

# High Prevalence of Transjugular Intrahepatic Portosystemic Shunt Creation Without Prior Endoscopy During Acute Variceal Bleeding Hospitalization in the United States

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Current clinical guidelines by both American Association for the Study of Liver Disease and European Association for the Study of the Liver recommend endoscopy in all patients admitted with acute variceal bleeding within 12 hours of admission. Transjugular intrahepatic portosystemic shunt (TIPS) creation may be considered in patients at high risk if hemorrhage cannot be controlled endoscopically. We conducted a cross-sectional observational study to assess how frequently TIPS is created for acute variceal bleeding in the United States without preceding endoscopy. Adult patients undergoing TIPS creation for acute variceal bleeding in the United States (n = 6,297) were identified in the last 10 available years (2007-2016) of the National Inpatient Sample. Hierarchical logistic regression was used to examine the relationship between endoscopy nonutilization and hospital characteristics, controlling for patient demographics, income level, insurance type, and disease severity. Of 6,297 discharges following TIPS creation for acute variceal bleeding in the United States, 31% (n = 1,924) did not receive first-line endoscopy during the same encounter. Rates of “no endoscopy” decreased with increasing population density of the hospital county (nonmicropolitan counties 43%, n = 114; mid-size metropolitan county 35%, n = 513; and central county with >1 million population 23%, n = 527) but not by hospital teaching status (n = 1,465, 32% teaching vs. n = 430, 26% nonteaching; P = 0.10). Higher disease mortality risk (odds ratio, 0.42; 95% confidence interval, 0.22-0.80; P = 0.02) was associated with lower odds of noncompliance. **Conclusion:** One third of all patients undergoing TIPS creation for acute variceal bleeding in the United States do not receive first-line endoscopy during the same encounter. Patients admitted to urban hospitals are more likely to receive guideline-concordant care. (*Hepatology Communications* 2021;5:1784-1790).

More than 600,000 Americans have liver cirrhosis, which is now the twelfth leading cause of mortality in the United States.<sup>(1)</sup> Esophageal varices are present in up to 85% of patients with decompensated cirrhosis<sup>(2,3)</sup> and rupture at a rate of 10%-15% per year,<sup>(4)</sup> resulting in life-threatening hemorrhage. Without treatment, variceal hemorrhage is associated with ~40% mortality and

*Abbreviations:* APR-DRG, All Patients Refined Diagnosis Related Groups; CI, confidence interval; ICD-9/10, International Classification of Diseases, Ninth/Tenth Revision; NIS, National Inpatient Sample; OR, odds ratio; TIPS, transjugular intrahepatic portosystemic shunt.

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up to 70% recurrence.<sup>(5,6)</sup> Endoscopic variceal ligation and administration of nonselective beta blockers reduces rebleeding to 40%-50% and mortality to 20%-35%.<sup>(5)</sup> In patients with acute variceal bleeding, current guidelines by both American Association for the Study of Liver Disease and European Association for the Study of the Liver recommend endoscopy within 12 hours of admission. Transjugular intrahepatic portosystemic shunt (TIPS) creation may be considered in patients with bleeding that cannot be controlled endoscopically and in those at high risk for rebleeding.<sup>(7,8)</sup>

Randomized controlled trial data indicate that TIPS reduces rebleeding and offers a significant survival advantage over endoscopic management in high-risk patients with variceal bleeding.<sup>(9-12)</sup> Guideline-supported endoscopy before TIPS is a consistent requirement of patients in clinical trials aimed at assessing risk and efficacy of TIPS creation for acute variceal bleeding. How often endoscopy precedes TIPS creation in real-world settings is not known. We therefore examined how often TIPS was created without first-line endoscopy among patients admitted with acute variceal bleeding in the United States. We secondarily examined which patient and hospital factors were associated with endoscopy nonutilization.

## Patients and Methods

### DATA SOURCE

We used discharge data from the National Inpatient Sample (NIS) of the Healthcare Cost and Utilization Project (HCUP),<sup>(13,14)</sup> created by the Agency for Healthcare Research and Quality (AHRQ). The NIS

is a 20% stratified sample of all nonfederal hospitals in 44 participating states, encompassing more than 95% of the US population. Clinical, resource use, and billing data submitted to statewide agencies by hospitals are aggregated in a survey-weighted national sample. This study was deemed exempt by our institutional review board as the data set contains no patient-level identifiers and is publicly available for purchase.

