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ORIGINAL ARTICLE

Comparison of the management of gastric variceal bleeding techniques

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alcoholism, balloon-occluded retrograde transvenous obliteration, endoscopic variceal ligation, transjugular intrahepatic portosystemic shunt.

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Abstract

Background and Aim: Managing gastric variceal (GV) hemorrhage is more complicated than managing esophageal variceal (EV) bleeding, resulting in significantly higher morbidity and mortality. We aim to compare the outcomes of endoscopic variceal ligation (EVL), transhepatic intrahepatic portosystemic shunt (TIPS), and balloon-occluded retrograde transvenous obliteration (BRTO) in the management of GV bleeding.
Methods: We utilized the National Inpatient Sample (NIS) database from January 2016 to December 2019 to include adult patients with GV hemorrhage.
Results: Our study identified 7160 hospitalizations with a primary diagnosis of GV hemorrhage who underwent the interventions of interest. EVL was performed in 69.83%, TIPS in 8.72%, and BRTO in 4.88%. Patients with liver cirrhosis had a higher frequency of undergoing BRTO (68.6%), followed by TIPS (64.0%) and esophagogastroduodenoscopy (EGD) + TIPS (63.7%) ($P < 0.001$). Patients with cirrhosis secondary to alcoholism had a higher prevalence of TIPS (62.4%), followed by EGD + TIPS (69.4%) and BRTO (52.9%) ($P < 0.001$). Overall, the inpatient mortality was 6.5%. Overall inpatient mortality was highest in the TIPS cohort (8.8%), followed by BRTO (7.1%), EGD + TIPS (6.5%), EVL (6.2%), and EGD + BRTO (2.8%) ($P < 0.001$); However, the Kaplan–Meier graph showed endoscopy with BRTO had the most favorable 30-day survival, trailed by TIPS alone and BRTO alone.
Conclusion: EVL remains a prominent therapeutic strategy. Remarkably, the combination of endoscopy with BRTO shows promising 30-day survival outcomes. Considering these observations, although EVL holds its primacy, it is essential to further explore the potential benefits of combined therapies in larger studies to ascertain the best treatment strategies.

Introduction

The development of varices and subsequent hemorrhage is a serious complication of portal hypertension. Gastric varices (GVs) are present in 18–70% of patients with portal hypertension[1–3] and gastroesophageal varices in about 50% of patients with cirrhosis.[1] GVs have ~25% risk of hemorrhage in 2 years.[1,4] Size (>5 mm), location (fundal varices), Child C class, and variceal red spots seen on endoscopy indicate an increased likelihood of hemorrhage.[4–7] Although less common and less likely to bleed than esophageal varices (EVs), GVs have a poorer prognosis due to more severe hemorrhage that is more difficult to control, along with a higher rebleeding rate (34–89%),[8,9] leading to further increase in mortality (10–30%).[10]

There are two major classifications for GVs. The Sarin classification focuses on the anatomical location, including the extension of the EV into the stomach,[11] whereas Hashizume *et al.*'s classification is based on endoscopic findings of GV, including color, form, and location.[12] Additionally, there are more recent classifications of GVs based on radiologic imaging and afferent and efferent flow hemodynamics. The Kiyosue classification divides GVs into three types for inflow hemodynamics and four types for outflow collaterals, whereas the Saad–Caldwell classification combines both into four types of GVs.[13,14] These radiologic classifications allow the identification of the presence or absence of afferent and efferent channels in the GV collateral complex to plan better effective treatment options for patients beyond

conventional endoscopic therapies. Understanding the hemodynamics of the portal circulation can assist in selecting the most effective treatment for GVs. They most commonly develop in the submucosal layer at the cardia or fundus, as these locations are fixed to the retroperitoneum and are closer to the systemic circulation via portosystemic shunts.[4,6,15] Rebleeding is, therefore, higher in GVs because of the persistence of collateral flow to the patent GV.[16,17]

The treatment choice for GVs often hinges on the technical challenges of each procedure and the availability of specialized centers equipped to handle them. Notably, the treatment of GVs is more intricate than other types of varices, and not all centers have the requisite expertise or facilities. As such, the number of centers proficient in managing GVs is limited, which can influence treatment decisions.

