Transjugular intrahepatic portosystemic shunt: Where are we?

ABSTRACT
Background/Aims: The purpose of this study was to evaluate the technical/hemodynamic success, complications, and biochemical/hematologic consequences of transjugular intrahepatic portosystemic shunt (TIPS) created with 10-mm bare stents in our patients.

Materials and Methods: Data of 27 cirrhotic patients (18 men and 9 women; mean age, 39.7±18.7 years) with a median MELD score 14 (range 7-31) treated with TIPS between January 2000 and August 2010 were evaluated retrospectively.

Results: The indications were refractory bleeding varices in 48.2%, refractory ascites in 22.2%, and Budd-Chiari syndrome in 29.6% of the patients. Technical and hemodynamic success rates were 96.3% and 92.3%, respectively. Mean portosystemic pressure gradient decreased from 21.5±5.3 mm Hg to 9±2.7 mm Hg (p<0.05). The rate of primary stent patency was 76.9% 1 year after the procedure. No statistically significant difference in shunt dysfunction was found between the groups of patients treated for Budd-Chiari syndrome and other indications (p>0.05). One patient (3.7%) had shunt dysfunction due to thrombosis within 24 hours. New and/or worsening hepatic encephalopathy occurred in 34.6% of patients. Increased age (≥40 years) was significantly related to hepatic encephalopathy in both univariate and multivariate analyses (p<0.05). Thirty-day mortality rate and 1-year transplant-free survival rate were 0% and 80.7%, respectively.

Conclusion: Transjugular intrahepatic portosystemic shunt procedure is a safe treatment for many patients with cirrhosis, but post-procedure hepatic encephalopathy and shunt dysfunction are still problems. Especially, patient age should be taken into consideration in predicting hepatic encephalopathy risk.

Keywords: Transjugular intrahepatic portosystemic shunt, bare stents, Budd-Chiari syndrome

INTRODUCTION
Transjugular intrahepatic portosystemic shunt (TIPS) reduces elevated portal pressure with a metallic stent placed between the hepatic and portal veins as a bridge. This shunt, created by percutaneous transjugular approach, functions as a side-to-side portacaval shunt (1). The purpose of TIPS is to decompress the portal system and therefore treat the complications of portal hypertension. TIPS has been proven to be an effective treatment for secondary prevention of variceal bleeding, as well as refractory cirrhotic ascites, with controlled trials (2-5). Besides these, TIPS has been used in a variety of different clinical conditions, including Budd-Chiari syndrome (BCS). Despite the results of different clinical trials, the role of TIPS in the management of BCS remains unclear (6,7).

The 1-year survival rates vary from 48% to 90% depending on both the indication for TIPS and the severity of liver disease (2). Due to the large spectrum of survival rates, a number of models have been developed to predict survival following TIPS. Modified MELD model, a model using bilirubin level, alanine aminotransferase level, and clinical conditions, such as pre-TIPS encephalo-
The purpose of this study was to evaluate the technical/ hemodynamic success, complications, and biochemical/hematologic consequences of TIPS created with 10-mm bare stents in our cirrhotic patients.

MATERIALS AND METHODS
Data of patients admitted to the Başkent University Ankara Hospital Gastroenterology Department and treated with TIPS between January 2000 and August 2010 were evaluated retrospectively. All patients were evaluated and followed by a multidisciplinary team, including transplant surgery, gastroenterology, and interventional radiology. All TIPS procedures and follow-up Doppler ultrasonographies were carried out by experienced interventional radiologists. Paracentesis was performed in patients with clinically evident ascites before the procedure.

The procedures were performed under conscious sedation in all patients. The right side of the patient’s neck was prepared for percutaneous puncture under real-time ultrasonography. An 8-French sheath was placed into the inferior vena cava (IVC) through the right internal jugular vein. Following the selection of the right hepatic vein under digital subtraction angiography, free and wedged hepatic vein pressures were measured to calculate the portosystemic pressure gradient (PSPG). The TIPS set needle was advanced into the portal system; then, the needle was exchanged with a 5-French cobra or Davis catheter. After portography and pressure measurement, a 0.035-inch Amplatz guidewire was advanced into the portal system. The intrahepatic tract was dilated with an 8-mm balloon and was stented with a 10-mm bare stent (Wallstent, Boston Scientific, Fremont, CA, USA). The sizes of the stents used were 10x42 mm in 3 patients, 10x68 mm in 16 patients, and 10x94 mm in 8 patients. Portography was performed, and portal vein and IVC pressures were measured again after placement of the stent.

