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Original Article

# Clinical outcomes of transjugular intrahepatic portosystemic shunt for portal hypertension: Korean multicenter real-practice data

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**Background/Aims:** This retrospective study assessed the clinical outcome of a transjugular intrahepatic portosystemic shunt (TIPS) procedure for managing portal hypertension in Koreans with liver cirrhosis.

**Methods:** Between January 2003 and July 2013, 230 patients received a TIPS in 13 university-based hospitals.

**Results:** Of the 229 (99.6%) patients who successfully underwent TIPS placement, 142 received a TIPS for variceal bleeding, 84 for refractory ascites, and 3 for other indications. The follow-up period was 24.9±30.2 months (mean±SD), 74.7% of the stents were covered, and the primary patency rate at the 1-year follow-up was 78.7%. Hemorrhage occurred in 30 (21.1%) patients during follow-up; of these, 28 (93.3%) cases of rebleeding were associated with stent dysfunction. Fifty-four (23.6%) patients developed new hepatic encephalopathy, and most of these patients were successfully managed conservatively. The cumulative survival rates at 1, 6, 12, and 24 months were 87.5%, 75.0%, 66.8%, and 57.5%, respectively. A high Model for End-Stage Liver Disease (MELD) score was significantly associated with the risk of death within the first month after receiving a TIPS ($P$=0.018). Old age ($P$<0.001), indication for a TIPS (ascites vs. bleeding, $P$=0.005), low serum albumin ($P$<0.001), and high MELD score ($P$=0.006) were associated with overall mortality.

**Conclusions:** A high MELD score was found to be significantly associated with early and overall mortality rate in TIPS patients. Determining the appropriate indication is warranted to improve survival in these patients. **(Clin Mol Hepatol 2014;20:18-27)**

**Keywords:** Liver cirrhosis; Transjugular intrahepatic portosystemic shunt; Portal hypertension

**Abbreviations:**

CP class, Child-Pugh classification; HE, Hepatic encephalopathy; LC, Liver cirrhosis; MELD, Model for End-stage Liver Disease; PPG, Portosystemic pressure gradient; TIPS, transjugular intrahepatic portosystemic shunt

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## INTRODUCTION

Since its introduction in the 1980s, transjugular intrahepatic portosystemic shunts (TIPS) have played an increasingly important role in the management and treatment of complications of portal hypertension, such as variceal bleeding and refractory ascites. In the early years following the introduction of the TIPS procedure, the mortality[1-4] and rates of stent dysfunction due to the use of bare metal stents were high.[5,6] Consequently, the role of the TIPS procedure in the long-term management of complications of portal hypertension was questioned.[7,8] Subsequently, however, the TIPS procedure was revolutionized by the introduction of covered stents, which dramatically improved long-term shunt patency.[9] Several practice guidelines for the use of TIPS in the management of portal hypertension were also published, and new studies detailing technical advances on TIPS were published.[10-12] The current use of TIPS has been influenced by a number of clinical trials, which enhanced the safety and efficacy of the procedure. The introduction of the Model of End-Stage Liver Disease (MELD) scoring system for assessing the risk of short-term mortality in patients undergoing TIPS also influenced the procedure.[13] Recently, the early use of TIPS has been shown to improve patient survival.[14]

Liver transplantation continues to be the only hope for those with portal hypertension. The number of liver transplants performed in Korea has increased markedly on an annual basis. However, the limited supply of organs continues to be limiting factor. Consequently, TIPS has become the management option for portal hypertension as a bridge to liver transplantation. However, few studies have investigated the clinical outcomes in TIPS patients in Korea in the era of liver transplantation, despite the advances in the TIPS procedure during the last 10 years.

This retrospective study assessed the clinical outcomes in Koreans with liver cirrhosis who underwent the TIPS procedure to manage portal hypertension during the past 10 years.