Previous studies have provided a stepwise methodology in managing EVs, but there is no such counterpart for GVs, which is due to the limited number of controlled clinical trials, making management of GVs challenging. Treatment should be based on the location, along with local expertise.[6,15] Current management of GVs is divided into endoscopic treatment, transhepatic intrahepatic portosystemic shunt (TIPS), surgery, and balloon-occluded retrograde transvenous obliteration (BRTO).[1,15] Traditional endoscopic therapy includes variceal sclerotherapy (EVS) along with variceal band ligation (EVL) and variceal obturation (EVO).[1,7] EVS has been less successful in the treatment of GVs, likely due to the high volume blood flow through the GV, leading to the sclerosant being rapidly flushed away in the bloodstream.[1] EVL can be effective for gastroesophageal varix 1 (GOV1) or small-sized GVs; however, it is not recommended for larger or actively bleeding GVs, and ulcer formation is, unfortunately, common.[1] TIPS is used in cirrhotic patients with bleeding EV and liver failure as a last resort if pharmacological or endoscopic treatment has failed. Still, it has a high risk of hepatic encephalopathy and other post-procedure complications. Regardless, TIPS can be a salvage treatment for GVs when endoscopic treatment is unsuccessful, particularly in patients with higher portal pressures.[1,6,15] Unfortunately, the success of TIPS is also dependent on the performer and the patient's vascular anatomy.[15] Surgical options include partial, selective, or total shunts and devascularization procedures. However, they can precipitate encephalopathy and have not been shown to improve survival.[7] BRTO is feasible only in patients with a known gastro-renal shunt.[1] It is effective for long-term GVs and rebleeding in isolated GVs.[15,18,19] It is also a fairly noninvasive procedure performed by interventional radiology. Still, its use has been mostly for prophylaxis or done on an elective basis, making it an unfavorable option for acute, active bleeding.[15]

Despite increased interest in the management of GVs, there is no consensus on their optimal management. GV is not a homogenous entity compared to EV, making management challenging. Additionally, few studies have specifically compared several different interventions in managing GVs. Our study aims to compare the outcomes of EVL, TIPS, and BRTO in managing bleeding GVs. This will give more insight into which interventions are favorable in improving outcomes in GV hemorrhage.

Materials and methods

Design and data source. The present study utilized the National Inpatient Sample (NIS) database from 1 January 2016 to 31 December 2019 [29183077]. NIS is the U.S.'s largest publicly available all-payer inpatient database and uses a 20% stratified sample of all U.S. community hospital discharges. NIS utilizes the International Classification of Diseases (ICD) 9 (before September 2015) and 10 (after October 2015) coding systems to store data. Detailed information on NIS's design and sampling methods is available at https://www.hcup-us.ahrq.gov. The exact codes utilized in this study for each variable can be found in Table S1. The inclusion criterion for the present study was patients with liver cirrhosis with a primary diagnosis of GVs. As there is no searchable diagnosis of "bleeding" GVs, we combined codes for gastric varices *and* gastrointestinal hemorrhage to include cases with bleeding GVs. Additionally, before 2016, ICD 9 had no specific diagnosis codes for GVs; therefore, only NIS databases with ICD 10 codes (2016–2019) were used for this study. Cases were further stratified based on the type of intervention the patients underwent during hospitalization: Endoscopic variceal ligation (EVL), TIPS, BRTO, esophagogastroduodenoscopy (EGD) + TIPS, and EGD + BRTO. Patients in the EVL and combined EGD + TIPS and EGD + BRTO groups initially presented with hematemesis and were first treated with endoscopy. If unsuccessful, TIPS or BRTO was added. In contrast, the TIPS and BRTO cohorts directly received their respective treatments without initial endoscopy based on clinical urgency. Because of the low number of patients undergoing BRTO + TIPS ($N = 24$), this cohort was not included in the final analysis. Exclusion criteria were hospitalizations with age <18 years, Budd–Chiari syndrome, end-stage renal disease (ESRD), liver transplant, and other upper gastrointestinal bleeding (gastric ulcer bleed, duodenal ulcer bleed, gastritis/duodenitis bleed, esophageal bleed, peptic ulcer bleed, gastric antral vascular ectasia [GAVE], dieulafoy lesions, or arteriovenous malformations [AVMs]). Hospitalizations without the aforementioned interventions or incomplete data were also excluded.