The patients received intravenous heparin during the first 24 hours after the procedure in the intensive care unit. Control Doppler ultrasonography was performed on Day 1 and 7 after the procedure, then monthly for the first 3 months, and every 3 months thereafter. Laboratory studies, including complete blood count, coagulation parameters (prothrombin time, international ratio), and biochemical parameters (serum total bilirubin, serum sodium, serum albumin, and serum creatinine), before TIPS and at the first visit 1 month after the procedure were analyzed. After the first visit, data were obtained both during routine visits (monthly for the first 3 months and every 3 months thereafter) as well as during unscheduled visits or hospitalizations due to complications or other reasons. Shunt dysfunction was defined as recurrence of the complications of portal hypertension as well as abnormal Doppler ultrasonographic features (degree of stenosis, decreased flow, or flow reversal) suggesting shunt dysfunction. A decrease in hemoglobin level of more than 2 g/dL was considered significant, and peripheral blood smear examination, serum haptoglobin, and unconjugated bilirubin measurements were performed to determine hemolysis, as were upper gastrointestinal endoscopy and stool heme tests for bleeding.

Child-Pugh score and Model for End-Stage Liver Disease (MELD) score were calculated before and 1 month after the procedure. MELD score was calculated according to the following formula (8):

\[ \text{MELD score} = 3.78 \cdot \ln(\text{serum bilirubin (mg/dL)}) + 11.2 \cdot \ln(\text{INR}) + 9.57 \cdot \ln(\text{serum creatinine (mg/dL)}) + 6.43. \]

Statistical analysis
Results are presented as mean±standard deviation (SD) and median (minimum-maximum). Continuous variables were compared with paired student’s t-test and Wilcoxon signed-ranks test. Categorical variables were compared with Fisher’s exact test. Univariate and multivariate logistic regression analysis was performed to identify predictors of post-procedure HES. For all variables with p<0.25 in the univariate analysis, multivariate analysis was performed. p<0.05 was considered statistically significant. All analyses were done using Statistical Package for the Social Sciences (SPSS) 19.0 (SPSS Inc. Chicago, IL, USA).

RESULTS
A total of 27 cirrhotic patients who underwent TIPS procedure with a median follow-up of 12 (range 3-60) months were evaluated. Among 27 patients, 66.7% (n=18) and 33.3% (n=9) were men and women, respectively. Mean age of the patients was 39.7±18.7 years.

Severity of cirrhosis, defined by Child-Pugh score, was Class A in 33.3% (n=9), Class B in 33.3% (n=9), and Class C in 33.3% (n=9), with a median MELD score of 14 (range 7-31). The etiology of cirrhosis was non-alcoholic in 92.6% (n=25) and alcoholic in 7.4% (n=2) of the patients.

The indications for TIPS were refractory bleeding varices in 48.2% (n=13), refractory ascites in 22.2% (n=6), and Budd-Chiari syndrome in 29.6% (n=8) of the patients.

Transjugular intrahepatic portosystemic shunt was successfully performed in 26 patients (96.3%). TIPS was unsuccessful, with capsular rupture and stent migration to the peritoneum, in only 1 (3.7%) of the 27 patients.
Table 1. The pre- and post-TIPS clinical and biochemical characteristics of the patients

<table>
<thead>
<tr>
<th></th>
<th>Pre-TIPS*</th>
<th>Post-TIPS*</th>
<th>p</th>
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</thead>
<tbody>
<tr>
<td>Serum total bilirubin (mg/dL)</td>
<td>2.1±1.5</td>
<td>2.9±1.9*</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Serum albumin (g/dL)</td>
<td>3.1±0.5</td>
<td>3.2±0.7*</td>
<td>NS</td>
</tr>
<tr>
<td>Serum creatinine (mg/dL)</td>
<td>1.04±0.8</td>
<td>0.85±0.66*</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Serum Na (mEq/L)</td>
<td>134.1±5.4</td>
<td>135.9±5.6</td>
<td>NS</td>
</tr>
<tr>
<td>Hemoglobin (g/dL)</td>
<td>10.7±1.7</td>
<td>10.7±1.8*</td>
<td>NS</td>
</tr>
<tr>
<td>White blood cells (/mm³)</td>
<td>6.3±4.1</td>
<td>6.2±3.5*</td>
<td>NS</td>
</tr>
<tr>
<td>Platelets (10³/mm³)</td>
<td>121±117</td>
<td>111±76*</td>
<td>NS</td>
</tr>
<tr>
<td>Portosystemic pressure gradient (mm Hg)</td>
<td>21.5±5.3</td>
<td>9±2.7</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

NS: non-significant; TIPS: transjugular intrahepatic portosystemic shunt
*p=mean±SD; *1 month after the procedure

After TIPS placement, the mean PSPG significantly decreased from 21.5±5.3 mm Hg to 9±2.7 mm Hg (p<0.05). Only 2 patients had post-TIPS gradient greater than 12 mm Hg. However, both of these patients had a decrease in pressure gradient of more than 50%.