## METHODS

### Patients

All TIPS patients treated at 13 medical centers distributed throughout Korea between January 2003 and July 2013 were reviewed retrospectively to identify consecutive patients with liver cirrhosis (n=238) who underwent TIPS placement for the treatment of portal hypertension. The medical records of the patients were reviewed to obtain the necessary demographic, clinical, laboratory, treatment, and follow-up data. The date of transplantation was established as an end point to the follow-up of TIPS placement. Thirteen (5.7%) patients who underwent the TIPS procedure were lost to follow-up. In this group, the last available date documenting a patent TIPS was used when calculating the duration of TIPS patency. Eight patients were excluded due to incomplete medical records.

The inclusion criteria for TIPS were hepatic cirrhosis diagnosed from typical histological or radiological findings, including ultrasound, computed tomography (CT), or magnetic resonance imaging (MRI), and complicated portal hypertension, such as acute or recurrent variceal bleeding that could not be controlled with endoscopic or medical therapy. Patients who underwent the TIPS procedure for refractory ascites, defined as ascites requiring large-volume paracentesis at least every other week that could not be controlled well with maximum-dose diuretics (spironolactone 400 mg/d and furosemide 160 mg/d) and those who could not tolerate high-dose diuretics as a result of side effects were included in the study. Patients with unsuccessful TIPS placement were excluded from the analysis.

### TIPS procedure and follow-up

The TIPS was placed using a technique described elsewhere,[1-5] in the interventional radiology unit. After direct portography between the portal and hepatic veins, shunt tracts were lined with various commercial stents: Niti-S (Taewoong Medical, Seoul, South Korea), Wallstents (Boston Scientific/Medi-Tech, Quincy, MA), etc. If necessary, balloon dilation was performed to reduce the pressure gradient.

After the procedure, all patients were followed clinically. Stent patency was monitored using color Doppler sonography and multidimensional CT at scheduled follow-up or in cases of suspected shunt malfunction.

### Measured outcomes

The outcome measures used in this study included technical success, defined as successful creation of a shunt between the hepatic vein and an intrahepatic portal venous branch,[15] and procedure-related complications, which were classified according to

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the Society of Interventional Radiology Standards of Practice Committee classification of complications.[16] Additional outcome measures were the primary patency rate, recurrent bleeding rate, early (within 3 month) and overall ascites response rate, 1-month mortality following the procedure, and overall patient survival. A complete response of ascites was defined as the absence of clinically detectable ascites, with or without diuretics and sodium restriction. A partial response was defined as the presence of clinically detectable ascites, without the need for further paracentesis. An absent response was defined as the persistence of severe ascites requiring repeated large-volume paracentesis.[17]

The time-to-event outcome was estimated as the interval from the time of TIPS placement to death. Data were obtained at the time of transplantation or at the last clinic visit before being lost to follow-up. Post-TIPS hepatic encephalopathy (HE) was graded according to the West Haven classification.[18] Shunt dysfunction was defined as loss of TIPS primary patency, evidenced by venographic shunt occlusion, thrombosis, or stenosis. Rebleeding was defined as recurrent variceal hemorrhage evidenced by clinical signs of bleeding, such as hematemesis. Endoscopic confirmation of the source of the recurrent variceal bleeding was obtained when possible.

### Statistical analysis

Data are presented as the means±SD for continuous variables and as frequencies for categorical variables. Quantitative variables were compared using Student's *t*-test and qualitative variables were compared using the chi-square test. Cumulative patency and survival rates were calculated with the Kaplan-Meier method, and the log-rank test was used to compare cumulative survival functions among groups. Logistic regression analyses were performed to assess factors influencing the 1-month mortality and HE. The Cox proportional-hazards test was used to perform multivariate analysis of overall mortality. Only variables that had a significant effect at the 0.10 level on univariate analysis were subjected to multivariate analysis. Ascites and bleeding were categorized as indications for TIPS placement. The MELD score and serum creatinine were categorized according to the median value. Statistical analysis was performed with SPSS ver. 12 (SPSS, Chicago, IL). A value of $P<0.05$ was taken to indicate statistical significance.

