

Impact of Esophagogastric Variceal Rupture Bleeding on 1-Year Mortality in Patients with Liver Cirrhosis and Analysis of Related Factors: Based on Propensity Score-Matched Samples

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Abstract

Background: Esophagogastric variceal bleeding (EGVB) is one of the most common and life-threatening complications of liver cirrhosis, and whether EGVB can affect the 1-year mortality outcome in cirrhotic patients remains unclear. **Objective:** To investigate the impact of EGVB on 1-year mortality outcomes in liver cirrhosis patients and analyze the associated factors, providing a basis for follow-up of cirrhotic patients. **Methods:** Clinical data of liver cirrhosis patients admitted to Changsha Central Hospital Affiliated to Nanhua University from January 2015 to May 2021 were collected and divided into an EGVB group and a control non-bleeding group. Logistic regression analysis was used to screen factors influencing 1-year mortality in liver cirrhosis patients. Propensity score matching (PSM) at a 1:2 ratio was employed to balance confounding factors, and binary logistic regression was used to comparatively analyze the factors influencing 1-year mortality outcomes between the EGVB and control non-bleeding groups. **Results:** A total of 812 liver cirrhosis patients were included, among which 158 (19.5%) had liver cirrhosis complicated by EGVB, with a 1-year mortality rate of 13.3%; 654 (80.5%) had liver cirrhosis without bleeding, with a 1-year mortality rate of 13.9%. There was no significant difference in 1-year mortality between the two groups. Pre-matching logistic regression analysis showed that serum sodium [OR=0.95, 95%CI (0.90-0.99)] and albumin [OR=0.95, 95%CI (0.91-0.99)] were protective factors for 1-year mortality in liver cirrhosis patients, while age [OR=1.04, 95%CI (1.02-1.06)] and hepatic encephalopathy (stage 3-4) [OR=3.72, 95%CI (1.21-11.37)] were risk factors. After PSM, 145 cases were obtained in the EGVB group and 290 cases in the control group, with both groups having a 1-year mortality rate of 12.4%, showing no significant difference. Post-matching logistic regres-

sion analysis indicated that blood urea nitrogen [OR=1.15, 95%CI (1.02-1.29)] was an independent risk factor for 1-year mortality in the EGVB group, while age [OR=1.09, 95%CI (1.04-1.14)] and neutrophil-to-lymphocyte ratio (NLR) [OR=1.09, 95%CI (1.00-1.18)] were independent risk factors in the control non-bleeding group. Conclusion: The occurrence of EGVB events has no significant impact on the 1-year mortality rate of liver cirrhosis patients, but the risk factors for 1-year mortality outcomes differ between the two groups, providing new reference for clinical follow-up of cirrhotic patients.

Full Text

Effect of Esophageal and Gastric Variceal Bleeding on 1-Year Mortality in Cirrhosis Patients: A Propensity Score Matching Study

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Abstract

Background: Esophageal and gastric variceal bleeding (EGVB) is one of the most common and life-threatening complications of liver cirrhosis. However, whether EGVB affects 1-year mortality in cirrhosis patients remains unclear.

Objective: To investigate the impact of EGVB on 1-year mortality in cirrhosis patients and analyze related factors to provide evidence for clinical follow-up.

Methods: Clinical data of cirrhosis patients admitted to the Affiliated Changsha Central Hospital from January 2015 to May 2021 were collected. Patients were divided into an EGVB group and a control group without bleeding. Logistic regression analysis was used to screen factors affecting 1-year mortality. Covariates were balanced between groups using 1:2 propensity score matching (PSM). Binary logistic regression was then applied to compare factors influencing 1-year mortality between the EGVB and control groups.

Results: A total of 812 cirrhosis patients were included, of whom 158 (19.5%) had EGVB with a 1-year mortality rate of 13.3%, while 654 (80.5%) patients

without bleeding had a 1-year mortality rate of 13.9%. There was no significant difference in 1-year mortality between the two groups. Before matching, logistic regression analysis showed that serum sodium [OR=0.95, 95%CI (0.90-0.99)] and albumin [OR=0.95, 95%CI (0.91-0.99)] were protective factors against 1-year mortality, whereas age [OR=1.04, 95%CI (1.02-1.06)] and hepatic encephalopathy (grades 3-4) [OR=3.72, 95%CI (1.21-11.37)] were risk factors. After PSM, 145 EGVB patients and 290 control patients were matched, with both groups showing a 1-year mortality rate of 12.4%. Post-matching logistic regression analysis revealed that blood urea nitrogen [OR=1.15, 95%CI (1.02-1.29)] was an independent risk factor for 1-year mortality in the EGVB group, while age [OR=1.09, 95%CI (1.04-1.14)] and neutrophil-to-lymphocyte ratio (NLR) [OR=1.09, 95%CI (1.00-1.18)] were independent risk factors in the control group.

Conclusion: The occurrence of EGVB did not significantly affect 1-year mortality in cirrhosis patients. However, the risk factors for 1-year mortality differed between the two groups, providing new insights for clinical follow-up and management of cirrhosis patients.

Keywords: liver cirrhosis; esophagogastric variceal bleeding; propensity score matching; risk factors

Introduction

Mortality remains high among patients with decompensated cirrhosis worldwide. Esophageal and gastric variceal bleeding (EGVB) is one of the most common complications and significantly increases mortality risk in these patients. Hepatic venous pressure gradient (HVPG) is the current gold standard for accurately assessing portal pressure changes and has predictive value for mortality in cirrhosis patients. Endoscopy is the most important tool for diagnosing and treating EGVB, with guidelines recommending that patients with decompensated cirrhosis undergo endoscopic examination every 6-12 months.

