Published in final edited form as:

J Gastroenterol Hepatol. 2017 April ; 32(4): 852–858. doi:10.1111/jgh.13593.

Early TIPS in U.S. Patients Hospitalized with Acute Esophageal Variceal Bleeding

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Abstract

Background and Aim—Early transjugular intrahepatic portosystemic shunt (TIPS) used as preventive therapy prior to recurrent bleeding has been recommended in patients presenting with acute esophageal variceal bleeding (EVB) who are at high risk of further bleeding and death. We investigated the impact of early TIPS on outcomes of U.S. patients hospitalized with EVB from 2000 to 2010.

Methods—The Nationwide Inpatient Sample database was queried to identify patients with EVB and decompensated cirrhosis (because early TIPS is recommended only in high-risk patients). The primary outcome was in-hospital death, and secondary outcomes included rebleeding and hepatic encephalopathy. Early preventive TIPS was defined by placement within 3 days of hospitalization for acute EVB after one session of endoscopic therapy. Rescue TIPS was defined as TIPS after two interventions for EVB.

Results—The study included 142,539 patients. From 2000 to 2010, the age-adjusted in-hospital mortality rate decreased 37.2% from 656 per 100,000 to 412 per 100,000 ($p < 0.01$), while early and rescue TIPS increased (0.22% to 0.70%; $p < 0.01$ and 1.1% to 6.1%; $p < 0.01$). On multivariate analysis, as compared to no TIPS, early TIPS was associated with decreased inpatient mortality (RR=0.87; 95% CI, 0.84–0.90) and rebleeding (RR=0.56; 95% CI, 0.45–0.71) without an increase in hepatic encephalopathy (RR=1.01; 95% CI, 0.93–1.11).

Conclusion—Early preventive TIPS in patients with EVB and decompensated cirrhosis was associated with significant in-hospital reductions in rebleeding and mortality without a significant increase in encephalopathy in “real-world” U.S. clinical practice.

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Author Contributions – Study concept and design: BN, TRM, LL; acquisition and analysis of data: BN; Interpretation of data: BN, TRM, LL; Initial draft: BN; Critical revision of manuscript: TRM, LL. All authors approved the final draft submitted.

Potential competing interests: None

Keywords

Esophageal Varices; Upper Gastrointestinal Bleeding; Liver Disease; Cirrhosis; Transjugular Intrahepatic Portosystemic Shunt (TIPS)

INTRODUCTION

Esophageal variceal bleeding (EVB) is a severe complication of portal hypertension with significant morbidity and mortality. The greatest risk of rebleeding in patients presenting with acute EVB occurs within the first 48–72 hours, and over 50% of rebleeding episodes occur within the first 10 days.¹ The current approach for acute EVB combines endoscopic band ligation and pharmacologic treatment as first-line therapy.^{2–6} However, 10–20% of patients will have persistent or recurrent bleeding necessitating alternative “rescue” treatment with transjugular intrahepatic portosystemic shunt (TIPS).⁷

Early TIPS (within 72 hours of presentation) as preventive therapy prior to recurrent bleeding has also been studied in patients presenting with acute EVB. Small, randomized trials of early TIPS report benefit in patients at high risk for further bleeding and death, such as those with a hepatic venous pressure gradient >20 mmHg or with Child-Pugh class C cirrhosis (Child-Pugh score 10–13) or Child-Pugh class B cirrhosis with active bleeding.^{8,9} However, population-based studies of the impact and timing of TIPS on outcomes of patients with EVB are not available. We used a United States (U.S.) nationwide database to determine the impact of early TIPS when utilized for prevention of rebleeding and of rescue TIPS used to treat persistent or recurrent bleeding in hospitalized patients with decompensated cirrhosis and EVB. We hypothesized that early TIPS would be associated with decreased mortality and rebleeding during hospitalization of decompensated cirrhotics with acute EVB.

METHODS**Data Source and Extraction**

The Nationwide Inpatient Sample (NIS) database was queried to identify patients with EVB in the U.S. from 2000 to 2010.¹⁰ The NIS is part of the Healthcare Cost and Utilization Project, sponsored by the Agency for Healthcare Research and Quality. The NIS is a database of hospital inpatient stays derived from billing data submitted by hospitals to statewide data organizations across the U.S. Inpatient data includes clinical and resource use information typically available from discharge abstracts. Each discharge is coded with a principal diagnosis for that specific hospitalization in addition to the potential for 14 secondary diagnoses and 15 associated procedures. The NIS is the largest U.S. inpatient care database, encompassing hospitals from a total of 46 states, which comprise 97% of the U.S. population.