### STUDY COHORT

We included patients >18 years old admitted with a principal diagnosis of acute variceal bleeding treated with TIPS creation in the last 10 available years of the NIS (2007-2016). We excluded patients transferred from another hospital due to absence of record linkage precluding verification of endoscopy use before transfer. Primary discharge diagnosis and procedure codes were identified using International Classification of Diseases, Ninth and Tenth (ICD-9/10) Revision codes, summarized in Supporting Table S1.

### PATIENT CHARACTERISTICS AND CLINICAL SEVERITY

Patient age, sex, race, primary payer, and median annual household income were extracted from the NIS. ICD-9/10 codes were used to identify clinical risk factors of interest<sup>(2,15-20)</sup>; these comprised congestive heart failure, chronic pulmonary disease, pulmonary hypertension, coagulopathy, alcohol abuse, hepatocellular carcinoma, spontaneous bacterial peritonitis, hepatic encephalopathy, ascites, sarcopenia, and portal vein thrombus. AHRQ comorbidity software provided by HCUP<sup>(21)</sup> was used to identify 29 Elixhauser comorbidities, using ICD-9-CM

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codes. Finally, All Patients Refined Diagnosis Related Groups (APR-DRG) severity of illness and mortality risk scores were extracted from the NIS severity files for adjustment of mortality risk. The APR-DRG is a proprietary formula developed by 3M for severity adjustment in the NIS and has specifically been validated as the best predictor of in-hospital mortality among patients with cirrhosis.<sup>(22)</sup>

## HOSPITAL CHARACTERISTICS

Hospital characteristics of interest extracted from the NIS included hospital bed size, location and teaching status (urban/rural, teaching/nonteaching), census region, and county population size.

## STATISTICS AND SENSITIVITY ANALYSIS

Categorical variables were compared using the chi-squared (Rao-Scott likelihood adjusted) test. Continuous variables were compared using a survey-weighted *t* test. To test the association between no endoscopy and hospital characteristics, we used a hierarchical logistic regression, controlling for baseline differences in patient demographics, comorbid risk factors, and the APR-DRG mortality risk, while accounting for clustering at the hospital level. Finally, we performed an internal validity analysis to assess rates of undercoding for endoscopy in the NIS by calculated rate of endoscopy use in all patients admitted with acute variceal bleeding over the same time period. Additionally, to assess whether elective planned admissions for TIPS creation accounted for endoscopy nonutilization, we performed a subset analysis excluding patients with a length of stay less than 2 days.

SAS, version 9.4 (SAS Institute, Cary, NC) and R 3.6.0 (Vienna, Austria) were used for data management, analysis, and visualization. Results were considered statistically significant for  $P < 0.05$ .

## Results

### PATIENT FACTORS

There were 6,297 discharges following TIPS creation for acute variceal bleeding in the United States

between 2007 and 2016. Overall, 31% ( $n = 1,924$ ) did not receive endoscopy during the same encounter. Baseline patient factors (demographics, socioeconomic indicators, and comorbid risk factors) stratified by whether or not they underwent endoscopy before TIPS are summarized in Table 1. A greater proportion of patients who received guideline-concordant endoscopy were men (72% endoscopy vs. 68% no endoscopy,  $P = 0.05$ ), had comorbid hepatic encephalopathy (24% endoscopy vs. 16% no endoscopy,  $P < 0.001$ ), coagulopathy (54% endoscopy vs. 46% no endoscopy,  $P = 0.01$ ), and belonged to the highest mortality risk category (45% endoscopy vs. 34% no endoscopy,  $P < 0.001$ ). Patient factors of age, race/ethnicity, and income status did not differ significantly by study group.

### HOSPITAL FACTORS

Rates of no endoscopy decreased with increasing population density of the hospital county ( $P < 0.001$ ) as follows: nonmicropolitan counties 43% ( $n = 114$ ), mid-size metropolitan county 35% ( $n = 513$ ), and central county with >1 million population 23% ( $n = 527$ ). Endoscopy nonutilization did not differ by hospital teaching status ( $n = 1,465$ , 32% teaching vs.  $n = 430$ , 26% nonteaching;  $P = 0.10$ ) or whether the admission occurred on a weekend ( $n = 454$ , 28% weekend vs.  $n = 1,470$ , 31% weekday;  $P = 0.29$ ). Endoscopy nonutilization was highest when TIPS creation occurred within a day of admission and decreased with increasing time to TIPS (Fig. 1). Inpatient mortality was higher for admissions with TIPS creation occurring on day 0 ( $n = 299/1,494$ , 20.0%) and day 1 ( $n = 313/1,507$ , 20.7%) as opposed to day 2 ( $n = 84/853$ , 9.8%) or day 3 and beyond ( $n = 231/2,439$ , 9.4%).

