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RESEARCH ARTICLE

Outcomes of Upper Gastrointestinal Bleeding in Hospitalized COVID-19 Patients in the United States: A Propensity-score Matched Analysis of a Large National Database

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Abstract

Patients with cirrhosis that are hospitalized with COVID-19 infection have been found to have worse outcomes. No comparative study has been conducted between gastrointestinal (GI) bleeding in patients with cirrhosis who are diagnosed with COVID-19. We utilized the National Inpatient Sample (NIS) database to perform a retrospective analysis of 24, 050 patients diagnosed with cirrhosis and COVID-19. The identified patients were separated into variceal bleeding, nonvariceal bleeding, and no (or neither) GI bleeding groups. After performing propensity sample matching and multivariate analysis of mortality, we found no significant differences in mortality among the three groups. However, the variceal bleed group had a shorter length of stay (5.67 days lower than the no-bleed group). Esophagogastroduodenoscopy (EGD) with intervention was associated with reduced mortality in the variceal and nonvariceal bleeding groups. Acute kidney injury was a strong predictor of mortality in both bleeding groups. A native American race was found to be associated with higher mortality in the nonvariceal bleeding group. Our study suggests that there are various pathophysiological processes among the three groups, with no significant mortality differences with cirrhosis complications of GI bleeding.

Keywords: Coronavirus disease, Liver cirrhosis, Esophageal varices, Gastrointestinal bleeding, Gastrointestinal complications, Acute kidney injury

1. Introduction

The COVID-19 pandemic caused by the novel coronavirus SARS-CoV-2 has emerged as one of the most significant global health challenges in recent history. While COVID-19 primarily manifests as a respiratory illness, emerging evidence in the literature has highlighted its potential impact on various organ systems, with high-risk comorbid conditions greatly increasing mortality and morbidity associated with COVID-19.[1] Since the emergence of the virus in early 2020, hepatic involvement has been demonstrated in several studies, with results varying significantly with

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respect to the degree of impact.[2–5] The global burden of patients with chronic liver disease is large, with some estimates noting almost two million deaths annually due to hepatic decompensation events and hepatocellular carcinoma.[2] Furthermore, immune dysregulation is a well-recognized phenomenon in cirrhosis, which makes these patients more susceptible to COVID-19 complications.[6] Several studies have compared outcomes between patients hospitalized with cirrhosis and COVID-19 versus patients with cirrhosis without COVID-19.[7–12] A multicenter study demonstrated that inpatient mortality was similar in patients with cirrhosis in COVID-19 and cirrhotic patients without COVID-19; however, the mortality rate was higher than that in a cohort of patients without cirrhosis who were admitted with COVID-19 infection.[7] Furthermore, some registry data have shown high mortality rates of up to 40 % for COVID-19 co-infection in patients with pre-existing liver disease and cirrhosis.[8]

Another significant concern arising from the COVID-19 pandemic with regard to cirrhotic patients is the potential impact of variceal bleeds. Variceal bleeding, a severe complication of advanced liver disease, results from the formation of enlarged blood vessels in the esophagus or stomach, secondary to portal hypertension. The interplay between COVID-19 and cirrhosis has been studied, but it also raises further questions about the risk of variceal bleeding in these patients, as the virus may exacerbate underlying hemodynamic disturbances and coagulopathy. Additionally, COVID-19 has been shown to induce systemic inflammation, alter coagulation pathways, and cause endothelial dysfunction, which may contribute to the eventual rupture of varices and increase the bleeding risk in patients.[13,14]

While there have been studies characterizing the outcomes of patients with cirrhosis and COVID-19 based on the etiology of cirrhosis, there have been no studies to date investigating secondary outcomes in cirrhotic patients, including variceal bleeds. We hypothesized that there is significant morbidity and mortality in patients with concomitant cirrhosis, COVID-19 infection, and variceal bleeding. Furthermore, we hypothesized that respiratory compromise is the driving force behind decompensatory episodes. The aim of this study was to evaluate outcomes associated with inpatient hospitalization in patients with cirrhosis and COVID-19, to assess disease severity and outcomes within subgroups of patients with and without variceal bleeds via an extensive literature review on the interactions between COVID-19, cirrhosis, and variceal bleeds, and to explore the underlying mechanisms, clinical implications, and potential management strategies.