Outcome measures. The outcomes of interest included biodemographical characteristics based on therapeutic interventions, liver- and hospital-related outcomes such as acute liver failure, spontaneous bacterial peritonitis (SBP), hepatocellular carcinoma (HCC), hepatic encephalopathy (HE), alcoholism, acute renal failure (ARF), septic shock, intensive care unit (ICU) admissions, new-onset hemodialysis, portal venous thrombosis (PVT), length of stay (LOS) in days, and hospitalization charges (US$). We also conducted a comparative analysis of inpatient mortality and hospital-related outcomes based on therapeutic intervention.

Statistical analysis. NIS is a nonparametric database; therefore, we employed Chi-square test for categorical data and the Kruskal–Wallis test for continuous data. Categorical variables are presented as frequency (N) and percentage (%), and continuous variables are reported as median with interquartile range (IQR) as appropriate. Hierarchical multivariate logistic regression was conducted to adjust the patient- or hospital-level factors for mortality, liver, and hospital-related outcomes as in previous studies.[20,21] The threshold for statistical significance was set at

Table 1 Summary of patient characteristics included in the study

Patient characteristics	Endoscopy cohort	TIPS cohort	BRTO cohort	Endoscopy + TIPS	Endoscopy + BRTO	Overall patients	*P*-value
No. (%) of patients	5000 (69.83%)	625 (8.72%)	350 (4.88%)	1005 (14.03%)	180 (2.51%)	7160	
Gender							<0.001
Male, no. (%)	3020 (60.4%)	475 (76.0%)	230 (65.7%)	600 (59.7%)	105 (58.3%)	4430 (61.9%)	
Female, no. (%)	1980 (39.6%)	150 (24.0%)	120 (34.3%)	405 (40.3%)	75 (41.7%)	22730 (38.1%)	
Median age in years (interquartile range)	58 (50–67)	58 (50–65)	58 (51–65)	57 (49–67)	57 (46–62)	58 (50–66)	0.004
Age group (years)							<0.001
18–34	230 (4.6%)	15 (2.4%)	15 (4.3%)	50 (5.0%)	5 (2.8%)	315 (4.4%)	
35–49	960 (19.2%)	120 (19.2%)	65 (18.6%)	205 (20.4%)	55 (30.6%)	1405 (19.6%)	
50–64	2330 (46.6%)	315 (50.4%)	155 (44.3%)	465 (46.3%)	85 (47.2%)	3350 (46.8%)	
65–79	1250 (25.0%)	160 (25.6%)	95 (27.1%)	270 (26.9%)	30 (16.7%)	1805 (25.2%)	
≥80	230 (4.6%)	15 (2.4%)	20 (5.7%)	15 (1.5%)	5 (2.8%)	285 (4.0%)	
Race/ethnicity, no. (%)							<0.001
White	3585 (73.9%)	470 (76.4%)	240 (71.6%)	680 (72.0%)	115 (69.7%)	5090 (73.7%)	
Black	435 (9.0%)	20 (3.3%)	5 (1.5%)	25 (2.6%)	5 (3.0%)	490 (7.1%)	
Hispanic	705 (14.5%)	105 (17.1%)	80 (23.9%)	225 (23.8%)	40 (24.2%)	1155 (16.7%)	
Asian or Pacific Islander/Native American	125 (2.6%)	20 (3.3%)	10 (3.0%)	15 (1.6%)	5 (3.0%)	175 (2.5%)	
Elixhauser Comorbidity Index score, no. (%)							0.1
1	145 (2.9%)	15 (2.4%)	10 (2.9%)	25 (2.5%)	0 (0.0%)	195 (2.7%)	
2	425 (8.5%)	45 (7.2%)	40 (11.4%)	50 (5.0%)	15 (8.3%)	575 (8.0%)	
≥3	4430 (88.6%)	565 (90.4%)	300 (85.7%)	930 (92.5%)	165 (91.7%)	6390 (89.2%)	
Hospital region							<0.001
Northeast	765 (15.3%)	140 (22.4%)	25 (7.1%)	135 (13.4%)	15 (8.3%)	1080 (15.1%)	
Midwest	955 (19.1%)	70 (11.2%)	70 (20.0%)	140 (13.9%)	40 (22.2%)	1275 (17.8%)	
South	1970 (39.4%)	265 (42.4%)	135 (38.6%)	410 (40.8%)	70 (38.9%)	2850 (39.8%)	
West	1310 (26.2%)	150 (24.0%)	120 (34.3%)	320 (31.8%)	55 (30.6%)	1955 (27.3%)	
Median annual income quartile in patient's zip code, no. (%)							<0.001
$1–24 999	1420 (29.0%)	190 (30.6%)	145 (42.0%)	350 (36.1%)	65 (36.1%)	2170 (30.9%)	
$25 000–34 999	1230 (25.1%)	130 (21.0%)	65 (18.8%)	255 (26.3%)	40 (22.2%)	1720 (24.5%)	
$35 000–44 999	1280 (26.1%)	130 (21.0%)	85 (24.6%)	215 (22.2%)	40 (22.2%)	1750 (24.9%)	
45 000 or more	975 (19.9%)	170 (27.4%)	50 (14.5%)	150 (15.5%)	35 (19.4%)	1380 (19.7%)	
Insurance type, no. (%)							<0.001
Medicare	1845 (38.3%)	230 (37.7%)	140 (40.6%)	395 (41.1%)	35 (20.0%)	2645 (38.3%)	
Medicaid	1075 (22.3%)	150 (24.6%)	75 (21.7%)	205 (21.4%)	85 (48.6%)	1590 (23.0%)	
Private	1500 (31.2%)	185 (30.3%)	85 (24.6%)	265 (27.6%)	50 (28.6%)	2085 (30.2%)	
Uninsured	395 (8.2%)	45 (7.4%)	45 (13.0%)	95 (9.9%)	5 (2.9%)	585 (8.5%)	
Hospital characteristics							
Hospital status							<0.001
Rural	225 (4.5%)	20 (3.2%)	20 (5.7%)	15 (1.5%)	0 (0.0%)	280 (3.9%)	
Urban non-teaching	955 (19.1%)	20 (3.2%)	60 (17.1%)	125 (12.4%)	25 (13.9%)	1185 (16.6%)	
Urban teaching	3820 (76.4%)	585 (93.6%)	270 (77.1%)	865 (86.1%)	155 (86.1%)	5695 (79.5%)	