Additional multivariable predictors of no endoscopy are summarized in Table 2 and included micropolitan counties (odds ratio [OR], 2.60; 95% confidence interval [CI] 1.24-5.47;  $P = 0.01$ ), female sex (OR, 1.54; 95% CI, 1.04-2.30;  $P = 0.03$ ), and Midwest census region (OR, 2.59; 95% CI, 1.23-5.44;  $P = 0.01$ ). Higher APR DRG mortality risk (OR, 0.42; 95% CI, 0.22-0.80;  $P = 0.02$ ), the presence of hepatic encephalopathy (OR, 0.55; 95% CI, 0.34-0.89;  $P = 0.01$ ), and greater time from admission to TIPS (OR, 0.85; 95% CI, 0.79-0.91;  $P < 0.001$ ) were associated with lower odds

**TABLE 1. BASELINE PATIENT DEMOGRAPHICS, INCOME LEVEL, PAYER INFORMATION, COMORBID RISK FACTORS, AND DISEASE SEVERITY SCORE STRATIFIED BY USE OF ENDOSCOPY BEFORE TIPS CREATION FOR ACUTE VARICEAL BLEEDING IN THE UNITED STATES (2007-2016)**

Patient Characteristics	No Endoscopy		Endoscopy	
	n = 1,924		n = 4,373	
Age in years, median (IQR)	54	(47-61)	54	(48-61)
18-40 years	166	(8.6%)	367	(8.4%)
40-60 years	1,164	(60.5%)	2,744	(62.8%)
60-80 years	570	(29.6%)	1,187	(27.1%)
>80 years	24	(1.3%)	74	(1.7%)
Race/ethnicity				
White	1,284	(66.7%)	2,707	(61.9%)
Black	87	(4.5%)	238	(5.4%)
Hispanic	343	(17.8%)	1,005	(23.0%)
Asian	18	(0.9%)	64	(1.5%)
Native	24	(1.2%)	30	(0.7%)
Other	39	(2.0%)	170	(3.9%)
Missing	129	(6.7%)	159	(3.6%)
Sex				
Male	1,304	(67.8%)	3,186	(72.8%)
Female	620	(32.2%)	1,188	(27.2%)
Census region				
Midwest	381	(19.8%)	584	(30.4%)
Northeast	293	(15.2%)	769	(17.59%)
South	875	(45.5%)	2,077	(47.50%)
West	375	(19.5%)	943	(21.56%)
Median zip code income*				
Quartile 1	635	(33.0%)	1,459	(33.4%)
Quartile 2	503	(26.1%)	1,216	(27.8%)
Quartile 3	422	(21.9%)	959	(21.9%)
Quartile 4	318	(16.5%)	607	(13.9%)
Missing	46	(2.4%)	132	(3.0%)
Expected primary payer				
Medicare	619	(32.2%)	1,154	(26.4%)
Medicaid	455	(23.6%)	1,233	(28.2%)
Private	588	(30.6%)	1,228	(28.1%)
Self-pay	154	(8.0%)	474	(10.8%)
No charge	20	(1.0%)	68	(1.6%)
Other	78	(4.1%)	201	(4.6%)
Missing	10	(0.5%)	15	(0.3%)
Comorbid risk factors				
Ascites	780	(40.5%)	1,894	(43.3%)
Portal vein thrombus	138	(7.2%)	250	(5.7%)
Spontaneous bacterial peritonitis	68	(3.6%)	98	(2.2%)
Hepatic encephalopathy	306	(15.9%)	1,065	(24.4%)
Hepatorenal syndrome	54	(2.8%)	122	(2.8%)
Hepatocellular carcinoma	34	(1.7%)	141	(3.2%)
Sarcopenia	0	(0.0%)	15	(0.3%)
Congestive heart failure	54	(3.2%)	131	(3.4%)
Pulmonary circulation disease	59	(3.5%)	24	(0.6%)

TABLE 1. Continued

Patient Characteristics	No Endoscopy		Endoscopy	
	n = 1,924		n = 4,373	
Chronic pulmonary disease	160	(9.5%)	360	(9.3%)
Coagulopathy	772	(46.0%)	2,069	(53.9%)
Alcohol abuse	681	(40.6%)	1,825	(47.5%)
Drug abuse	68	(4.1%)	181	(4.7%)
APR DRG mortality risk				
Moderate	229	(11.9%)	229	(5.2%)
Major	819	(42.6%)	1,643	(37.6%)
Extreme	666	(34.6%)	1,956	(44.7%)

Data show number (%) except where indicated.

