | .008 |
| Child class A (%) | 10 | 7 | .06 |
| Child class B (%) | 72 | 55 |
| Child class C (%) | 18 | 38 |

| Table 2 Etiology of cirrhosis for patients undergoing TIPS alone versus TIPS before orthotopic liver transplantation (OLT) |
|-----------------|------------------|-------------------|
| TIPS alone | TIPS before OLT | P value |
| Alcohol (%) | 43 | 22 | .26 |
| Viral hepatitis (%) | 20 | 26 |
| Alcohol/viral hepatitis (%) | 29 | 43 | .26 |
| Cryptogenic (%) | 9 | 9 |

Viral indicates hepatitis B and/or hepatitis C.
TIPS was performed on an emergency basis for 9% of patients who underwent TIPS alone, whereas only 1 patient subsequently undergoing transplantation underwent TIPS in an emergency setting (Table 3). Overall, patients underwent TIPS in an elective setting 83% of the time (Table 3). For patients who did not undergo transplantation, 59% required TIPS placement primarily because of variceal bleeding refractory to endoscopic/medical therapy; 62% of patients who subsequently underwent transplantation had undergone TIPS primarily because of ascites. There was a significant difference in the indications for TIPS between patients who underwent subsequent liver transplantation compared with patients who underwent TIPS alone (Table 3, $P = .03$). In other words, patients undergoing transplantation after TIPS were less likely to undergo TIPS for variceal bleeding.

Covered stents were used in 176 patients (72%), whereas 70 patients (28%) received uncovered stents. TIPS significantly decreased portal vein–Inferior vena cava (IVC) gradients from 17 to 5 mm Hg ($P = .001$) (Table 4). Fifty-four patients (21%) underwent reinterventions after TIPS. A total of 89 reinterventions were undertaken (Table 4). Six patients had to have their TIPS occluded: 4 because of encephalopathy, 1 because of renal failure, and 1 because of right-sided heart failure. Stenosis or occlusion was the indication for 54 reinterventions (61%), whereas ascites, encephalopathy, and variceal bleeding were an indication for 10 reinterventions (11%) each (Table 4). Reinterventions for stenosis and/or occlusion were undertaken in 33% with uncovered stents, whereas only 19% underwent reintervention with covered stents ($P = .01$).

The predicted median survival of 256 patients undergoing TIPS is 31 months (95% CI, 24.6–37.4 months) (Fig. 1). For the 221 patients (86%) who underwent TIPS alone, the predicted median survival was 26 months (95% CI, 18.9–32.5 months), whereas the 35 patients (14%) who underwent subsequent liver transplantation have a predicted median survival of 87 months (95% CI, 61.6–108.0 months). Forty-five of the 256 patients (18%) have survived at least 5 years. There was a significant survival benefit for patients who underwent liver transplantation after TIPS (Fig. 2).

### Table 3

<table>
<thead>
<tr>
<th></th>
<th>TIPS alone</th>
<th>TIPS before OLT</th>
<th>$P$ value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elective (%)</td>
<td>81</td>
<td>94</td>
<td>.20</td>
</tr>
<tr>
<td>Urgent (%)</td>
<td>10</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Emergency (%)</td>
<td>9</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Variceal bleeding (%)</td>
<td>59</td>
<td>35</td>
<td>.03</td>
</tr>
<tr>
<td>Ascites (%)</td>
<td>40</td>
<td>62</td>
<td></td>
</tr>
<tr>
<td>Pleural effusion (%)</td>
<td>1</td>
<td>3</td>
<td></td>
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</table>

### Table 4

<table>
<thead>
<tr>
<th></th>
<th>TIPS alone</th>
<th>TIPS before OLT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gradient before TIPS (mm Hg)</td>
<td>17 (18 ± 5.1)</td>
<td>20 (20 ± 6.1)</td>
</tr>
<tr>
<td>Gradient after TIPS (mm Hg)</td>
<td>5 (6 ± 2.8)</td>
<td>6 (6 ± 2.4)</td>
</tr>
<tr>
<td>No. of patients who underwent reinterventions (%)</td>
<td>47/220 (21)</td>
<td>7/35 (20)</td>
</tr>
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#### Indications for reinterventions undertaken

- Stenosis/occlusion: 45/77 (58) vs. 9/12 (75)
- Variceal bleeding: 10/77 (13%) vs. 0/12 (0%)
- Encephalopathy: 9/77 (12) vs. 1/12 (8%)
- Ascites: 8/77 (10) vs. 2/12 (17%)
- Right-sided heart failure: 1/77 (1%) vs. 0/12 (0%)
- Portal vein thrombosis: 1/77 (1%) vs. 0/12 (0%)
- Malplacement: 1/77 (1%) vs. 0/12 (0%)
- Renal failure: 1/77 (1%) vs. 0/12 (0%)
- Multisystem organ failure: 1/77 (1%) vs. 0/12 (0%)

Figure 1 The predicted survival of all patients after TIPS.