Inclusion and Exclusion Criteria

Patients were identified by hospitalizations related to EVB through appropriate International Classification of Diseases, Ninth Edition, Clinical Modification (ICD-9-CM) codes. Patients

were initially included with a primary diagnosis of esophageal varices with bleeding or patients who had a secondary diagnosis of bleeding varices but a primary diagnosis of cirrhosis. We used previously defined criteria for decompensated liver disease by using the Baveno V classification of cirrhosis severity.²

The Baveno five-stage classification system has been devised as follows: 1) compensated cirrhosis with no varices; 2) compensated cirrhosis with varices; 3) upper gastrointestinal bleeding without ascites; 4) ascites (and/or hepatocellular carcinoma, encephalopathy, or jaundice) without bleeding; and 5) ascites and bleeding (with/without hepatocellular carcinoma, hepatic encephalopathy, or jaundice).^{11,12} Only patients with decompensated liver disease as defined by Baveno V classification (Stages 3 and 5) were included in our analyses.

Clinical Characteristics and Covariates

Demographic information was collected, including gender, age, and race/ethnicity. Additional characteristics extracted included etiology of liver disease as well as disease complications: hepatorenal syndrome, hepatocellular carcinoma, ascites, sepsis, encephalopathy, or development of spontaneous bacterial peritonitis. Procedures examined included esophagogastroduodenoscopy (EGD) and endoscopic therapy for variceal bleeding, balloon tamponade, interventional radiology, surgery, and TIPS occurring during hospital stay. The Elixhauser comorbidity index was calculated based upon the Agency for Healthcare Research and Quality comorbidity measures obtained from the NIS.¹³ The original index contained 30 comprehensive categories of comorbidity; however the list of specific ICD diagnoses was expanded to 31 categories in 2012.^{13,14} An Elixhauser comorbidity index of >2 is associated with adverse outcomes and can be used to predict in-hospital mortality.¹⁵

Early TIPS was defined by placement within 3 days of hospitalization for acute EVB after one EGD with endoscopic therapy. This definition was chosen to simulate recommended practice in which initial endoscopy to diagnose EVB and provide endoscopic therapy prior to the early TIPS is recommended.^{6,13} Rescue TIPS, used to treat patients with persistent or recurrent bleeding, was defined by two or more EGD's with endoscopic therapy or one EGD plus a non-endoscopic intervention for control of variceal bleeding (i.e., balloon tamponade, interventional radiology, or surgery) prior to TIPS. Rebleeding was defined as at least 2 blood transfusions following initial endoscopic or non-endoscopic intervention for control of variceal bleeding or repeat endoscopic or non-endoscopic intervention for control of variceal bleeding. Additional hospitalization data included day of admission (weekday or weekend), route of admission, mean length of stay, hospitalization charges, and primary payor source. Further details are highlighted in Appendix 1.

Measured Outcomes

The primary outcome measure was in-hospital death. Secondary outcomes included rebleeding, hepatic encephalopathy, sepsis, length of hospital stay, and hospitalization cost.

Data Synthesis and Statistical Analysis

Data were analyzed using the Stata 13.0 software package (Stata Corp LP, College Station, TX). Healthcare Cost and Utilization Project NIS data are provided in a 2-stage cluster design incorporating clustering at the hospital level and discharge level. The project provides weighting of discharges based on the hospital type and volume of discharges relative to the sampling region. Quantitative variables were expressed as means $\pm$ standard deviation (SD). Two-way chi-square analyses were performed on categorical variables. The age-adjusted mortality rate was calculated for each year of study by summing the product of age-specific mortality rates by the age-specific weights. For trends in overall population, the total number of cases were standardized per 100,000 based upon total population derived from the U.S. census data for specific year (2000 to 2010).¹⁶ The weights used in the age adjustment of the data were the proportion of the year 2000 standard U.S. population within each age group.¹⁷

Secular trends in mortality rates were observed in linear Poisson regression models. The models were used to observe the effect of the period of diagnosis (independent variable) on the in-hospital mortality rate (dependent variable), while controlling for other independent variables. Risk estimates and 95% confidence intervals (CI's) were calculated for all independent variables in the final model. Poisson regression with robust (Huber–White) standard errors was also used to determine incident risk ratios (RR) for predictors of in-hospital mortality. Prior to our analysis we tested the Poisson models for over-dispersion using a Pearson goodness-of-fit test. Models were not over dispersed and were appropriate for our analyses.