**Table 1.** General characteristics of the patients (n=229)

| Characteristic | | |
|---|---|---|
| Age (yr) | | 56.6±10.9 (17-84) |
| Sex (M:F) | | 192 (83.8): 37 (16.1) |
| Etiology | Virus | 125 (54.6) |
| | Alcohol | 75 (32.8) |
| | Alcohol and virus | 6 (2.6) |
| | Cryptogenic | 21 (9.2) |
| | Autoimmune | 1 (0.4) |
| | Budd-Chiari syndrome | 1 (0.4) |
| Child–Pugh class | A | 42 (18.3) |
| | B | 134 (58.5) |
| | C | 53 (23.1) |
| Mean MELD score | | 14.3±5.6 |
| Hemoglobin (g/dL) | | 9.58±2.04 |
| Platelets (×1,000/mm$^3$) | | 98.2±65.9 |
| T-Bilirubin (mg/dL) | | 2.37±3.24 |
| Albumin (g/dL) | | 2.83±0.57 |
| Creatinine (mg/dL) | | 1.25±1.13 |
| Prothrombin time (INR) | | 1.53±0.56 |
| Indication for TIPS placement | Varix bleeding | 142 (62.0) |
| | Refractory ascites | 84 (36.7) |
| | Hydrothorax | 2 (0.9) |
| | Budd-Chiari syndrome | 1 (0.4) |
| Hepatic encephalopathy | None | 194 (84.7) |
| | Grade I-II | 28 (12.2) |
| | Grade III-IV | 7 (3.1) |

Data are mean±SD (range) or N (%) value.
INR, international normalized ratio; MELD, Model for End-Stage Liver Disease; TIPS, transjugular intrahepatic portosystemic shunt.

## Results

### Patients' characteristics

This retrospective study identified 229 patients (99.6%) who underwent technically successful TIPS placement for potential inclusion. The patients' demographics and clinical and laboratory data are summarized in Table 1. The patient age averaged 56.6±10.9 (range 17-84) years, and 83.8% (n=192) were male. Underlying liver disease was due predominantly to hepatitis B or C virus (54.6%), alcohol (32.8%), or both (2.6%). Other causes included cryptogenic cirrhosis (9.2%), autoimmune hepatitis (0.4%), and Budd-Chiari syndrome (0.4%).


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Indications for the TIPS procedure were uncontrolled/recurrent variceal bleeding not responding to medical and endoscopic treatment (n=142, 62.0%), refractory ascites, including diuretic-resistant and intractable ascites (n=84, 36.7%), hydrothorax (n=2, 0.9%), and Budd-Chiari syndrome (n=1, 0.4%). Of the patients, 42, 134, and 53 had Child-Pugh (CP) class A, B, and C cirrhosis, respectively.

The mean follow-up duration was 24.9±30.2 months. During follow-up, 128 patients (55.9%) died, 72 patients (28.4%) alived and 13 patients (5.8%) were lost to follow-up. Sixteen patients (7.0%) underwent liver transplantation.

## Shunt procedure and procedure-related complications

The mean period from TIPS placement to primary patency state was 18.5±27.2 months. Covered stents were inserted in 171 (74.7%) patients, uncovered stents in 30 (13.1%), and the type was unknown in 28 (12.2%) (Table 2).

The stent diameters were 10 mm (n=202, 88.2%), 9 mm (n=8, 3.5%), 8 mm (n=9, 3.9%), and others (n=10, 4.4%). The dilation balloon diameters were 10 mm (n=107, 59.1%), 8 mm (n=62, 34.3%), and other. The mean stent length was 7.8±1.4 mm. The following lengths were used: 6, 7, 8, 9, and 10 mm in 23, 51, 78, 30, and 19 patients respectively. Some other lengths were used. Adjunctive stents were required in five patients to cover long tracks.

The portal pressure gradient (PPG) was reduced from a mean of 22.8±6.9 mm Hg to 11.1±5.1 mm Hg in the patient group (129 patients, 56.3%) for whom the PPG was available. The mean decrease in post-TIPS PPG was 11.9±5.4 mm Hg ($P$<0.001) (Table 2).

Procedure-related complications (during or immediately after TIPS) occurred in 9 (3.9%) patients. Hemobilia developed in two patients, contrast-induced nephropathy in two, and intraperitoneal bleeding, hypotension of unknown origin, sepsis, hemolysis, and hepatic infarction in one patient each. Two patients died of TIPS procedure-related complications despite technical success.