2. Methods

The NIS database in its sample recorded 6.47 million discharges across the US which is equivalent to 32.35 million weighted patients across the US. A total, 25 of 670 patients were diagnosed with COVID-19 and cirrhosis. However, after removing patients with missing data for the variables of interest, the sample size was reduced to 24,050. Initially, raw data from the NIS were processed in SAS and later statistically analyzed using R and Python.

Chi-squared tests were used to assess the relationships between cirrhosis and COVID-19 infection (divided into three categories) and categorical variables such as disposition, sex, race, CAD, MI, and hospital status. Low p-values for the chi-squared tests indicated the existence of relationships between the three cohorts and the categorical variable. For continuous variables (length of hospital stay and total hospitalization charge), we used a multivariate linear regression model to study the differences among the three cohorts.

Logistic regression models were used to obtain odds ratios. In the logistic regression models, only the significant variables (p-value <0.2 were retained, while for the multivariate linear regression model, the threshold to retain predictors was p-value <0.05. Propensity matching among the three groups was performed using the MatchIt library package in the R programming language. Hazard ratios were obtained using the survival analysis package in R using a multivariate model for each cohort. Major libraries used in the Python environment included Pandas, Numpy, Pyreadstat, and Statsmodels.

3. Results

3.1. Patient characteristics

Our analysis of 24,050 hospitalized cirrhosis and COVID-19 patients identified three groups: 910 with variceal bleeding (VB), 275 with nonvariceal bleeding (NVB), and 22,865 without GI bleeding (NB). Most patients were aged 50–69, particularly in NB (55.5 %, $p < 0.001$), with VB having more in the 30–49 age range (31.3 %, $p < 0.001$). Medicaid coverage was highest in VB (36.8 %, $p < 0.001$). Aside from these characteristics, no other variables such as gender, race, median household income and several others had statistically significant differences as shown in Table 1.

Table 1. COVID + Cirrhotics, no bleed, non-variceal bleed, and variceal bleed patient-level characteristics.

Characteristics	COVID+ & Cirrhosis			P-Value
	Neither Bleed	Non-variceal Bleed	Variceal Bleed	
N = 24,050	N = 22,865 (95.07 %)	N = 275 (1.14 %)	N = 910 (3.79 %)	
Gender (%)				0.071
Male	9070 (39.67 %)	130 (47.27 %)	295 (32.42 %)	
Female	13,795 (60.33 %)	145 (52.73 %)	615 (67.58 %)	
Mean Age Years (SD)				
Female	64.29 (12.98)	62.00 (13.73)	60.37 (12.27)	
Male	61.28 (12.60)	58.69 (15.20)	54.78 (12.15)	
AGE Groups (%)				<0.001
18-29	180 (0.79)	5 (1.82)	0 (0.00)	
30-49	3240 (14.17)	60 (21.82)	285 (31.32)	
50-69	12,690 (55.50)	145 (52.73)	465 (51.10)	
≥70	6755 (29.54)	65 (23.64)	160 (17.58)	
Race (%)				0.347
Asian or Pacific Islander	560 (2.45)	5 (1.82)	25 (2.75)	
Black	2855 (12.49)	35 (12.73)	60 (6.59)	
Hispanic	6375 (27.88)	80 (29.09)	325 (35.71)	
Native American	585 (2.56)	10 (3.64)	35 (3.85)	
Other	980 (4.29)	10 (3.64)	45 (4.95)	
White	11,510 (50.34)	135 (49.09)	420 (46.15)	
Median Household Income (%)				0.283
≤49,999	8935 (39.08)	100 (36.36)	315 (34.62)	
50,000–64,999	5875 (25.69)	65 (23.64)	190 (20.88)	
65,000–85,999	4560 (19.94)	60 (21.82)	220 (24.18)	
≥86,000	3495 (15.29)	50 (18.18)	185 (20.33)	
Insurance Status (%)				<0.001
Medicaid	5320 (23.27)	85 (30.91)	335 (36.81)	
Medicare	11,705 (51.19)	130 (47.27)	315 (34.62)	
No Charge	60 (0.26)	0 (0.00)	5 (0.55)	
Other	860 (3.76)	15 (5.45)	20 (2.20)	
Private Insurance	3995 (17.47)	30 (10.91)	150 (16.48)	
Self-Pay	925 (4.05)	15 (5.45)	85 (9.34)	
Hospital Division (%)				0.170
East North Central	3360 (14.69)	25 (9.09)	115 (12.64)	
East South Central	1240 (5.42)	20 (7.27)	40 (4.40)	
Middle Atlantic	2975 (13.01)	35 (12.73)	125 (13.74)	
Mountain	1915 (8.38)	10 (3.64)	90 (9.89)	
New England	1205 (5.27)	15 (5.45)	20 (2.20)	
Pacific	3155 (13.80)	55 (20.00)	200 (21.98)	
South Atlantic	3835 (16.77)	35 (12.73)	160 (17.58)	
West North Central	1255 (5.49)	15 (5.45)	40 (4.40)	
West South Central	3925 (17.17)	65 (23.64)	120 (13.19)	
Hospital Bed Size (%)				0.473
Large	11,525 (50.40)	150 (54.55)	420 (46.15)	
Medium	6665 (29.15)	90 (32.73)	300 (32.97)	
Small	4675 (20.45)	35 (12.73)	190 (20.88)	
Hospital Teaching Status (%)				0.142
Rural	1415 (6.19)	15 (5.45)	15 (1.65)	
Urban Nonteaching	3795 (16.60)	40 (14.55)	145 (15.93)	
Urban Teaching	17,655 (77.21)	220 (80.00)	750 (82.42)	
Comorbidities (%)				
CAD	4205 (18.39)	75 (27.27)	95 (10.43)	0.005
MI	790 (3.45)	30 (10.90)	35 (3.84)	0.011
HTN	15,280 (66.82)	180 (65.45)	425 (46.70)	<0.001
Diabetes	11,485 (50.22)	110 (40.00)	390 (42.85)	0.05
Cancer	1945 (8.50)	15 (5.45)	75 (8.24)	0.717
Drug Abuse	1320 (5.77)	25 (9.09)	45 (4.94)	0.511
Smoking	8075 (35.31)	115 (41.81)	315 (34.61)	0.591
Alcohol	5605 (24.51)	95 (34.54)	385 (42.30)	<0.001
Chronic Pulmonary Disease	5125 (22.41)	50 (18.18)	95 (10.43)	<0.001
CKD	3675 (16.07)	45 (16.36)	70 (7.69)	0.009