We also hypothesized that improved care and incorporation of guidelines for variceal bleeding may have improved survival and would be reflected in decreasing mortality risk ratios from year to year. Therefore, we created interaction terms between each diagnosis and year of discharge (EVB 2000, EVB 2001, and so forth). To validate our results in patients with a Child-Pugh Score of <14 , we carried out a sensitivity multivariate analysis limited to patients without ascites because the maximum Child-Pugh score for patients without ascites is 13.

RESULTS

Demographic and Clinical Characteristics

A total of 142,539 patients with a discharge diagnosis of EVB were included in our study. Demographic and baseline characteristics are shown in Table 1. A majority of the study population was White (65%) and male (68%). The mean age was 58 (SD 0.6) years. The average Elixhauser comorbidity index of patients was 2.9 (SD 1.7). Early TIPS was performed in 0.5% (n=713) of the population studied. The primary method or route of admission was through the emergency department (n=97,924 or 68.7%) with a mean hospital stay of 5.5 days. The mean hospitalization cost accrued for one visit was \$35,453 with the largest proportion of patients covered by Medicare (n=60,722 or 42.6%). Elixhauser comorbidities of included patients is shown in Supplemental Table 1.

Trends in Variceal Bleeding

From 2000 to 2010, the number of patients with EVB increased by approximately 2-fold [n=7,839 (2.8 per 100,000) to n=16,391 (5.3 per 100,000)] with a gradual increase each year during this period (Supplemental Table 2).¹⁸ During the same period, a decline in overall in-hospital age-adjusted mortality rate was seen among patients with EVB [decreased 37.2% from 656 per 100,000 to 412 per 100,000 ($p < 0.01$); Figure 1]. The age-adjusted mortality rates were consistently higher in males as compared to females during the study period and both sexes demonstrated decreasing mortality rates over the study period. Age-adjusted in-hospital mortality rate for males decreased from 749 per 100,000 to 505 per 100,000 from 2000 to 2010. Similarly, the age-adjusted in-hospital mortality rate for females decreased from 557 per 100,000 to 313 per 100,000 over the study period (Figure 1).

Use of TIPS

Utilization of TIPS (early and rescue) significantly increased over the study period [(0.22% to 0.70%; $p < 0.01$ and 1.1% to 6.1%; $p < 0.01$, respectively); Figure 2]. Linear univariate poisson regression analysis showed a significant inverse association of TIPS utilization and the mortality rate ratio of EVB from 2000 to 2010 (RR 0.88; 95% CI: 0.83–0.92). Overall, early TIPS had a lower rate of in-hospital death compared to patient with no TIPS and rescue TIPS, [(1.5% versus 5.6%; $p < 0.01$ and 1.5% versus 8.1%; $p < 0.01$, respectively) Table 2]. Early TIPS also showed a lower rate of rebleeding when compared to no TIPS and rescue TIPS (0.5% versus 15.4%; $p < 0.01$ and 0.5% versus 2.2%; $p < 0.01$, respectively). When comparing in-hospital rate of encephalopathy, early TIPS was similar to no TIPS and rescue TIPS (30.1% versus 27.3%; $p = 0.19$ and 30.1% versus 29.5%; $p = 0.15$, respectively).

Multivariate Analysis

A multivariate logistic regression analysis was also performed with variables controlled for age, ethnicity, sex, Elixhauser comorbidities, and Baveno V stage (Table 2). On multivariate analysis, as compared to no TIPS and rescue TIPS, early TIPS was associated with decreased inpatient mortality (aRR 0.87; 95% CI, 0.84–0.90 and aRR 0.85; 95% CI, 0.82–0.88, respectively). A significant decrease in inpatient rebleeding rates was also noted in the early TIPS group compared to no TIPS and rescue TIPS (aRR 0.56; 95% CI, 0.45–0.71 and aRR 0.57; 95% CI, 0.50–0.64, respectively). Patients who had early TIPS had a decrease in hospital stay by 4.6 days (95% CI, 4.3–5.1; $p < 0.01$) compared to rescue TIPS. Early TIPS was also associated with a decrease in hospitalization costs by \$7,288.37 (95% CI, \$6,697.62–\$8,922.45) compared to rescue TIPS. Although there was no significant difference in length of hospital stay for early TIPS compared to no TIPS (adjusted difference of 0.6 days; 95% CI, –0.3 to 1.0; $p = 0.18$), patients who had early TIPS accrued a higher hospitalization cost than those with no TIPS (absolute difference of \$8,226.68, 95% CI \$3,807.33 to \$18,137.42).