## Shunt patency

Shunt dysfunction occurred in 44 (19.2%) of 229 patients. The causes of shunt dysfunction were stent thrombosis (n=20, 45.4%), stent stenosis (n=19, 43.2%), hepatic vein stenosis (n=1, 2.3%),

**Table 2.** Characteristics of the stents and procedures

| Characteristic | |
|---|---|
| Mean follow-up period of stent (months) | 18.5±27.2 |
| Stents (covered: uncovered: unknown) | 171: 30 :28 |
| PPG (mm Hg) (n=129) | |
| Before TIPS | 22.8±6.0 |
| After TIPS | 11.1±5.1 |
| Mean reduction of PPG (mm Hg) | 11.9±5.4 |
| Short-term complications of TIPS* (n=9) | |
| Hemobilia | 2 |
| Contrast-induced nephropathy | 2 |
| Intraperitoneal bleeding | 1 |
| Hypotension of unknown origin | 1 |
| Sepsis | 1 |
| Hemolysis | 1 |
| Hepatic infarction | 1 |
| Cause of stent dysfunction (n=44) | |
| Thrombosis | 20 |
| Stenosis | 19 |
| Hepatic vein stenosis | 1 |
| Others | 4 |

Data are mean±SD.
PPG, portosystemic pressure gradient; TIPS, transjugular intrahepatic portosystemic shunt.
*, within 1 month.

**Table 3.** Analysis of shunt patency in patients with TIPS

| Variables | Univariate | | | Multivariate | | |
|---|---|---|---|---|---|---|
| | HR | (95% CI) | *P*-value | HR | (95% CI) | *P*-value |
| Platelet count (×1,000/μL) | 1.006 | 1.003-1.009 | <0.001 | 1.005 | 1.001-1.009 | 0.008 |
| Alcoholic cirrhosis (vs. viral) | 1.775 | 0.928-3.395 | 0.083 | 1.516 | 0.787-2.918 | 0.213 |
| Hemoglobin level | 0.900 | 0.776-1.043 | 0.162 | | | |
| MELD score | 1.017 | 0.957-1.080 | 0.592 | | | |
| Covered stent (vs. uncovered) | 0.764 | 0.231-2.533 | 0.660 | | | |
| Systolic blood pressure | 0.989 | 0.971-1.007 | 0.235 | | | |

CI, confidence interval; HR, hazards ratio; TIPS, transjugular intrahepatic portosystemic shunt.


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and unknown (n=4, 9.1%) (Table 2).

The primary patency cumulative rate was 78.7, 73.9, 71.1, and 65.5% at the 1-, 2-, 3-, and 5-year follow-ups, respectively. On Cox univariate regression analysis, elevated platelet count and alcoholic cirrhosis (vs. viral) significantly affected the primary patency rate. Multivariate analysis of these factors showed that an elevated platelet count was independently related to shunt patency (Table 3).

## Recurrent bleeding after TIPS placement

During follow-up, 30 (21.1%) patients experienced recurrent variceal bleeding, and one had gastric ulcer bleeding. The CP class distribution in the same patients was 6, 21, and 3, patients in class A to C, respectively. The mean time to the onset of rebleeding after the TIPS procedure was 11.4±14.6 months. Four (2.8%) patients had variceal rebleeding within 30 days, 13 (9.2%) within 6 months, and 20 (14.1%) within the first year of TIPS insertion. Twenty-eight (93.3%) patients with variceal rebleeding had stent dysfunction. The overall rebleeding rate after TIPS placement was 21.1 and 16.7% in the uncovered and covered stent groups, respectively, but the difference was not significant (*P*=0.791). A low hemoglobin and stent dysfunction were risk factors for recurrent hemorrhage after TIPS placement (Table 4).

## Ascites response

At 1, 3, 6, 12, and 24 months after TIPS placement, any type of response (either complete or partial) was seen in 62.7, 67.0, 70.0, 61.1, and 75% of the respective patients who were alive and present at follow-up.