The VB group had lower rates of several comorbidities compared to NB and NVB groups: coronary artery disease (10.4 % VB vs. 18.4 % NB vs. 27.3 % NVB, $p = 0.005$), chronic pulmonary disease (10.4 % VB vs. 22.4 % NB vs. 18.2 % NVB, $p < 0.001$), chronic kidney disease (7.7 % VB vs. 16.1 % NB vs. 16.4 % NVB, $p = 0.009$), and hypertension (46.7 % VB vs. 66.82 % NB vs. 65.45 % NVB, $p < 0.001$). NVB had a higher incidence of myocardial infarction (10.9 %, $p = 0.011$) compared to VB and NB. Diabetes was most prevalent in NB (50.22 %, $p = 0.05$), and alcohol consumption was highest in VB (42.3 %, $p < 0.001$). No significant differences were found for cancer, smoking, or other substance use.

In our analysis of propensity score matched samples of 825 COVID-19 positive patients with cirrhosis with 275 in each of the GI bleed groups, significant differences emerged across sub-groups classified by bleeding status: NB, NVB, and VB groups. Notably, gender distribution varied significantly ($p < 0.001$), with the VB group being majority female (96.36 %). The mean age in this group was also lower compared to the other two, particularly for females (47.50 years). Insurance status varied again significantly across groups ($p < 0.001$), with a higher prevalence of Medicaid in the VB cohort (43.64 %). The results of the propensity score matched samples is depicted in Table 2.

For comorbidities, there were several statistically significant differences; hypertension was higher in both the NB group and NVB groups but lower in the VB group (9.09 %, $p < 0.001$). Reported alcohol use was disproportionately higher in the VB group (65.45 %, $p < 0.001$). In contrast, factors such as race, median household income, and hospital characteristics did not exhibit statistically significant variation among the sub-groups (Table 2).

3.2. In-hospital outcomes

We employed propensity score matching to balance variables like age, hospital features, Elixhauser comorbidities, race, insurance status and income ensuring a fair comparison between patient groups. Patient outcomes, such as the need for home healthcare (higher in NVB group at 21.8 %) and routine discharges (most common in VB group at 67.3 %), varied significantly. Notably, there was no significant difference in in-hospital mortality among the groups. The average hospital stay was shortest for VB patients (8.1 days) and longest for NB patients (10 days, $p = 0.006$). The mean total hospitalization charge varied slightly, with the highest being in the VB group ($126,684.50), but these differences were not statistically significant in the matched sample. Blood transfusions were significantly higher in the VB group (38.2 %, $p = 0.005$), and portal vein thrombosis was significantly more diagnosed in this group as well (5.4 %, $p = 0.002$). Vasopressor use, acute kidney injury (AKI), and hepatic encephalopathy showed no significant difference among the groups (Table 3).