Early TIPS was not associated with higher rates of hepatic encephalopathy or sepsis compared to no TIPS or rescue TIPS (Table 2). A sensitivity analysis limited to patients without ascites revealed similar results (Supplemental Table 3): compared to no TIPS and rescue TIPS, early TIPS was associated with decreased inpatient mortality (aRR 0.80; 95% CI, 0.82–0.92 and aRR 0.81; 95% CI, 0.79–0.89, respectively). A significant decrease in

inpatient rebleeding rates was also noted in our sensitivity analysis in the early TIPS group compared to no TIPS and rescue TIPS (aRR 0.49; 95% CI, 0.44–0.77 and aRR 0.52; 95% CI, 0.49–0.69, respectively).

DISCUSSION

This U.S. nationwide database study showed that early TIPS was associated with decreased rebleeding, inpatient mortality, and length of hospital stay amongst inpatients with decompensated cirrhosis and acute EVB. Sensitivity analysis with early TIPS performed for EVB in decompensated cirrhotics without ascites (which guarantees all patients had Child-Pugh Score <14) also showed similar results. A significant decrease in inpatient mortality among decompensated cirrhotics with EVB in the U.S. was also seen from 2000 to 2010, with a concurrent increase in the utilization of TIPS.

Previous small, randomized trials have supported the use of early TIPS as a treatment for prevention of rebleeding and death in selected patients with acute EVB. Cello et al showed no significant difference in outcomes during initial hospitalization, and EVB was significantly less frequent in the early TIPS group (mean follow-up 570 days).¹⁹ Other outcomes measured were not significantly different. Monescillo and colleagues demonstrated significantly improved inpatient mortality and control of acute bleeding with early TIPS in a randomized trial of 52 patients with hepatic venous pressure gradients 20mm Hg; however, TIPS was again not compared to current standard therapy, ligation, but rather to sclerotherapy.⁸ More recently, García-Pagán et al compared early TIPS to combined medical therapy and endoscopic ligation and showed significantly lower rates of uncontrolled bleeding/rebleeding and mortality at 6 weeks and 1 year [1-year actuarial survival of 61% in the pharmacotherapy-ligation group versus 86% in the early TIPS group ($p<0.001$)].⁹ A subsequent retrospective observational study of 75 patients with the same criteria in the same centers after completion of the randomized trial reported a benefit of early TIPS in control of bleeding or rebleeding at 2 years (but not 6 weeks) and a trend to a mortality benefit over 2 years.²⁰

Thus, randomized trials indicate a benefit of early TIPS in prevention of long-term further bleeding. Results, however, are mixed regarding the short-term benefit of early TIPS, with one study reporting benefit during the initial hospitalization¹³, and two others not documenting this.^{14,23} Nevertheless, these studies were small and only one compared early TIPS to the current standard of care. Furthermore, these studies were generally performed at centers with expertise in the management of cirrhotic patients with variceal bleeding. To our knowledge, no population-based studies have assessed the impact of early TIPS on EVB outcomes in clinical practice.

We found a steady rise in the annual number of patients with cirrhosis and acute EVB in the U.S. from 2000 to 2010. This occurred despite evidence-based recommendations to employ medical therapy and/or ligation for primary and secondary prevention of variceal bleeding.^{3,18} This increase is likely secondary to the maturation of the hepatitis C epidemic and the rise in non-alcoholic fatty liver disease (NAFLD). Previous data extracted from the NIS database has shown a growing number of patients with cirrhosis from 2002 to 2010

(discharge diagnosis n=71,899 to n=99,252, respectively).²¹ Despite the increase in EVB over the 10-year study period, we did find a nearly 40% decrease in hospital mortality in patients with EVB. This presumably is due at least in part to improved management of EVB, including use of TIPS, but also may relate to improvements in overall management of cirrhosis.