Viral-induced liver cirrhosis, the presence of a covered stent-graft, systolic blood pressure, and serum creatinine level were significant predictors of an early response of ascites, but only a viral cause was significant in the multivariate analysis.

**Table 4.** Risk factors for rebleeding in patients with TIPS

| Variables | Univariate | | | Multivariate | | |
|---|---|---|---|---|---|---|
| | OR | (95% CI) | *P*-value | OR | (95% CI) | *P*-value |
| Stent dysfunction (vs. patent) | 12.622 | 4.921-32.377 | <0.001 | 12.551 | 4.685-33.625 | <0.001 |
| Hemoglobin | 0.718 | 0.562-0.917 | 0.008 | 0.714 | 0.535-0.953 | 0.022 |
| Platelet count (×1,000/μL) | 1.006 | 0.999-1.013 | 0.072 | 1.004 | 0.996-1.013 | 0.333 |
| Stent diameter | 0.661 | 0.174-2.506 | 0.542 | | | |
| Albumin (g/dL) | 1.441 | 0.743-2.794 | 0.280 | | | |
| MELD score | 1.037 | 0.956-1.125 | 0.381 | | | |

CI, confidence interval; OR, odds ratio; MELD, Model for End-stage Liver Disease; TIPS, transjugular intrahepatic portosystemic shunt.

**Table 5.** Risk factors for hepatic encephalopathy in patients with TIPS

| Variable | Univariate | | | Multivariate | | |
|---|---|---|---|---|---|---|
| | OR | (95% CI) | *P*-value | OR | (95% CI) | *P*-value |
| Uncovered stent (vs. covered) | 2.293 | 0.898-5.855 | 0.083 | 2.887 | 1.033-8.068 | 0.043 |
| Age (yr) | 1.031 | 1.003-1.060 | 0.030 | 1.043 | 1.006-1.081 | 0.021 |
| ALT (IU/L) | 0.987 | 0.974-0.999 | 0.040 | 0.989 | 0.974-1.004 | 0.138 |
| Albumin (g/dL) | 1.309 | 0.772-2.219 | 0.318 | | | |
| Stent diameter | 1.120 | 0.541-2.321 | 0.760 | | | |
| MELD score | 0.937 | 0.878-0.999 | 0.047 | 0.953 | 0.891-1.019 | 0.161 |
| Systolic blood pressure on TIPS | 0.992 | 0.974-1.011 | 0.412 | | | |
| Stent dysfunction (vs. patent) | 0.900 | 0.423-1.916 | 0.785 | | | |

CI, confidence interval; OR, odds ratio; MELD, Model for End-stage Liver Disease; TIPS, transjugular intrahepatic portosystemic shunt.


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**Table 6.** Risk factors for overall survival in patients with TIPS

| Variables | Univariate | | | Multivariate | | |
|---|---|---|---|---|---|---|
| | HR | (95% CI) | *P*-value | HR | (95% CI) | *P*-value |
| Age (yr) | 1.03 | 1.014-1.047 | <0.001 | 1.036 | 1.017-1.055 | <0.001 |
| Indication for TIPS (ascites vs. bleeding) | 2.583 | 1.793-3.271 | <0.001 | 2.007 | 1.229-3.278 | 0.005 |
| Systolic blood pressure on TIPS | 0.985 | 0.974-0.997 | 0.014 | 0.982 | 0.971-0.994 | 0.003 |
| Albumin | 0.481 | 0.363-0.639 | <0.001 | 0.552 | 0.396-0.770 | <0.001 |
| Platelet count (×1,000/μL) | 1.003 | 1.000-1.005 | 0.037 | 1.002 | 1.000-1.005 | 0.068 |
| MELD score | 1.08 | 1.053-1.108 | <0.001 | 1.045 | 1.013-1.078 | 0.006 |
| Serum sodium | 0.939 | 0.914-0.965 | <0.001 | 0.962 | 0.927-0.998 | 0.040 |
| Presence of HE on TIPS | 1.518 | 0.939-2.453 | 0.089 | 1.070 | 0.638-1.794 | 0.799 |
| Stent dysfunction (vs. patent ) | 0.594 | 0.380-0.928 | 0.022 | 0.705 | 0.424-1.173 | 0.178 |
| Stent diameter | 0.952 | 0.604-1.498 | 0.831 | | | |
| Alcoholic cirrhosis (vs. viral) | 1.196 | 0.822-1.740 | 0.349 | | | |

CI, confidence interval; HR, hazards ratio; MELD, Model for End-stage Liver Disease; TIPS, transjugular intrahepatic portosystemic shunt.