(*Continues*)

Table 1 (Continued)

Patient characteristics	Endoscopy cohort	TIPS cohort	BRTO cohort	Endoscopy + TIPS	Endoscopy + BRTO	Overall patients	*P*-value
Disposition of patient							<0.001
Discharged to home or self-care (routine discharge)	2815 (56.3%)	385 (61.6%)	215 (61.4%)	655 (65.2%)	125 (69.4%)	4195 (58.6%)	
Transfer to short-term hospital	950 (19.0%)	15 (2.4%)	45 (12.9%)	50 (5.0%)	15 (8.3%)	1075 (15.0%)	
Transfer other: includes skilled nursing facility (SNF), intermediate care facility (ICF), another type of facility	360 (7.2%)	70 (11.2%)	35 (10.0%)	130 (12.9%)	10 (5.6%)	605 (8.4%)	
Home health care (HHC)	460 (9.2%)	85 (13.6%)	25 (7.1%)	100 (10.0%)	25 (13.9%)	695 (9.7%)	
Against medical advice (AMA)	105 (2.1%)	15 (2.4%)	5 (1.4%)	5 (0.5%)	0 (0.0%)	130 (1.8%)	
Died	310 (6.2%)	55 (8.8%)	25 (7.1%)	65 (6.5%)	5 (2.8%)	460 (6.4%)	
Liver-related outcomes							
Acute liver failure	170 (3.4%)	60 (9.6%)	15 (4.3%)	75 (7.5%)	15 (8.3%)	335 (4.7%)	<0.001
Spontaneous bacterial peritonitis	0 (0.0%)	0 (0.0%)	5 (1.4%)	0 (0.0%)	0 (0.0%)	5 (0.1%)	<0.001
Hepatocellular carcinoma	25 (0.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	25 (0.3%)	0.028
Hepatic encephalopathy	0 (0.0%)	0 (0.0%)	5 (1.4%)	0 (0.0%)	0 (0.0%)	5 (0.1%)	<0.001
Alcoholism	2315 (46.3%)	390 (62.4%)	185 (52.9%)	485 (48.3%)	125 (69.4%)	3500 (48.9%)	<0.001
Hospital-related outcomes							
ARF	1060 (21.2%)	135 (21.6%)	95 (27.1%)	210 (20.9%)	35 (19.4%)	1535 (21.4%)	0.11
Septic shock	285 (5.7%)	75 (12.0%)	25 (7.1%)	95 (9.5%)	5 (2.8%)	960 (13.4%)	<0.001
New-onset dialysis	5 (0.1%)	0 (0.0%)	0 (0.0%)	5 (0.5%)	0 (0.0%)	10 (0.1%)	0.022
PVT	455 (9.1%)	60 (9.6%)	20 (5.7%)	75 (7.5%)	20 (11.1%)	630 (8.8%)	0.070
Length of stay (days)	4 (2–6)	6 (4–9)	4 (3–6)	7 (5–10)	7 (5–9)	5 (3–7)	0.001
Hospitalization charges (US$)	56 207 (31 530–108 334)	143 401 (90 587–143 401)	49 792 (31 962–90 753)	145 049 (101 721–216 163)	85 010 (44 952–138 047)	72 476 (36 918–138 897)	0.001
Blood transfusion	1960 (39.20%)	245 (39.22%)	134 (38.24%)	418 (41.58%)	93 (51.43%)	2850 (39%)	0.001