3.3. Predictors of mortality

In our study, we analyzed mortality predictors in COVID-19 positive cirrhotic patients. For NVB patients, undergoing EGD with intervention (HR: 0.05, $p = 0.02$) and being male (HR: 0.07, $p = 0.03$) significantly lowered mortality risk, while Native American race (HR: 8.05, $p = 0.04$) and requiring blood transfusions (HR: 8.18, $p = 0.044$) were associated with increased mortality. In the VB group, chronic kidney disease (HR: 0.04, $p = 0.001$) and EGD with intervention (HR: 0.23, $p = 0.004$) reduced mortality risk, while sudden cardiac arrest (HR: 5.1, $p = 0.004$) and AKI (HR: 5.7, $p < 0.001$) increased it. NB patients showed that diagnostic EGD (HR: 0.33, $p < 0.001$) reduced mortality, whereas positive predictors of mortality included vasopressor use (HR: 1.55, $p < 0.001$), AKI (HR: 1.91, $p < 0.001$), age over 70 (HR: 2.63, $p = 0.035$), cardiogenic shock (HR: 3.44, $p < 0.001$), and sudden cardiac arrest (HR: 4.06, $p < 0.001$) (Fig. 1).

4. Discussion

Our study, drawing from the NIS database of patients with cirrhosis and COVID-19 infection, offers insights into outcomes across three subgroups: those with variceal gastrointestinal bleeding, NVB, and those with no GI bleeding. The VB group had the lowest proportions of chronic diseases, such as hypertension, coronary artery disease, and chronic kidney disease, which contrasts with the NB group, which had the highest prevalence of these conditions. The VB group also had significantly higher alcohol use, which likely contributed to the progression of cirrhosis and subsequent development of esophageal varices.[15] The VB group had a statistically significantly shorter length of hospital stay than the other groups. There was also a non-significant highest overall hospitalization charge for the VB group, possibly indicating the cost of additional interventions, such as blood transfusions and endoscopic interventions. The shorter hospital stay may be due to the COVID-19 infection being relatively less severe than the other groups with earlier discharges after endoscopic intervention, allowing for earlier discharge. VB was more likely a primary

Table 2. COVID + Cirrhotics, no bleed, non-variceal bleed, and variceal bleed patient-level characteristics (Matched Sample).