A previous study by Schmidt and colleagues demonstrated a steady decline in inpatient mortality among hospitalized cirrhotic patients in the U.S. from 9.1% in 2002 to 5.4% in 2010.²¹ In addition to the increase in use of early TIPS, a much larger absolute increase in the use of rescue TIPS was identified from 2000 to 2010. This group represents a high-risk population with further bleeding in the hospital and, as expected, has a higher mortality than those with no TIPS or early TIPS. However, the marked increase in rescue TIPS from 2000 to 2010 also may account for at least a portion of the improvement in mortality, as TIPS replaced no therapy or therapies that are less effective and/or more morbid for treatment of further bleeding after hospital admission (i.e., balloon tamponade, surgery).

Our study had several limitations. Laboratory data to compute the Child-Pugh score or MELD score in our cohort of patients cannot be obtained from the NIS database. The Child-Pugh Score and MELD score have been shown to predict outcomes in patients with EVB.^{17,22,23} However, we were able to use the Baveno classification for cirrhosis severity to select decompensated patients and based on the absence of ascites we were also able to identify a subgroup of decompensated patients who had a Child-Pugh Score of <14. This notion that patients at high risk of rebleeding should receive consideration for early TIPS was again demonstrated in retrospective studies and more recent guidelines including the updated Baveno VI report.^{9,20,24,25} However, while early TIPS with polytetrafluoroethylene (PTFE) covered stents have demonstrated impressive results (improved survival 86% with early TIPS vs 61% with band ligation and pharmacotherapy, at 1 year)⁹, the NIS database does not allow for the ability to differentiate between different stent types. While PTFE stents are more common in traditional U.S. practice today, an inability to differentiate between different stent types remains another limitation to our study.

Furthermore, the diagnosis of EVB and identification of comorbidities are dependent on the accuracy of coding procedures. While large datasets based upon insurance reimbursement may be affected due to the several assumptions in the analysis, a recent study demonstrated administrative data can identify patients with cirrhosis with high accuracy.²⁶ Additionally, previous studies have defined a combination of codes for EVB to improve the sensitivity, and we adapted the codes from these studies.^{21,27} Although, we found no significant increase in hepatic encephalopathy in patients with early TIPS compared to no TIPS or rescue TIPS, this does not confirm that there was no difference in incident hepatic encephalopathy with use of early TIPS because the NIS database does not differentiate between outcomes that develop during an inpatient stay versus those present prior to hospitalization. Nevertheless, recent randomized trials in high-risk patients also failed to show an increase in hepatic encephalopathy with early TIPS as compared to endoscopic and medical therapy^{13,14}, possibly because a reduction in rebleeding also reduced subsequent hepatic decompensation. Moreover, additional management questions are unable to be answered by our analysis including changes in pharmacotherapy standard of care over time

(i.e. type and duration of antibiotics, choice of vasoactive agent, and the transition from sclerotherapy to band ligation).

In addition, our definition of early TIPS, requiring TIPS after initial endoscopy with endoscopic therapy, was chosen to simulate the recommended practice of performing initial diagnostic and therapeutic endoscopy prior to early TIPS. However, because NIS is not a medical records database, we cannot rule out that some early TIPS cases were mis-categorized because the hospitalization for EVB represented a second or third episode of rebleeding after prior hospitalizations or because patients had clinical evidence of persistent bleeding after their initial endoscopy, which led to rescue TIPS rather than early preventive TIPS. Given the nature of the dataset, we cannot rule out that patients were admitted for their first variceal bleed as compared to a recurrent bleed. Also, because TIPS is not readily performed at all hospitals, the results of this study may not be generalizable.

Despite these limitations, our study has several strengths and clinical implications. All of the patients included in this database were admitted with EVB and had decompensated cirrhosis. The sampling of EVB patients spanning the U.S. population over a decade is also an advantage over smaller, single-centered studies. Furthermore, the use of data from a nationwide population-based sample minimizes the possible biases that may be seen in single-center studies and provides strong data for generalizing the observations from this study to clinical practice in the U.S.

In conclusion, this population-based study from the U.S. demonstrates the significant impact of early TIPS on EVB outcomes in patients with decompensated cirrhosis. The early use of TIPS as a preventive treatment was associated with significant short-term reductions in rebleeding and mortality. The small percentage of eligible cases receiving early TIPS suggests that there is room for further improvement in the treatment of patients with decompensated cirrhosis and EVB. Early use of TIPS, together with patient and physician education on current guidelines and treatment protocols, should continue to be a priority to improve patient outcomes.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Financial Support: Supported by NIH T32 DK007017 (BN)

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Figure 1.