ARF, acute renal failure; BRTO, balloon-occluded retrograde transvenous obliteration; PVT, portal venous thrombosis; TIPS, transhepatic intrahepatic portosystemic shunt.

0.05, and all *P*-values were two-sided. All analyses were performed using Statistical Software for Data Science (STATA) version 16.0.

Results

Baseline characteristics. The present study included 7160 patients with liver cirrhosis hospitalized with gastric variceal (GV) bleeding who underwent interventions of interest. Of the patients, 69.83% underwent EVL, 14.03% underwent EGD + TIPS, 8.72% underwent TIPS, 4.88% underwent BRTO, and 2.51% underwent EGD + BRTO. There was no difference in Elixhauser's comorbidity score in the cohorts ($P = 0.1$). There was a higher prevalence of males than females in all therapeutic cohorts ($P < 0.001$). The median age for GV bleed hospitalizations was 58 years (IQR, 50–66). The most prevalent age group was 50–64 years for all cohorts ($P < 0.001$). Overall, inpatient mortality was 6.5%. Mortality was highest in the TIPS cohort (8.8%), followed by BRTO (7.1%), EGD + TIPS (6.5%), EVL (6.2%), and EGD + BRTO (2.8%) ($P < 0.001$). Additional discharge disposition was home for 58.6% of hospitalizations, transfer to short-term hospital (15%), home health care (HHC) (9.7%), nursing or assisted-living facility (8.4%), and leaving against medical device (AMA) (1.8%) ($P < 0.001$). Hospitalizations that underwent EVL, TIPS, and EGD + BRTO had a higher prevalence of discharge with HHC. In comparison, those with EGD + TIPS and BRTO had a higher prevalence of discharges to nursing facilities (Table 1).

An additional comparison of comorbidities for these hospitalizations is shown in Table S2.