Characteristics	COVID+ & Cirrhosis			P-Value
	Neither Bleed	Non-variceal Bleed	Variceal Bleed	
N = 825	N = 275 (33.33 %)	N = 275 (33.33 %)	N = 275 (33.33 %)	
Gender (%)				<0.001
Male	135 (49.09)	130 (47.27)	10 (3.64)	
Female	140 (50.91)	145 (52.73)	265 (96.36)	
Mean Age Years (SD)				
Female	61.92 (14.13)	62.00 (13.73)	47.50 (17.67)	
Male	59.39 (11.35)	58.69 (15.20)	51.09 (10.51)	
AGE Groups (%)				<0.003
18-29	0 (0.00)	5 (1.82)	0 (0.00)	
30-49	55 (20.00)	60 (21.82)	125 (45.45)	
50-69	145 (52.73)	145 (52.73)	140 (50.91)	
≥70	75 (27.27)	65 (23.64)	10 (3.64)	
Race (%)				0.247
Asian or Pacific Islander	5 (1.82)	5 (1.82)	10 (3.64)	
Black	30 (10.91)	35 (12.73)	0 (0.00)	
Hispanic	75 (27.27)	80 (29.09)	120 (43.64)	
Native American	15 (5.45)	10 (3.64)	5 (1.82)	
Other	15 (5.45)	10 (3.64)	25 (9.09)	
White	135 (49.09)	135 (49.09)	115 (41.82)	
Median Household Income (%)				0.409
≤49,999	85 (30.90)	100 (36.36)	105 (38.81)	
50,000–64,999	80 (29.09)	65 (23.64)	30 (10.90)	
65,000–85,999	65 (23.64)	60 (21.82)	75 (27.27)	
≥86,000	45 (16.37)	50 (18.18)	65 (23.65)	
Insurance Status (%)				<0.001
Medicaid	80 (29.09)	85 (30.91)	120 (43.64)	
Medicare	145 (52.73)	130 (47.27)	35 (12.73)	
No Charge	0 (0.00)	0 (0.00)	5 (1.82)	
Other	10 (3.64)	15 (5.45)	0 (0.00)	
Private Insurance	30 (10.91)	30 (10.91)	65 (23.64)	
Self-Pay	10 (3.64)	15 (5.45)	50 (18.18)	
Hospital Division (%)				0.491
East North Central	40 (14.55)	25 (9.09)	10 (3.64)	
East South Central	10 (3.64)	20 (7.27)	15 (5.45)	
Middle Atlantic	45 (16.36)	35 (12.73)	45 (16.36)	
Mountain	30 (10.91)	10 (3.64)	20 (7.27)	
New England	10 (3.64)	15 (5.45)	10 (3.64)	
Pacific	30 (10.91)	55 (20.00)	80 (29.09)	
South Atlantic	60 (21.82)	35 (12.73)	50 (18.18)	
West North Central	10 (3.64)	15 (5.45)	5 (1.82)	
West South Central	40 (14.55)	65 (23.64)	40 (14.55)	
Hospital Bed Size (%)				0.214
Large	115 (41.82)	150 (54.55)	95 (34.55)	
Medium	95 (34.55)	90 (32.73)	105 (38.18)	
Small	65 (23.64)	35 (12.73)	75 (27.27)	
Hospital Teaching Status (%)				0.206
Rural	5 (1.82)	15 (5.45)	0 (1.65)	
Urban Nonteaching	20 (7.27)	40 (14.55)	16 (15.93)	
Urban Teaching	250 (90.91)	220 (80.00)	84 (82.42)	
Comorbidities (%)				
CAD	25 (9.09)	75 (27.27)	10 (3.63)	<0.001
MI	5 (1.81)	30 (10.90)	5 (1.81)	0.037
HTN	180 (65.45)	180 (65.45)	25 (9.09)	<0.001
Diabetes	135 (49.09)	110 (40.00)	105 (38.18)	0.463
Cancer	10 (3.63)	15 (5.45)	30 (10.90)	0.281
Drug Abuse	15 (5.45)	25 (9.09)	0 (0.00)	0.082
Smoking	85 (30.90)	115 (41.81)	85 (30.90)	0.381
Alcohol	85 (30.90)	95 (34.54)	180 (65.45)	<0.001
Chronic Pulmonary Disease	55 (20.00)	50 (18.18)	0 (0.00)	0.002
CKD	30 (10.90)	45 (16.36)	15 (5.45)	0.185

Table 3. In-Hospital Outcomes in COVID + Cirrhotic patients with no bleed, nonvariceal, and variceal bleeds (Matched Sample).