In the group of 26 patients, only 1 patient (3.7%) with Budd-Chiari syndrome had TIPS dysfunction due to thrombosis within 24 hours. The patency of the shunt was re-established through percutaneous transluminal angioplasty and thrombolysis. Hematologic consultation was done to investigate whether the patient could have a hypercoagulable state, and we found that the patient had a factor V Leiden mutation.

The pre-and postprocedure clinical and biochemical characteristics of the patients are reported in Table 1. There were no statistically significant differences between pre- and post-TIPS serum albumin, serum sodium, and hemoglobin levels as peripheral white blood cells and platelets counts. Besides, mean serum creatinine level was significantly decreased (1.04±0.8 to 0.85±0.66, p<0.05) and mean serum total bilirubin level was significantly increased (2.1±1.5 to 2.9±1.9, p<0.05) after the procedure.

Fourteen patients (53.8%) had a decrease in Hgb levels. Seven patients (26.9%) had a 0-1-g/dL, 6 patients (23%) had a 1-2-g/dL, and 1 patient (3.9%) had a 2-3-g/dL decrease in serum Hgb levels. Peripheral blood smear examination, serum haptoglobin, and unconjugated bilirubin measurements were performed in the patient who had a more than 2-g/dL decrease, and no signs associated with hemolysis were found.

The rate of primary stent patency was 76.9% 1 year after the TIPS procedure. Shunt dysfunction occurred in 9 of 26 patients (34.6%) within a median period of 10 (range 3-30) months. Four patients with recurrent bleeding were re-treated with balloon angioplasty, and 3 required additional stents. One patient who was treated for refractory bleeding was treated with balloon angioplasty for persistence of high-risk varices and TIPS stenosis, identified by Doppler ultrasound. Four patients treated for BCS were re-treated with balloon angioplasty for recurrence of ascites with need of repeated paracentesis.

The indication of TIPS was BCS in 5 of 9 patients with shunt dysfunction, and no statistically significant difference in shunt dysfunction was found between the groups of patients treated for BCS and other indications (p>0.05).

During follow-up, new and/or worsening HE occurred in 9 of 26 patients (34.6%). Shunt caliber was reduced with a 6-mm bare stent in 1 patient (3.8%) due to refractory HE who did not respond to the medical therapy. Variables of age, gender, pre-procedure MELD and Child-Pugh scores, serum creatinine, serum Na, total bilirubin, albumin levels, post-procedure PSPG, and previous history of HE were evaluated as potential predictors of post-procedure HE in both univariate and multivariate analyses (Table 2,3). Only increased age (≥40 years) was significantly related to post-procedure HE in both the univariate and multivariate analyses (p<0.05).

Thirty-day mortality rate was 0%. One-year transplant-free survival rate was 80.7%. One-year transplant-free survival rates were similar between patients with MELD <14 and MELD ≥14 (81.8% vs 80%; p>0.05). Four patients died due to liver failure, and 1 patient died due to sepsis in 1 year.

DISCUSSION

Transjugular intrahepatic portosystemic shunt has been in use since the early 1970s to treat the complications of portal hypertension (12). The use of new technologies, such as PTFE-covered stents, improved the outcomes of this procedure over time. However, even with these improvements, shunt dysfunction and HE remain the main complications as well as technical complications (2).

Our technical and hemodynamic success rates were 96.3% and 92.3%, respectively. TIPS was unsuccessful with capsular rupture and stent migration to the peritoneum in 1 patient. In that patient, we controlled bleeding by embolization of the tract with gel foam. Freeman et al. (13) have reported that the incidence of transcapsular puncture is approximately 33%. However, obvious clinical hemoperitoneum due to capsular rupture is relatively rare (14). We thought that it may have been related to relatively small and hard liver parenchyma due to advanced cirrhosis, and we think that relatively small livers should warn physicians of such unexpected complications. Only 2 patients had a post-TIPS gradient greater than 12 mm Hg. However, both of the patients had a decrease in pressure gradient of more than 50%. The indications for TIPS were refractory bleeding varices for both of these patients. Although the gold standard for prevention of rebleeding remains a PSPG of less than 12 mm
more recent studies suggest that achieving a PSPG of less than 12 mm Hg may not be required and that a decrease of more than 50% may reduce the risk of rebleeding significantly (2,15,16).