In-hospital age-adjusted mortality rate among patients with cirrhosis and acute esophageal variceal bleeding in the U.S. from 2000 to 2010. From 2000 to 2010, the overall age-adjusted in-hospital mortality rate decreased 37.2% from 656 per 100,000 to 412 per 100,000 ($p < 0.01$).

Figure 2.

Proportion of discharges who had a TIPS procedure among patients with cirrhosis and acute esophageal variceal bleeding in the U.S. from 2000 to 2010. Utilization of TIPS (early and rescue) significantly increased over the study period (0.22% to 0.70%; $p < 0.01$ and 1.1% to 6.1%; $p < 0.01$, respectively).

Table 1

Demographic and Clinical Characteristics of Hospitalized Patients with Cirrhosis and Acute Esophageal Variceal Bleeding in the U.S. from 2000 to 2010 (n = 142,539).

Variable	Frequency (n)	Percentage (%)
Sex		
Male	97212	68.2
Female	45327	31.8
Age, years		
<40	8695	6.1
41–50	30931	21.7
51–60	46325	32.5
61–70	28650	20.1
71–80	19243	13.5
>80	8695	6.1
Race/ethnicity		
White	92650	65
Black	15252	10.7
Hispanic	25942	18.2
Other race	8695	6.1
Liver complications		
Hepatorenal syndrome	4133	4.2
Hepatocellular carcinoma	5416	5.6
Ascites	47180	48.6
Sepsis	7269	7.4
Encephalopathy	29078	30.1
Spontaneous bacterial peritonitis	3991	4.1
Comorbidities		
Elixhauser comorbidity index (SD)	2.9 (1.7)	
Procedures		
EGD	124864	87.6
EGD 1 day from admission	117595	82.5
Balloon tamponade	855	0.6
Non-TIPS IR procedure	161	0.1
Surgery	98	0.07
TIPS		
Early TIPS	713	0.5
Rescue TIPS	5844	4.1
Hospitalization data		

Variable	Frequency (n)	Percentage (%)
Admitted on weekend	30646	21.5
Routine admission	35777	25.1
Admitted through emergency room	97924	68.7
Admitted from outside hospital	6129	4.3
Admitted from another facility	2423	1.7
Admitted through court/law	285	0.2
Primary payor		
Private insurance	32927	23.1
Medicaid	30646	21.5
Medicare	60722	42.6
Other payment source	6129	4.3
Self-pay	10690	7.5
No charge	1283	0.9

IR – interventional radiology

Table 2

Multivariable Regression Analysis for Outcomes with Early TIPS vs. No TIPS or Rescue TIPS in Patients with Cirrhosis and Acute Esophageal Variceal Bleeding (n = 142,539).

Outcome	Early TIPS	No TIPS	P value	RR ^a (95% CI)	P value
Early TIPS versus No TIPS					
In-hospital death	1.5%	5.6%	<0.01	0.87 (0.84, 0.90)	<0.01
In-hospital rebleeding	0.5%	15.4%	<0.01	0.56 (0.45, 0.71)	<0.01
Hepatic encephalopathy	30.1%	27.3%	0.19	1.01 (0.93, 1.11)	0.62
Sepsis	7.5%	7.1%	0.38	1.28 (0.75, 2.19)	0.40
Mean length of stay (days)	5.1	4.7	0.05	0.6 (−0.3 to 1.0) ^b	0.18
Mean hospitalization cost (U.S. \$)	42,789	34,154	<0.01	8,226.68 (3,807.33 to 18,137.42) ^b	<0.01
Early TIPS versus Rescue TIPS					
In-hospital death	1.5%	8.1%	<0.01	0.85 (0.82, 0.88)	<0.01
In-hospital rebleeding	0.5%	2.2%	<0.01	0.57 (0.50, 0.64)	<0.01
Hepatic encephalopathy	30.1%	29.5%	0.15	0.97 (0.95, 1.02)	0.22
Sepsis	7.5%	7.3%	0.22	0.83 (0.66, 1.04)	0.32
Mean length of stay (days)	5.1	9.6	<0.01	−4.6 (−5.1 to −4.3) ^b	<0.01
Mean hospitalization cost (U.S. \$)	42,789	58,982	<0.01	−7,288.37 (−8,922.45 to −6,697.62) ^b	<0.01

^a Adjusted for age, ethnicity, sex, Elixhauser Comorbidities, and Baveno V stage (i.e. presence or absence ascites)

Adjusted absolute difference (95% CI)
b

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