\*Income level increases with increasing quartile number (1, lowest; 4, highest) and is based on median income reported for the zip code in which the patient resides.

Abbreviation: IQR, interquartile range.

of noncompliance (or, conversely, higher odds of endoscopy use).

## INTERNAL VALIDITY ANALYSIS

There were 224,600 admissions for acute variceal bleeding in the United States between 2007 and 2016. A claim for endoscopy use was present in 182,375 (81%) of encounters in this aggregate mixed-severity population. In the subset analysis, 410 patients with a length of stay less than 2 days were excluded to assess for possible impact of unrecognized elective admissions. Of the remaining 5,887 encounters, 1,667 (28.3%) did not bill for endoscopy use.

## Discussion

In this retrospective cross-sectional study of discharges following TIPS creation for acute variceal bleeding in the United States, we observed a high rate (31%) of endoscopy nonutilization during the same encounter, discordant with current clinical practice guidelines. Rates of noncompliance were highest among hospitals in small/rural counties and lowest among hospitals in dense/urban counties, suggesting that lower access to endoscopists may underlie the observed nonadherence.

High-risk patients with hepatic encephalopathy and/or major/extreme risk of death had lower odds of undergoing TIPS creation without first-line

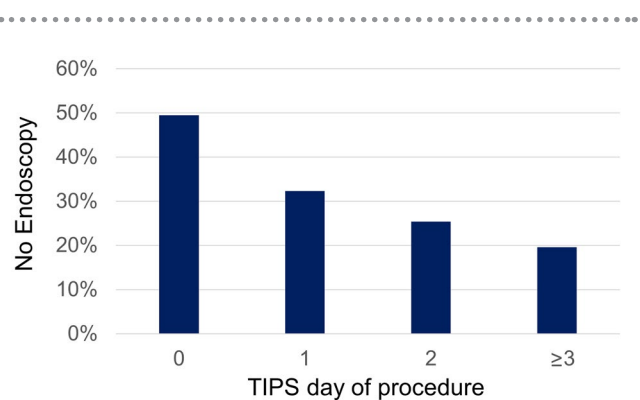


FIG. 1. Proportion of admissions for acute variceal bleeding in which TIPS creation was performed without first-line endoscopy, stratified by day of procedure.

endoscopy, indicating greater consideration afforded for this sicker subset. Although endoscopy nonutilization was significantly higher when TIPS creation occurred within a day of admission, it is unlikely that previously planned elective admissions primarily account for endoscopy nonuse for two reasons. First, inpatient mortality was significantly higher for patients undergoing TIPS on day 0 and day 1 compared with days 2 and beyond, which we do not expect of a healthier elective-procedure population. Second, in a subset analysis that excluded patients with a short length of stay as would be expected of elective cases, the proportion of TIPS without preceding endoscopy remained high (28%). We also studied the association between patient demographics and endoscopy use,

**TABLE 2. HIERARCHICAL LOGISTIC REGRESSION FOR THE OUTCOME OF NO ENDOSCOPY OCCURRING BEFORE TIPS CREATION (n = 6,297) FOR ACUTE VARICEAL BLEEDING IN THE UNITED STATES**