Figure 2 The predicted survival of patients after TIPS alone compared with the survival of patients who underwent TIPS followed by orthotopic liver transplantation (OLT).
A total of 153 (60%) patients died. One hundred forty-three of the patients who underwent TIPS alone (65%) and 10 patients after liver transplantation (27%) died. When considering all patients who underwent TIPS, there was no significant difference in survival when comparing patients who underwent TIPS because of ascites and TIPS because of bleeding varices (Fig. 3). However, there was a significant difference in survival when comparing all patients who underwent TIPS by Child class (Fig. 4).

**Comments**

TIPS is an effective intervention to achieve portal decompression. We agree with others that note that TIPS consistently reduces portal pressures, with portal vein to hepatic vein pressure gradients of ≤ 12 mm Hg achieved over 90% of the time and with a 57% reduction in pre-TIPS portal vein pressures.\(^5,17\) TIPS gains control of acute gastrointestinal bleeding in some reports over 90% of the time with early rebleeding rates of about 10%.\(^5,15\) When TIPS is placed for refractory ascites, reaccumulation of ascites within 1 year occurs 45% of the time.\(^3,15\) Unfortunately, these benefits are often transient because of shunt stenosis, occlusion, and/or malfunction. Because of this, TIPS often provides a short-term solution to the long-term problem of the complications of portal hypertension, specifically variceal bleeding and ascites refractory to endoscopic/medical therapy. Although we have a pejorative bias about TIPS, that does not preclude an objective review of outcome after TIPS. Whatever our bias might be, the data are what the data are. This report, like many others, denotes that TIPS does not offer prolonged survival or increase the propensity toward subsequent liver transplantation. This cannot be denied but is often ignored.

The patients in this study were not unusual or unique for patients undergoing TIPS; they were generally middle-aged alcoholic men with two thirds Child class B and one fifth Child class C. The primary indication for TIPS was variceal bleeding refractory to medical/endoscopic therapy, and TIPS was regularly performed in an elective setting. For our patients, as in most reports, the portal vein–inferior vena cava (IVC) gradient was significantly lower after TIPS.

Primary patency rates have been approximately 22% to 48% at 1 year and 17% to 26% at 2 years with reintervention rates of 48% to 82%.\(^6,12-14,18\) We found a reintervention rate of 21%, most commonly caused by stenosis/occlusion. Additionally, hepatic encephalopathy is reportedly found in 18% to 45% of patients after TIPS.\(^19\)

Notably, the majority of our patients had covered stents. Covered stents, which were approved by the Food and Drug Administration in 2004, have improved patency in the opinion of many when compared with their uncovered counterparts with primary patency rates as high as 76% to 84% at 1 year.\(^3\) There are seemingly innumerable reports about improved outcomes with covered stents. Without fail, these reports are uncontrolled trials or reports with few patients at risk with long-term follow-up. Notably, reported primary patency rates are still disappointing. In this series, covered stents provided improved patency; however, uncovered stents did not mitigate or prevent postshunt hepatic dysfunction and do not lead to improved survival.\(^16\)

The optimal method to achieve portal decompression has been a highly debated topic over the last decade for cirrhotic patients of Child class A or B. Before the advent of TIPS, surgical shunting was the only modality available for portal decompression. With TIPS becoming readily available and easy to “order,” there has been a shift such that surgeons are generally not involved in the care of patients suffering from complications caused by portal hypertension. A multicenter prospective randomized controlled trial comparing distal splenorenal shunts with TIPS (a selective shunt vs a nonselective shunt) in patients with Child A or B cirrhosis documented equivalent rebleeding rates and similar survival rates at 2 and 5 years. However, shunt stenosis/occlusion and
reinterventions were more frequent in patients who received TIPS therapy, denoting that TIPS became a more expensive intervention for the treatment of refractory variceal bleeding caused by portal hypertension.20,21 A prospective randomized trial comparing small-diameter prosthetic H-graft portocaval shunts with TIPS (both partial portal decompressive nonselective shunts) documented that survival was significantly improved at both 2 and 5 years after shunting for patients who were Child class A or B who underwent small-diameter prosthetic portocaval H-graft shunts.13,21 Also, shunt failure was superior after H-graft shunts for patients with MELD scores less than 14. In this latter trial, there was essentially nothing promoting TIPS, not even peri-procedural mortality. For patients who had Child class C cirrhosis, resource consumption was greater after TIPS.22 A systematic review comparing surgical shunting with TIPS denotes the superiority of surgical shunting.21 Yet, despite these randomized trials and many nonrandomized trials, TIPS continues to be used preferentially relative to surgical shunts because of the ease of “ordering” TIPS, the misconception that surgical intervention is riskier, the misperception that outcomes favor TIPS, and the illusion that TIPS is a “bridge” to transplantation.