## Hepatic encephalopathy

Hepatic encephalopathy was seen in 35 patients before the TIPS procedure. Of these, seven developed aggravated HE. After TIPS placement, 54 (23.6%) patients developed a new episode of clinical encephalopathy, with mild and severe encephalopathy in 27 (50%) patients each. Most patients with precipitating factors (e.g., dehydration, infection, constipation, and recurrent bleeding) were treated successfully with the administration of lactulose. Aggravation or a new episode of HE occurred in 44 (72.1%) patients within 3 months after the TIPS procedure. The univariate analysis of overall HE showed that age, use of an uncovered stent (vs. covered), serum alanine aminotransferase level and MELD score were predictors. Multivariate analysis revealed that old age and the use of an uncovered stent were independent predictors of the overall development of HE (Table 5).

## Mortality

In all, 128 patients died after a mean of 16.2±21.1 months; 30 patients died within the first 30 days after the procedure. The causes of the early morality were acute hepatic failure (n=11), variceal bleeding (n=4), TIPS-related bleeding (n=2), hepatorenal syndrome (n=2), sepsis (n=2), asphyxia (n=1), acute renal failure (n=1), and unknown origin (n=7).

The causes of death by the end of the follow-up were hepatic failure (n=34), complication of portal hypertension without variceal bleeding (HE, hepatorenal syndrome) (n=16), sepsis or infection (n=12), gastrointestinal bleeding, including variceal bleeding (n=8), hepatocellular carcinoma (n=8), TIPS-related complication (n=2), intracranial hemorrhage (n=2), and others (n=46).

The cumulative survival rates at 1, 6, 12, and 24 months were 87.5, 75.0, 66.8, and 57.5%, respectively. The mortality differed significantly ($P$<0.001) in the bleeding and ascites groups. The respective cumulative survival rate at 3, 12, and 24 months was 86.1, 72.5, and 65.5% in the bleeding group, and 62.0, 48.9, and 28.9% in the ascites group.

Factors associated with death within the first month after TIPS in the univariate analysis were female (vs male), low serum albumin, low systolic blood pressure during the TIPS procedure, presence of HE on TIPS, and high MELD score. When all the significant variables in the univariate analysis were included, low serum albumin and high MELD score were significantly related to the risk of death within the first month after TIPS in the multivariate analysis.

In the Cox univariate analysis of overall survival, age, indication for TIPS (ascites vs. bleeding), systolic blood pressure during the TIPS procedure, presence of HE on TIPS, platelet count, serum albumin, serum sodium, stent dysfunction (vs. patent), and MELD score were significantly associated with survival. In the multivariate analysis, old age, indication for TIPS (ascites vs. bleeding), low systolic blood pressure during the TIPS procedure, low serum albumin, low serum sodium, and high MELD score were associated with the risk of overall mortality (Table 6).

There was a survival difference between patients with MELD scores higher or lower than 14 ($P$<0.001) (Fig. 1). Kaplan–Meier analysis also showed a significant survival difference between