Variable	Level	OR	95% CI	PValue
Age (years), centered		0.99	(0.98, 1.01)	0.49
Female sex		1.54	(1.04, 2.30)	0.03
Patient race	Black	1.13	(0.47, 2.73)	0.78
	Hispanic	0.91	(0.57, 1.47)	0.71
	Other	1.36	(0.60, 3.10)	0.45
	Missing	0.37	(0.14, 0.98)	0.04
Residential zip code income level*	Quartile 2	0.70	(0.44, 1.13)	0.14
	Quartile 3	0.95	(0.57, 1.59)	0.85
	Quartile 4	1.02	(0.56, 1.87)	0.95
Primary payer	Medicaid	0.85	(0.52, 1.40)	0.51
	Medicare	1.23	(0.75, 1.99)	0.41
	Other	0.80	(0.45, 1.42)	0.45
Comorbidities	Ascites	1.06	(0.73, 1.53)	0.76
	Encephalopathy	0.55	(0.34, 0.89)	0.01
	Portal vein thrombus	1.59	(0.76, 3.35)	0.22
	SBP	1.51	(0.54, 4.21)	0.43
	Coagulopathy	0.81	(0.56, 1.17)	0.25
	Alcohol abuse	0.75	(0.51, 1.10)	0.14
APR DRG mortality risk	Major/extreme risk	0.42	(0.22, 0.80)	<0.01
Hospital location/teaching status	Rural	0.17	(0.01, 1.98)	0.15
	Urban nonteaching	0.99	(0.62, 1.59)	0.97
Hospital census region	Midwest	2.59	(1.23, 5.44)	0.01
	South	1.40	(0.74, 2.63)	0.30
	West	1.94	(0.95, 3.97)	0.06
Hospital county size	Fringe >1 million	1.29	(0.76, 2.19)	0.35
	Metro 250,000-1 million	1.65	(0.99, 2.74)	0.05
	Metro 50,000-250,000	1.89	(0.93, 3.84)	0.07
	Metropolitan counties	2.60	(1.24, 5.47)	0.01
Weekend admission		1.08	(0.72, 1.61)	0.71
Day of TIPS (from admission)		0.85	(0.79, 0.91)	<0.0001

\*Income level increases with increasing quartile number (1, lowest; 4, highest) and is based on median income reported for the zip code in which the patient resides.

Abbreviation: SBP, spontaneous bacterial peritonitis.

incidentally observing higher odds of guideline non-adherence for female patients. Sex disparity in guideline adherence has been noted in management of many other acute conditions, including percutaneous coronary intervention for myocardial infarction.<sup>(23)</sup> This finding is difficult to explain but deserves further focused investigation.

Admission to hospitals in the Midwest was also associated with higher odds of noncompliance, suggesting regional practice pattern variation. To reduce rates of guideline nonadherence, public health efforts must focus on improving access/resources among hospitals in more rural locations. Finally, future studies

need to evaluate whether endoscopy nonutilization before TIPS is associated with worse outcomes, particularly because current guidelines are largely based on expert opinion.

Several study limitations deserve mention. The primary limitation to consider is the possibility of undercoding for endoscopy. To assess its impact on the reported findings, we performed an internal validity analysis studying rate of endoscopy use within the larger cohort of all national admissions for acute variceal bleeding. We found a significantly higher rate of endoscopy use in this control population (81% among 224,600 discharges over the same

study period), suggesting that undercoding does not primarily explain the reported findings. Some degree of undercoding is nonetheless expected. Second, the NIS does not contain records before or following hospital admission. It is possible that some of the patients who did not receive endoscopy before TIPS were candidates for the shunt based on findings from prior endoscopic encounters. Our subset analysis suggests that planned elective admissions do not primarily account for endoscopy nonutilization but may inflate the reported rate. Third, while we did adjust for comorbid conditions and severity of illness, the NIS does not have granular laboratory data to assess severity of liver disease based on traditional metrics, such as the Model for End-Stage Liver Disease score.

In summary, approximately one third of patients undergoing TIPS creation for acute variceal bleeding in the United States do not receive recommended first-line endoscopy during the same admission. Guideline nonadherence is more likely to occur in female patients and in hospitals located in less populated areas. Further studies are necessary to determine the impact of endoscopy nonutilization on TIPS outcomes to ultimately inform practice guidelines moving forward.