Characteristics	COVID+ & Cirrhosis			P-Value
	Neither Bleed	Non-variceal Bleed	Variceal Bleed	
N = 825	N = 275 (33.33 %)	N = 275 (33.33 %)	N = 275 (33.33 %)	
Disposition (%)				0.003
Against Medical Advice	5 (1.82)	0 (0.00)	0 (0.00)	
Died in Hospital	65 (23.64)	35 (12.73)	50 (18.18)	
Discharged Alive, Unknown Destination	0 (0.00)	0 (0.00)	0 (0.00)	
Home Health Care	20 (7.27)	60 (21.82)	15 (5.45)	
Routine	100 (36.36)	125 (45.45)	185 (67.27)	
Transfer Other	80 (29.09)	50 (18.18)	15 (5.45)	
Transfer to Short-Term Hospital	5 (1.82)	5 (1.82)	10 (3.64)	
Comorbidities (%)				
Hemorrhagic Shock	5 (1.81)	5 (1.81)	15 (5.45)	
		Adjusted Odds Ratio[a]		
		1.07 (95 % CI 0.106–18.78)	1.96 (95 % CI 0.51–8.29)	
	P-Value	0.962	0.601	
Sudden Cardiac Arrest	5 (1.81)	0 (0.00)	15 (5.45)	
		Adjusted Odds Ratio[a]		
		NA	1.07 (95 % CI 0.51–8.29)	
	P-Value	NA	0.556	
Mean Total Hospitalization Charge (S)	$113,355.94	$121,305.78	$126,684.50	
		Adjusted Total Charge		
		$2001.80 lower	$32598.2 lower	
	P-Value	0.947	0.351	
Mean Length of Stay (days)	10.03	8.60	8.10	
		Adjusted Length of Stay[a]		
		2.16 days lower	5.67 days lower	
	P-Value	0.233	0.006	
In Hospital Mortality	65 (23.63)	35 (12.72)	50 (18.18)	
		Adjusted Odds Ratio[a]		
		0.39 (95 % CI 0.13–1.17)	1.08 (95 % CI 0.36–3.21)	
	P-Value	0.096	0.885	
Vasopressor Use	10 (3.63)	10 (3.63)	10 (3.63)	
		Adjusted Odds Ratio[a]		
		1.11 (95 % CI 0.12–5.72)	1.38 (95 % CI 0.40–2.96)	
	P-Value	0.920	0.456	
Mechanical Circulatory Support	0 (0.00)	0 (0.00)	0 (0.00)	
		Adjusted Odds Ratio[a]		
		NA	NA	
	P-Value	NA	NA	
Acute Kidney Injury	115 (41.81)	80 (29.09)	95 (34.54)	
		Adjusted Odds Ratio[a]		
		0.48 (95 % CI 0.21–1.11)	0.76 (95 % CI 0.28–2.02)	
	P-Value	0.089	0.583	
Hepatic Encephalopathy	35 (0.15)	0 (0.00)	0 (0.00)	
		Adjusted Odds Ratio[a]		
		NA	NA	
	P-Value	NA	NA	
Cardiogenic Shock	0 (0.00)	0 (0.00)	0 (0.00)	
		Adjusted Odds Ratio[a]		
		NA	NA	
	P-Value	NA	NA	
Hemodialysis	40 (14.54)	25 (9.09)	15 (5.45)	
		Adjusted Odds Ratio[a]		
		0.53 (95 % CI 0.13–2.03)	0.66 (95 % CI 0.09–4.66)	
	P-Value	0.355	0.683	
Blood Transfusion	30 (10.90)	75 (27.27)	105 (38.18)	
		Adjusted Odds Ratio[a]		
		3.40 (95 % CI 1.13–10.19)	5.21 (95 % CI 1.64–16.54)	
	P-Value	0.028	0.005	

(*continued on next page*)

Table 3. (continued)

Characteristics	COVID+ & Cirrhosis			P-Value
	Neither Bleed	Non-variceal Bleed	Variceal Bleed	
Portal Vein Thrombosis	5 (1.81)	5 (1.81)	15 (5.45)	
		Adjusted Odds Ratio[a]		
		1.13 (95 % CI 0.06–9.74)	2.59 (95 % CI 1.24–7.72)	
	P-Value	0.93	0.002	
Spontaneous Bacterial Peritonitis	5 (1.81)	5 (1.81)	15 (5.45)	
		Adjusted Odds Ratio[a]		
		0.96 (95 % CI 0.05–15.95)	2.77 (95 % CI 0.27–28.32)	
	P-Value	0.981	0.389	
EGD Diagnostic	15 (5.45)	65 (23.63)	115 (12.72)	
		Adjusted Odds Ratio[a]		
		5.39 (95 % CI 1.41–20.56)	1.96 (0.45–8.42)	
	P-Value	0.013	0.362	
EGD with Intervention	0 (0.00)	65 (23.63)	95 (34.54)	
		Adjusted Odds Ratio[a]		
		NA	NA	
	P-Value	NA	NA	
IR Arterial Embolization	0 (0.00)	0 (0.00)	0 (0.00)	
		Adjusted Odds Ratio[a]		
		NA	NA	
	P-Value	NA	NA	

[a] Adjusted Odds Ratios, adjusted length of stay, and adjusted total charge are adjusted for Age, Hospital Bed Size, Race, Gender, Hospital location, Hospital teaching status, Hospital region, Median Household Income, Expected primary payer (insurance status), ELIXHAUSER COMORBIDITIES.

admission diagnosis with COVID-19 infection being possibly an incidental or secondary diagnosis, which can also possibly explain these findings. The VB group also demonstrated the highest prevalence of Medicaid insurance, which may indicate the socioeconomic factors that influence healthcare access and outcomes.