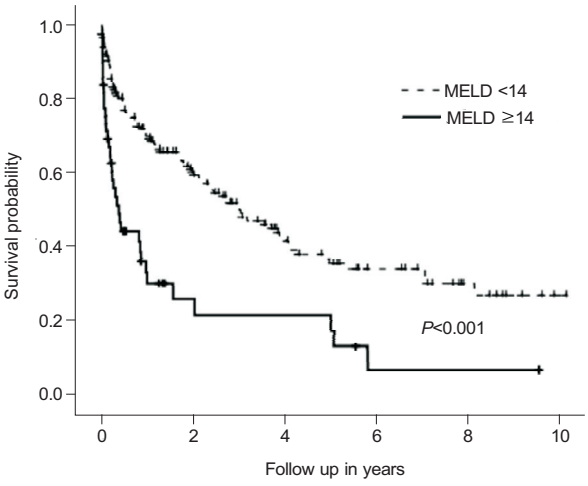


**Figure 1**. Kaplan-Meier curve of patients' survival based on the MELD score.

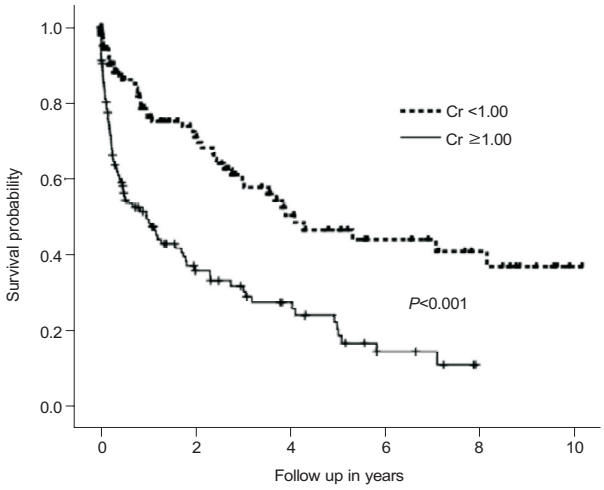


**Figure 3**. Kaplan-Meier analysis of survival based on the serum creatinine level.

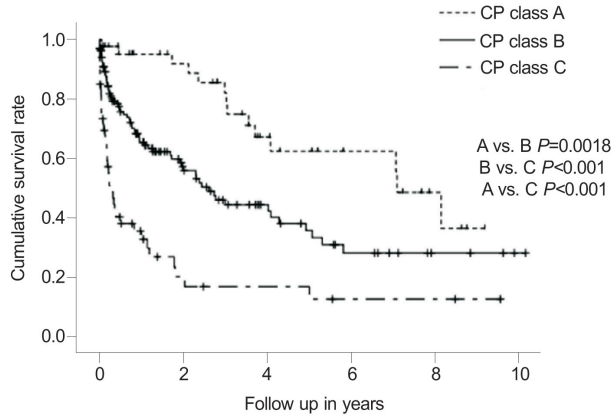


**Figure 2.** Kaplan-Meier analysis of survival grouped by Child-Pugh (CP) class adjusted with Bonferroni correction.

patients with CP class A vs. B ($P$=0.0018), class B vs. C ($P$<0.001), and class A vs. C ($P$<0.001) (Fig. 2) and a serum creatinine higher or lower than 1.0 mg/dL ($P$<0.001) (Fig. 3). But, response of ascites was not significant survival factor in patients with TIPS ($P$=0.28).

## DISCUSSION

Current guidelines recommend withholding TIPS in patients with severe disease in whom a poor outcome can be predicted.[19] Recent reports have focused on the usefulness of the MELD score as a marker of severity to predict survival in patients after TIPS placement.[20] This study found significantly higher early mortality and a higher overall mortality rate in patients with MELD scores ≥ 14 compared with patients with MELD scores <14. Gaba et al reported that a MELD score >25 was clearly associated with a significant mortality risk and that a careful approach to TIPS placement is warranted.[21] Similar to Gaba et al,[21] high-risk patients (4.4%) with a MELD score ≥25 who underwent TIPS placement in our study also had higher early mortality and higher overall mortality than the other group. In patients who require liver transplantation, TIPS placement seems to be the only therapeutic option.

Our cutoff value for the MELD score differed from that used in studies that used cutoff values of 15,[22] 18,[20] or 24.[19] These studies also reported different short- and long-term outcomes depending on the MELD score. The differences between those and our findings might be the result of patient selection.[22] The MELD score might facilitate identification of patients who might not benefit significantly from TIPS placement.