For our patients who underwent TIPS placement because of bleeding varices, the chance of subsequent liver transplantation is less than 1 in 10. In contrast, for our patients who underwent TIPS for ascites, the chance of subsequent liver transplantation is about 1 in 5. Unlike MELD score, Child class, etiology of cirrhosis, and urgency of TIPS placement, Child-Pugh score and indication for TIPS predicted subsequent transplantation.

The predicted median survival for patients undergoing TIPS without transplantation was just over 2 years, which is not impressive given that only a small minority of patients were Child class C. There was a survival advantage when patients undergoing TIPS were stratified by Child Class but not by indication for TIPS. Patients with worse baseline liver function had worse survival. This should not be a surprise; sickest patients generally do worse. With over half of the patients being dead and with follow-up early in some patients, the median survival may decrease as other patients die, but it will not increase. Given this relatively short survival, the number of reinterventions and failures are particularly concerning. Although survival after TIPS alone is poor, survival after transplantation after TIPS is dramatically better and quite admirably better. Given the short period between TIPS and transplantation, the number of reinterventions to maintain TIPS function is, again, concerning. Transplantation after TIPS is a worthwhile endeavor in promoting survival. It just does not happen often in our experience and in the experience of others.

There was no significant survival benefit for patients undergoing TIPS based on indication alone. However, patients who undergo TIPS secondary to ascites have an increased propensity for subsequent transplantation. Methods to predict which patients who undergo TIPS will proceed to subsequent liver transplantation are still sought. Worse baseline liver function promoted subsequent liver transplantation given that patients of Child class C who underwent TIPS were most likely to undergo transplantation but only with a 1 in 4 chance. Based on occurrences, TIPS is not a “bridge” to transplantation. However, TIPS promotes worsening of liver function and promotes the need for liver transplantation because of excess diminution of effective hepatic blood flow.23 The portal and hepatic arterial hemodynamic consequences of TIPS are essentially ignored.

There was a confirmed significant survival benefit for patients who underwent subsequent transplantation after TIPS. However, liver transplantation is seldom undertaken because of insufficient organ allocation and availability. Currently, there are approximately 18,000 patients awaiting liver transplantation in the United States, yet only about 5,700 liver transplantations are undertaken in the United States yearly as reported by the Organ Procurement and Transplantation Network.24 Consistent with this study, only about 14% of patients after TIPS placement undergo liver transplantation.21,25 Prospects of transplantation after TIPS are unlikely although survival after transplantation is far superior to survival after TIPS alone.24 Liver transplantation after TIPS occurs so infrequently that the “bridge” therapy is truly the end of the road and no “bridge” at all.

Results after TIPS do not justify its general application. We must revisit why surgical shunting has been cast aside. Reinstituting surgical shunting is of paramount importance in the current era because the technique is slipping from the armamentarium of surgeons. The 2009 American Association for the Study of Liver Disease (AASLD) guidelines for the management of portal hypertension, which are followed in our institution, stated the following: “the decision to perform or not perform a TIPS in a high risk patient should be reached by the gastroenterologist/hepatologist and the interventional radiologist together.” Only under “ideal” circumstances is it even appropriate to involve a transplant surgeon. Surgeons have unwittingly been “shunted” away from performing surgical shunts.

Who should receive TIPS? Patients who are imminently going to be transplanted (ie, within 6 months), patients with high cardiopulmonary risk for abdominal surgery (eg, aortic stenosis and mitral regurgitation), patients with a “hostile abdomen” (eg, multiple previous celiotomies), and poor candidates for abdominal surgery secondary to extreme obesity should be considered for TIPS therapy. Other than this select group, patients should not undergo TIPS without any expectation other than a short survival complicated by shunt surveillance and shunt failure. For patients with poor hepatic function (eg, Child class C), resource allocation is promoted by surgical shunting.22 The concept of operative shunting needs to be reconsidered and revisited.

References