Table 2 Complication associations

Variables	95% Confidence intervals	*P*-value
Acute liver failure		
TIPS	3.27 [2.39–4.48]	<0.001
BRTO	1.48 [0.86–2.55]	0.15
Endoscopy + TIPS	2.76 [2.07–3.68]	<0.001
Endoscopy + BRTO	2.08 [1.1–4.03]	0.03
Alcoholism		
TIPS	1.88 [1.56–2.27]	<0.001
BRTO	1.21 [0.95–1.53]	0.11
Endoscopy + TIPS	1.01 [0.87–1.18]	0.80
Endoscopy + BRTO	2.60 [1.82–3.73]	<0.001
ARF		
TIPS	1.01 [0.82–1.24]	0.90
BRTO	1.31 [1.01–1.70]	0.037
Endoscopy + TIPS	1.02 [0.85–1.21]	0.80
Endoscopy + BRTO	1.11 [0.76–1.63]	0.57
Septic shock		
TIPS	2.21 [1.67–2.94]	<0.001
BRTO	1.35 [0.87–2.08]	0.16
Endoscopy + TIPS	1.92 [1.50–2.47]	<0.001
Endoscopy + BRTO	0.50 [0.20–1.24]	0.13
ICU admission		
TIPS	1.87 [1.49–2.35]	< 0.001
BRTO	0.96 [0.67–1.39]	0.85
Endoscopy + TIPS	2.03 [1.68–2.45]	<0.001
Endoscopy + BRTO	3.04 [2.11–4.36]	<0.001
PVT		
TIPS	1.04 [0.77–1.40]	0.77
BRTO	0.71 [0.44–1.13]	0.15
Endoscopy + TIPS	0.97 [0.75–1.26]	0.84
Endoscopy + BRTO	1.55 [0.96–2.52]	0.07

ARF, acute renal failure; BRTO, balloon-occluded retrograde transvenous obliteration; ICU, intensive care unit; PVT, portal venous thrombosis; TIPS, transhepatic intrahepatic portosystemic shunt.

Hospital-related outcomes. Among the hospitalizations due to GVs, 21.4% had ARF, 13.4% had septic shock, 0.1% had new-onset hemodialysis requirement, and 8.8% had PVT (Table 1). The median LOS was 5 (IQR 3–7) days. The median hospitalization cost was $72 476 ($36 918–$138 897). There was no statistical difference in ARF among therapeutic cohorts, although the frequency was higher in hospitalizations with BRTO ($P = 0.11$). Septic shock was the most prevalent in hospitalizations with TIPS (12%), followed by EGD + TIPS (9.5%), BRTO (7.1%), EVL (5.7%), and EGD + BRTO (2.8%) ($P < 0.001$), as seen in Table 2. Overall, 39% of patients required blood transfusion, with the highest requirements being in patients undergoing BRTO and TIPS after endoscopy (51% and 41%, respectively).

Among hospitalizations due to GVs, 4.7% had acute liver failure, 0.1% had SBP, 0.3% had HCC, and 0.1% had hepatic encephalopathy. In comparison, 48.9% of hospitalizations had a secondary diagnosis of alcoholism (Table 1). Hospitalizations with alcoholism had a higher prevalence of TIPS (62.4%), followed by EGD + TIPS (69.4%) and BRTO (52.9%) ($P < 0.001$).

Compared to those who had undergone EVL, those who underwent TIPS (AOR 3.27 [95% CI: 2.39–4.48]; $P < 0.001$), EGD + TIPS (AOR 2.76 [95% CI: 2.07–3.68]; $P < 0.001$), and EGD + BRTO (AOR 2.08 [95% CI: 1.1–4.03]; $P = 0.030$) had a higher association with a secondary diagnosis of ALF. Compared to EVL, BRTO had a higher association with ARF (AOR 1.31 [95% CI: 1.01–1.70]; $P = 0.037$). Compared to EVL, TIPS (AOR 2.21 [95% CI: 1.67–2.94]; $P < 0.001$), and endoscopy + TIPS (AOR 1.92 [95% CI: 1.50–2.47]; $P < 0.001$) had a higher association with a secondary diagnosis of septic shock. No significant difference in mortality risk existed for BRTO, EGD + TIPS, and EGD + BRTO compared to EVL (Table 3).

Kaplan–Meier (KM) graph revealed that patients undergoing a combination of endoscopy with BRTO exhibited the highest 30-day survival. This was followed by those receiving

Table 3 Mortality outcomes

Variables	95% Confidence intervals	*P*-value
Endoscopy	—	—
TIPS	1.39 [1.02–1.91]	0.037
BRTO	1.29 [0.84–0.84]	0.23
Endoscopy + TIPS	1.20 [0.91–1.59]	0.18
Endoscopy + BRTO	0.49 [0.20–1.22]	0.13

BRTO, balloon-occluded retrograde transvenous obliteration; TIPS, transhepatic intrahepatic portosystemic shunt.