Notably, the NB group had the highest proportion of patients with diabetes. The NB group also had the highest mortality, followed by the VB and NVB groups. This could suggest that patients without GI bleeding but with other complications may be at a higher risk, possibly due to hospitalization for a more severe form of COVID-19 infection rather than a primary admission diagnosis of GI bleeding. This aligns with other studies that found an association between cirrhosis-associated comorbidities and higher mortality.[7,8,16] One significant factor may be that patients with more cirrhosis-associated comorbidities likely have a greater extent of immune dysfunction, resulting in more severe COVID-19 infections.[3]

Our mortality analysis underscores the complexity of predicting the outcomes in this heterogeneous patient population. There were no significant differences in mortality in the matched samples, possibly because of various factors. These might include a similar severity of illness across groups or effective medical and endoscopic interventions that mitigate the effect of the independent variables on mortality. In addition, our study was limited to the hospital stay and was unable to further extrapolate post-discharge outcomes, which may have significant differences. Additional studies are required to elucidate the underlying mechanisms.

There were several statistically significant findings in the analysis of the mortality predictors. In the NVB group, endoscopic treatment (EGD with intervention) significantly reduced the mortality. The positive mortality predictor of blood transfusions in the non-variceal group also suggests that significant bleeding requiring transfusion is associated with higher mortality. A native-American race was seen to be a positive predictor of mortality, likely related to socioeconomic barriers and healthcare disparities.[17,18] Male sex was a negative predictor of mortality in our study; however, the reason for this is not immediately clear. Other studies have suggested that males typically have worse in-hospital outcomes than females with variceal bleeding.[19] Our study may not have been able to see the same result given the significant proportion of female patients in the VB group.

In the NB group, diagnostic EGD was a potent negative predictor and variables such as vasopressor use and AKI were strong positive predictors, suggesting the role of circulatory and renal complications in influencing outcomes. Vasopressor use likely indicated progression to shock requiring ICU