In this study, the rebleeding rate in the group that underwent TIPS with a covered stent (16.7%) was higher than the <10% reported previously.[23,24] Stent dysfunction and low hemoglobin were risk factors for recurrent hemorrhage after TIPS placement in our series. In particular, stent dysfunction had a very high hazard ratio compared with Sanyal et al.[25] Most (93.3%) cases of recurrent variceal bleeding were associated with stent dysfunction, which can lead to recurrent portal hypertension and put patients at risk for further variceal hemorrhage. However, early management of subclinical shunt dysfunction through stricter surveillance of shunts might decrease the variceal rebleeding rate.

TIPS placement proved to be effective in the control of recurrent


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ascites,[26] with about 70% of the patients with refractory ascites achieving a reduction without the need for further paracentesis. However, there was a high 12-month mortality rate of 55% in the ascites group. The TIPS procedure might provide long-term control of previously refractory ascites. However, once ascites becomes refractory to medical treatment, the median patient survival is ~6 months, despite management. Our study demonstrated a significant survival difference between the ascites and variceal bleeding groups according to their indication for TIPS ($P$<0.001). Ascites is a poor prognostic factor in patients with cirrhosis, and the clinical management of ascites appears to be problematic.[7]

In addition, we found a significantly higher serum creatinine level and CP score in the ascites group than in the bleeding group. This is consistent with Membreno et al.[26] Differences in the severity of liver disease and renal function between the ascites and rebleeding groups likely reflect the survival differences between the two groups.

One of the major drawbacks of TIPS is the development or worsening of HE, which occurred in 26.2% of our patients. The majority (72.1%) of these developed HE within 3 months, similar to Bai et al.[27] Recently, Wróblewski et al investigated the ability of two-stage TIPS to prevent the development of HE in patients with an extremely high risk of this condition and found that patients with uncovered stents had a significantly higher occurrence of HE than those with covered stents.[28] This is unexpected because greater patency results in increased portosystemic shunting and, therefore, greater anticipated encephalopathy. The same finding was reported in a randomized controlled study of TIPS.[29] The reason is not clear, but it might be related to the need for fewer interventions for shunt insufficiency compared with bare stents.[29] Another potential reason could be improved control of ascites and congestion of the bowel wall with decreased bacterial translocation or even overt bacteremia.[30] However, further studies are needed to develop a better strategy to select patients who can obtain a survival advantage from TIPS, while minimizing the incidence of HE.

In this study, TIPS placement was used to manage variceal rebleeding and refractory ascites, and these indications account for 99% of TIPS procedures in Korea. The technical success rate and procedure-related complication rate with TIPS in Korea were comparable to those reported by Song et al.[31] The stent patency rate showed more favorable results compared with previous Korean data.[31,32] Although this might be due to the use of covered stents, there was no difference in the stent dysfunction rate between the groups with covered and uncovered stents. This might be explained by the fact that 74.7% of the stents in our study were covered. Another reason might be the different surveillance protocols for stent patency used by the various hospitals. When interpreting data on shunt patency, the influence of the surveillance method should be considered.[9]

There were several limitations to this study. First, TIPS might have been performed in patients selected according to the protocol of each medical center. As this was a retrospective study, the analysis is subject to potential patient selection bias, such as omitting patients with technical TIPS failure. Second, as already noted, the different surveillance programs of the individual hospitals after TIPS placement might have affected the shunt patency and rebleeding rates. Third, 13 patients were lost to follow-up. These patients also were regarded as lost to follow-up in the analysis of TIPS patency. Fourth, the percentage of patients with refractory ascites as an indication for TIPS placement in this study was larger than that in other studies. Despite these limitations, there were a large number of patients enrolled in this study, and they were followed for a long period.

In conclusion, the TIPS procedure is an option for managing patients with refractory ascites and variceal bleeding refractory to pharmacological or endoscopic management. However, recurrent bleeding was significantly associated with shunt dysfunction. Therefore, stricter surveillance of shunt patency is required to prevent recurrent variceal bleeding. The MELD score is a useful decision-making tool regarding TIPS procedures. Although there has been an improvement in stent patency and survival with TIPS, older patients and those with advanced liver dysfunction still have high mortality. In the era of liver transplantation, further study is required to re-assess the role of and indications for TIPS.

## Conflicts of Interest

The authors have no conflicts to disclose.

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