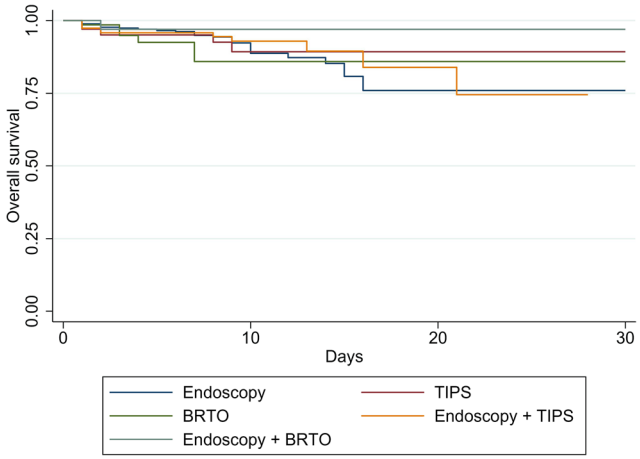

Figure 1 Kaplan–Meier curves for 30-day inpatient mortality for variceal bleeding based on treatment.

TIPS alone, BRTO alone, endoscopy alone, and a combination of endoscopy with TIPS (Fig. 1).

Discussion

The present study aimed to compare EVL, TIPS, and BRTO in managing GV bleeding in liver cirrhosis patients. Despite technological advances, no epidemiological trials are available to understand the risk factors triggering GVs to bleed. Moreover, there is a severe paucity of randomized, prospective data to standardize the management strategies of patients presenting with these bleeding GVs.[22] EVL may be beneficial in treating lesser curve bleeding GVs, and rebleeding rates are superior to those of sclerotherapy.[22,23] TIPS is effective in reducing portal pressure, reducing long-term rebleeding, compared with endoscopic cyanoacrylate injection but may increase rates of HE. BRTO has hemostasis rates and procedure-related complications similar to those of TIPS; however, there is less rebleeding and HE.[22,24]

We found that bleeding GVs are more common in older White males, between 50 and 64 years of age, with a high comorbidity burden and low socioeconomic class. These baseline characteristics are consistent with previous retrospective and prospective trials comparing various therapeutic options in bleeding GVs.[24,25] Our study indicated that EVL remains the predominant management strategy in patients with GV bleeding, with nearly three-quarters of our patients undergoing this procedure. The choice of using either TIPS with or without EGD was higher compared to BRTO alone or BRTO and EGD. The high rates of EVL compared to TIPS and BRTO can be explained by the location of GV bleeding, patient and clinical characteristics, operator preference, institutional facilities, and cost effectiveness.[22,26] TIPS and BRTO with or without EGD led to higher median LOS and hospitalization costs than EVL in our study.

The mortality rates were highest in the TIPS (8.8%) and BRTO (7.1%) cohorts; the 30-day KM graph revealed that patients undergoing a combination of endoscopy with BRTO showed the highest 30-day survival. These minimally invasive procedures were developed because of the limited efficacy and long-term success with endoscopic options due to the anatomic location and high blood flow.[27,28] TIPS aims to shunt blood away from portal hepatic circulation by redirecting it into the systemic circulation.[27] BRTO is a percutaneous procedure where a balloon catheter is inserted into an outflow shunt (gastric-renal or gastric-inferior vena cava) to occlude blood flow. A sclerosing agent is then directly injected into the varix. In a 2020 meta-analysis and systematic review of seven studies, Paleti *et al.* compared BRTO and TIPS to treat portal hypertension-related GVs. There was a statistically significant risk of rebleeding associated with TIPS compared with BRTO. TIPS was associated with an increased incidence of HE compared to BRTO. Our analysis found overall low rates of HEs. Five-year mortality was high for both interventions, 49% for TIPS and 31–39% for BRTO.[27] BRTO can lead to increased blood flow to the portal vein, with the resultant development or exacerbation of portal hypertensive gastropathy, hydrothorax/pleural effusion, and ascites.[28] Unlike the acute liver dysfunction seen after TIPS, liver synthetic function can improve after BRTO as a result of increased portal blood flow to the liver.[29] This may explain our study's higher association of ALF with TIPS compared to BRTO.