Thrombosis of the TIPS usually occurs within first 24 hours. The frequency of this complication varies from 10% to 15% (17,18). The probable causes of thrombosis are leakage of bile into the shunt, hypercoagulable syndromes, and inadequate coverage of the intrahepatic tract (19). In our study, only 1 patient (3.7%) had TIPS thrombosis within first 24 hours. After the investigation, we found that the patient had a factor V Leiden mutation. The patency of the shunt was re-established through percutaneous transluminal angioplasty and thrombolysis. Afterwards, lifelong coumadin treatment was offered to the patient.

Hemolytic anemia is the main hematologic complication of TIPS. Transjugular intrahepatic portosystemic shunt is associated with hemolysis in about 10% of patients. Most patients do not require therapy, and hemolysis resolves within 12 to 15 weeks (11). In patients without anemia, hemolysis is diagnosed only if new onset reticulocytosis, indirect hyperbilirubinemia, or decreased haptoglobin is present. In our study, 14 patients had a decrease in Hgb levels. Only 1 patient had a decrease more than 2 g/dL. Peripheral blood smear examination, serum haptoglobin, and unconjugated bilirubin measurements were performed in that patient, and no signs associated with hemolysis were found.

Pancytopenia due to hypersplenism is another problem of cirrhotic patients with portal hypertension. The effect of portal decompression on both platelet and white blood cell counts is unpredictable (20). In a prospective study including 60 patients undergoing TIPS, no significant changes in both platelet and white blood cell counts were observed (11). Like in our study, no statistically significant differences between pre- and post-TIPS peripheral white blood cell and platelet counts were observed.

Budd-Chiari syndrome (BCS) results from blockage of blood outflow from the liver as a result of an obstruction anywhere from the hepatic veins to the right atrium. Most patients have an underlying prothrombotic disorder. Symptomatic treatments with diuretics and drugs aiming at reduction of portal pressure, anticoagulants, TIPS, and liver transplantation are treatment options in different stages of the disease (21). Despite the results of some clinical trials, the role of TIPS in the management of Budd-Chiari syndrome remains unclear (6,7,22). The AASLD practice guideline recommendation is for creation of TIPS in patients who fail to improve with anticoagulation (23). Contrary to prevalent opinion, a recent review of the literature showed that the frequency of TIPS dysfunction in BCS patients is higher than in patients with other etiologies, especially with bare stents (2,24). The indication of TIPS was Budd-Chiari syndrome in 8 patients, and shunt dysfunction appeared in 5 of 8 patients in our study. Contrary to a recent review, no statistically significant difference in shunt dysfunction was found between the groups of patients treated for Budd-Chiari syndrome and other indications in our study. It should be noted that this result may be due to the small number of patients.

Hepatic encephalopathy is one of the two main complications that limit the effectiveness of TIPS. The incidence of new/worsening HE following TIPS is 10% to 44% (2). Encephalopa-
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thy usually becomes clinically apparent 2-3 weeks after the procedure (25,26). Many univariate and multivariate analyses of potential predictors of post-TIPS HE in different studies have been conducted; however, the results of these studies are conflicting. In a recent meta-analysis, including 30 studies that evaluated 60 variables by univariate and 32 variables by multivariate analyses, older age, prior HE, and Child-Pugh score were found to be the most commonly reported risk factors of post-TIPS HE. In addition, three studies concluded that non-alcoholic etiology and two studies concluded that gender and hypoalbuninemia were risk factors of post-TIPS HE by multivariate analyses (27). In our study, new/worsening HE occurred in 9 of 26 patients (34.6%). Variables of age, gender, pre-procedure MELD and Child-Pugh scores, serum creatinine, serum Na, total bilirubin, albumin levels, post-TIPS PSPG, and prior HE were evaluated as potential predictors of post-TIPS HE in both univariate and multivariate analyses (Table 2-3). Only increased age (≥40 years) was significantly related to post-TIPS HE in both the univariate and multivariate analyses (p<0.05).

In conclusion, we think that the etiologies of patients, especially for hypercoagulable states, should be verified clearly before TIPS in order to take more serious precautions. Patient age should be taken into consideration, especially in predicting HE risk. Radiologists should be even more careful with patients with relatively small livers for unexpected complications, such as capsule rupture and stent migration.

Ethics Committee Approval: N/A.

Informed Consent: Written informed consent was obtained from patients who participated in this study.

Peer-review: Externally peer-reviewed.


Conflict of Interest: No conflict of interest was declared by the authors.

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