## REFERENCES

- Scaglione S, Kliethermes S, Cao G, Shoham D, Durazo R, Luke A, et al. The epidemiology of cirrhosis in the United States: a population-based study. *J Clin Gastroenterol* 2015;49:690-696.
- Garcia-Tsao G, Abraldes JG, Berzigotti A, Bosch J. Portal hypertensive bleeding in cirrhosis: Risk stratification, diagnosis, and management: 2016 practice guidance by the American Association for the study of liver diseases. *Hepatology* 2017;65:310-335. Erratum in: *Hepatology* 2017;66:304.
- Kovalak M, Lake J, Mattek N, Eisen G, Lieberman D, Zaman A. Endoscopic screening for varices in cirrhotic patients: data from a national endoscopic database. *Gastrointest Endosc* 2007;65:82-88.
- Nett A, Binmoeller KF. Endoscopic management of portal hypertension-related bleeding. *Gastrointest Endosc Clin N Am* 2019;29:321-337.
- Strunk H, Marinova M. Transjugular intrahepatic portosystemic shunt (TIPS): pathophysiologic basics, actual indications and results with review of the literature. *Rofo* 2018;190:701-711.
- D'Amico G, De Franchis R; Cooperative Study Group. Upper digestive bleeding in cirrhosis. Post-therapeutic outcome and prognostic indicators. *Hepatology* 2003;38:599-612.
- Boyer TD, Haskal ZJ; American Association for the Study of Liver Diseases. The role of transjugular intrahepatic portosystemic shunt (TIPS) in the management of portal hypertension: update 2009. *Hepatology* 2010;51:306.
- de Franchis R; Baveno VI Faculty. Expanding consensus in portal hypertension: report of the Baveno VI Consensus Workshop: stratifying risk and individualizing care for portal hypertension. *J Hepatol* 2015;63:743-752.
- García-Pagán JC, Caca K, Bureau C, Laleman W, Appenrodt B, Luca A, et al.; Early TIPS (Transjugular Intrahepatic Portosystemic Shunt) Cooperative Study Group. Early use of TIPS in patients with cirrhosis and variceal bleeding. *N Engl J Med* 2010;362:2370-2379.
- García-Pagán JC, Di Pascoli M, Caca K, Laleman W, Bureau C, Appenrodt B, et al. Use of early-TIPS for high-risk variceal bleeding: results of a post-RCT surveillance study. *J Hepatol* 2013;58:45-50.
- Deltenre P, Trépo E, Rudler M, Monescillo A, Fraga M, Denys A, et al. Early transjugular intrahepatic portosystemic shunt in cirrhotic patients with acute variceal bleeding: a systematic review and meta-analysis of controlled trials. *Eur J Gastroenterol Hepatol* 2015;27:e1-e9.
- Sauerbruch T, Mengel M, Dollinger M, Zipprich A, Rössle M, Panther E, et al.; German Study Group for Prophylaxis of Variceal Rebleeding. Prevention of rebleeding from esophageal varices in patients with cirrhosis receiving small-diameter stents versus hemodynamically controlled medical therapy. *Gastroenterology* 2015;149:660-668.e1.
- Agency for Healthcare Research and Quality. Healthcare Cost and Utilization Project (HCUP): NIS overview. <https://www.hcup-us.ahrq.gov/nisoverview.jsp#about>. Updated April 2021. Accessed April 2021.
- Steiner C, Elixhauser A, Schnaier J. The healthcare cost and utilization project: an overview. *Eff Clin Pract* 2002;5:143-151.
- Lee SS, Liu H. Cardiovascular determinants of survival in cirrhosis. *Gut* 2007;56:746-748.
- Fasullo M, Al-Abboodi Y. The mortality of hepatorenal syndrome from etiology of cirrhosis: 990. *Am J Gastroenterol* 2017;112:S554.
- Praktiknjo M, Clees C, Pigliacelli A, Fischer S, Jansen C, Lehmann J, et al. Sarcopenia is associated with development of acute-on-chronic liver failure in decompensated liver cirrhosis receiving transjugular intrahepatic portosystemic shunt. *Clin Transl Gastroenterol* 2019;10:e00025.
- Bajaj JS, O'Leary JG, Tandon P, Wong F, Garcia-Tsao G, Kamath PS, et al. Hepatic encephalopathy is associated with mortality in patients with cirrhosis independent of other extrahepatic organ failures. *Clin Gastroenterol Hepatol* 2017;15:565-574.e4.
- Arvaniti V, D'Amico G, Fede G, Manousou P, Tsochatzis E, Pleguezuelo M, et al. Infections in patients with cirrhosis increase mortality four-fold and should be used in determining prognosis. *Gastroenterology* 2010;139:1246-1256, 1256.e1-e5.
- Fede G, D'Amico G, Arvaniti V, Tsochatzis E, Germani G, Georgiadis D, et al. Renal failure and cirrhosis: a systematic review of mortality and prognosis. *J Hepatol* 2012;56:810-818.
- Elixhauser A, Steiner C, Harris DR, Coffey RM. Comorbidity measures for use with administrative data. *Med Care* 1998;36:8-27.
- Myers RP, Quan H, Hubbard JN, Shaheen AAM, Kaplan GG. Predicting in-hospital mortality in patients with cirrhosis: results differ across risk adjustment methods. *Hepatology* 2009;49:568-577.
- Birkemeyer R, Schneider H, Rillig A, Ebeling J, Akin I, Kische S, et al. Do gender differences in primary PCI mortality represent a different adherence to guideline recommended therapy? a multi-center observation. *BMC Cardiovasc Disord* 2014;14:71.

## Supporting Information

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