More than one-quarter of our patients underwent endoscopy with either TIPS (14.03%) or BRTO (2.51%). EGDs are generally done periodically after TIPS or BRTO to assess the eradication of GVs or when there is rebleeding.[30] Given the challenging and highly variable anatomy, continued flow through the varices is likely following TIPS if direct obliteration of cardio-fundal GV is not performed. These may require additional therapy with BRTO or ECl.[22] This may account for our findings showing higher hospitalizations with TIPS + EGD *versus* BRTO + EGD. Interestingly, we also observed that more patients in the EGD cohorts (65.2% for TIPS + EGD and 69.4% for BRTO + EGD) were discharged directly to home compared to the other cohorts (56.3% for EVL, 61.6% for TIPS and 61.4% for BRTO).

BRTO was associated with an increased frequency of ARF (95% CI: 1.31 [1.01–1.70]). One theory could be the increased incidence of ascites and hepatorenal syndrome observed with BRTO, as shown by Yu *et al.* in their meta-analysis comparing BRTO and TIPS for GV management.[24] A significantly larger number of hospitalizations with TIPS also had septic shock; however, it remains unclear whether this was due to the procedural aspects, including complications, or due to an alternate metabolic phenomenon. More patients in the EGD cohorts (TIPS + EGD and BRTO + EGD) had concomitant ICU admissions. These patients may have had rebleeding and hemodynamic instability, requiring ICU stay and early EGD for resuscitation.[31]

In the context of global guidelines, many centers, especially in Europe and the United States, prioritize sclerotherapy as an initial treatment, followed by interventions to reduce portal vein pressure for rebleeding prevention, as found by De Franchis *et al.* and Aithal *et al.* The Baveno consensus, particularly Baveno VI and VII, strongly advocates for early TIPS intervention.[32,33] Our findings, which indicate higher adverse outcomes in the TIPS and BRTO cohorts, might be influenced by factors such as patient selection, intervention timing, technical aspects, and higher comorbidity burden. Although both TIPS and BRTO have their merits, it is crucial to tailor their application based on individual patient profiles and the broader clinical context.

Limitations

Our study has limitations that must be mentioned. First, the NIS database comprises approximately 20% of the hospitals in the United States. The final data is a national estimate calculated using sampling weights to extrapolate national numbers. Second, an entry into the NIS database represents a single hospitalization. A single patient could have multiple entries into the database through readmissions and hospital transfers. Third, our study uses ICD codes to identify GVs and procedures. There is no ICD code for bleeding GVs; hence, we combined codes for GVs *and* gastrointestinal hemorrhage. We cannot exclude some degree of underreporting due to the inherent limitations of nonstandardized clinical documentation outside clinical studies. While we recognize the significance of understanding long-term outcomes after therapeutic interventions, our study is constrained by the limitations of the database regarding the unavailability of long-term data. In its effort to protect patient privacy, the NIS database does not provide the granularity of data needed for specific clinical details, such as liver function metrics or detailed patient histories. Lastly, although our study looks at a large database over 4 years, this study is retrospective, so the analysis is subject to potential patient selection bias. In the absence of randomization, confounding factors cannot be ignored.

Conclusion

In our national cohort analysis spanning 4 years, we found that hospitalizations with bleeding GVs undergoing either TIPS or BRTO were the costliest, with the highest rates of ICU stay and liver cirrhosis. Hospitalizations with TIPS had the highest mortality and prevalence of acute liver failure and septic shock. BRTO admissions had more ARF but a lower prevalence of ALF. EVL was the most practiced intervention, and hospitalizations had comparatively low mortality and lower diagnosis of ALF and septic shock. It is prudent to individualize treatment plans for patients with GVs. There is a pressing need for large epidemiological and randomized controlled trials to recognize high-risk patients for bleeding GVs and evolve a standardized approach for interventional management in these patients.

Ethics statement

National inpatient sample database contains de-identified third-party data. Therefore, it was exempted from review by the institutional review board. NIS also does not include patient identifiers; thus, patient consent was waived.

Patient consent statement

Patient consent was not required for this retrospective study.

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Supporting information

Additional supporting information may be found in the online version of this article at the publisher's website:

Data S1. Supporting information.