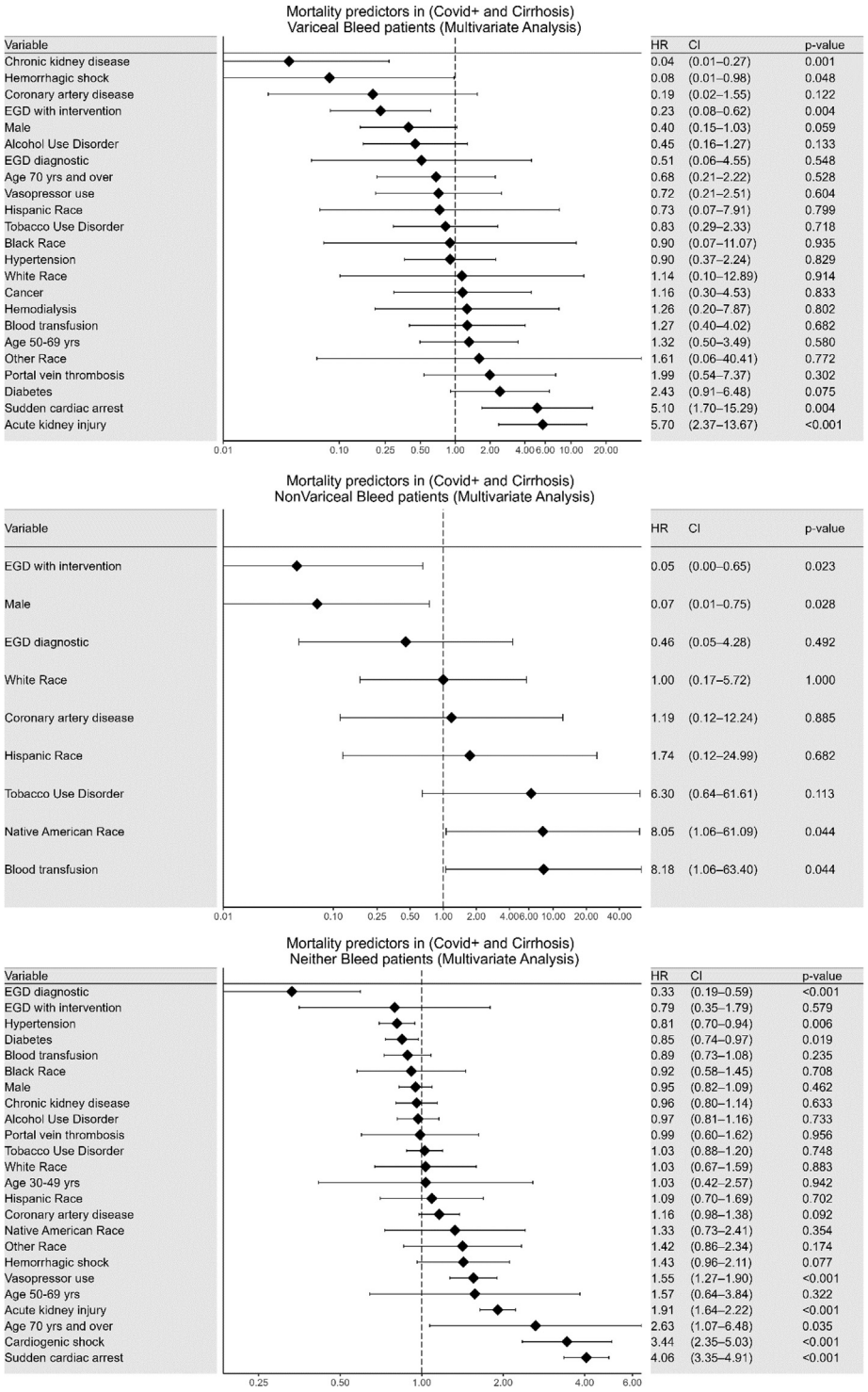

Fig. 1. Panel figure consisting of (a) Mortality predictors for the non-variceal bleed (NVB) group; (b) Mortality predictors for the variceal bleed (VB) group; and (c) Mortality predictors for the no or neither GI bleed (NB) group.

stay. AKI has been shown to be significantly associated with increased length of stay, mortality during hospitalization, and decreased survival in previous studies.[20] It is interesting to note that variables such as hypertension and diabetes acted as negative predictors in this group, possibly serving as markers for more careful medical management.

Lastly, in the VB group, chronic kidney disease and EGD with intervention emerged as negative predictive factors for mortality. There is no clear

explanation given in previous literature suggesting that CKD is associated with worse outcomes in patients with cirrhosis.[21] However, there was no difference in the acute settings, as demonstrated by an analysis finding no significant difference in adjusted HR for six-week mortality in end-stage renal disease (ESRD) and cirrhosis patients with esophageal variceal bleeding.[22] In contrast, AKI and sudden cardiac arrest were ominous indicators aligned with the NB group and previous studies.

It is worth noting that our study has some limitations. The retrospective method relying on administrative diagnostic coding data limits the understanding of the complete clinical context, as the treatment course and severity of disease cannot be analyzed. The unavailability of the degree or timing of pertinent diagnoses, such as when the relevant GI bleeding was diagnosed, is a challenge when interpreting the results. However, this study had several advantages. Conducting our analysis using the NIS database allows us to access a database of significant sample sizes that are diverse and representative to ascertain outcome data that would be difficult without a national database.

Our study underscores the criticality of customized management and preventive approaches for upper gastrointestinal bleeding in COVID-19 patients, particularly in those with cirrhosis. The identification of acute kidney injury as a significant mortality predictor necessitates enhanced clinical alertness. The proactive detection and management of AKI, alongside the advantageous role of esophagogastroduodenoscopy, are crucial in clinical decision-making. Clinicians should prioritize early EGD intervention and engage gastroenterology and nephrology teams for integrated care. Furthermore, our findings advocate for revising hospital protocols and resource distribution to better manage these complex cases, ultimately aiming to improve patient outcomes in this challenging clinical landscape.

5. Conclusions

In summary, our study elucidated different mortality predictors and characteristics across various groups of patients with cirrhosis and COVID-19. Our findings suggest that there were no mortality differences among the three groups of GI bleeding, but the heterogeneity of predictors across the three groups could be indicative of different underlying pathophysiological processes, warranting more personalized clinical approaches. The significance of EGD with intervention in reducing mortality across both bleeding groups reinforce its critical role in patient management suggests that such suggests that intervention can significantly improve the outcomes. AKI seems to be a consistent and strong predictor of mortality across both the NB and VB groups, indicating the critical role of renal function in these patients and demonstrating the higher mortality of AKI in patients with cirrhosis, as seen in prior studies. Special attention should be paid to unique demographic trends, such as the varying impacts of insurance status and association with the Native American race, with higher mortality in the nonvariceal bleeding group. These findings have significant implications for the management of this vulnerable patient population, and suggest avenues for future research to more comprehensively understand the underlying societal mechanisms.

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Ethical considerations

The study was conducted in accordance with the ethical standards of the Responsible Committee on Human Experimentation and with the Helsinki Declaration of 1975, as revised in 2005.

Conflicts of interest

The authors have no conflicts of interest to report.

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