However, both HVPG and endoscopy are invasive procedures requiring specialized technical expertise, limiting their applicability in community and remote settings. Therefore, non-invasive assessments are crucial for follow-up and treatment of cirrhosis patients with EGVB. Child-Pugh score and Model for End-Stage Liver Disease (MELD) are classic non-invasive tools for evaluating cirrhosis prognosis. While both scores have some value in predicting outcomes in cirrhosis patients with EGVB, consistent conclusions are lacking. The Child-Pugh score includes subjective components such as hepatic encephalopathy and ascites. MELD offers greater objectivity and discrimination but suffers from calibration errors. Overall, consensus on accurately predicting mortality in cirrhosis patients with EGVB has not been reached, and existing scoring systems require extensive validation, with further research needed to develop updated or new models based on MELD.

Identifying factors that independently affect prognosis in cirrhosis patients with EGVB could help improve non-invasive prediction models. This study utilizes logistic regression and propensity score matching (PSM) to investigate the impact of EGVB on 1-year mortality in cirrhosis patients and analyze related factors, aiming to provide reliable evidence for developing more effective non-invasive models to guide follow-up and treatment.

Methods

1.2 Inclusion and Exclusion Criteria **Inclusion Criteria:** Cirrhosis patients aged 18-80 years with or without EGVB.

- (1) **Cirrhosis diagnosis criteria:** Evidence of liver dysfunction and/or portal hypertension, plus any of the following: Histological confirmation of cirrhosis; Endoscopic evidence of esophagogastric varices with exclusion of non-cirrhotic portal hypertension; Imaging evidence (ultrasound or CT) suggesting cirrhosis or portal hypertension.
- (2) **Cirrhosis with EGVB group:** Met criteria (1) above, plus endoscopic evidence of any of the following: (a) Active bleeding from varices; (b) “White nipple” sign over varices; (c) Blood clot over varices or varices without other identifiable bleeding sources. Diagnosis was made by experienced endoscopists, and patients received standard endoscopic variceal ligation and/or tissue glue/sclerotherapy injection.
- (3) **Cirrhosis without bleeding group:** Met criteria (1) above, with no clinical symptoms of hematemesis or melena, negative fecal occult blood test, and no endoscopic signs of bleeding, as determined by the attending physician.

Exclusion Criteria: (1) Hepatocellular carcinoma; (2) Post-TIPS, shunt surgery, devascularization, splenic embolization, or splenectomy; (3) Post-liver transplantation; (4) Severe cardiac, cerebral, pulmonary, renal, hematological, or connective tissue diseases; (5) Severe infection; (6) Other types of gastrointestinal bleeding besides EGVB or unconfirmed bleeding without endoscopy; (7) Refusal of follow-up, missing information, or loss to follow-up.

1.3 Study Methods Clinical data were collected within 24 hours of admission through the electronic medical record system, including demographic information (age, sex), bleeding history (EGVB within past 6 months), comorbidities (diabetes), complications (ascites, hepatic encephalopathy, portal vein thrombosis), laboratory tests (complete blood count, blood biochemistry, coagulation profile, liver and kidney function), and antiviral therapy history (regular antiviral treatment within 1 year). Patients were divided into an EGVB group and a control group without bleeding based on the presence of esophagogastric

variceal bleeding at presentation. All patients underwent routine follow-up until death from cirrhosis or completion of 1-year follow-up.

First, univariate and multivariate logistic regression analyses were performed on all included cirrhosis patients to identify risk factors for 1-year mortality. Second, based on the identified risk factors, propensity score matching (PSM) was used to balance variables that might affect mortality outcomes (matching factors: age, albumin, serum sodium, hepatic encephalopathy). Finally, univariate and multivariate logistic regression analyses were conducted to compare factors influencing 1-year mortality between the EGVB and control groups.

[Figure 1: see original paper] Flow chart of the current study

1.4 Ethics Review This study protocol was approved by the Ethics Committee of Changsha Central Hospital (Affiliated Changsha Central Hospital, University of South China) (Approval No.: 2022-S0019).

1.5 Statistical Methods Statistical analysis was performed using SPSS 23.0 and R 4.0.2 software. Normally distributed continuous variables were expressed as mean \pm standard deviation and compared between groups using independent samples t-test. Non-normally distributed continuous variables were expressed as median (interquartile range) and compared using Mann-Whitney U test. Categorical variables were expressed as percentages (%) and compared using χ^2 test or Fisher's exact test. The caliper value for propensity score matching was set at 0.1 with a 1:2 matching ratio. $P < 0.05$ (two-tailed) was considered statistically significant.

Results

2.1 Baseline Characteristics A total of 812 cirrhosis patients were included in the analysis, comprising 158 (19.5%) with EGVB and 654 (80.5%) without bleeding. The cohort included 542 males (67%) and 220 females (33%), with a mean age of 62 ± 12 years. Etiologies of cirrhosis included viral (hepatitis B and C) (38%), alcoholic (24%), and other etiologies (38%) (see Table 1).

Table 1 Baseline Characteristics of Cirrhotic Patients

Characteristic	Total (n=812)	Survival Group (n=700)	Death Group (n=112)
EGVB (n, %)	158 (19.5%)	137 (19.6%)	21 (18.8%)
Age (years)	62 ± 12	61 ± 11	66 ± 13
Sex (n, %)			
Female	270 (33%)	227 (32%)	43 (38%)
Male	542 (67%)	473 (68%)	69 (62%)

Characteristic	Total (n=812)	Survival Group (n=700)	Death Group (n=112)
Etiology (n, %)			
Viral	308 (38%)	279 (40%)	29 (26%)
Alcoholic	192 (24%)	159 (23%)	33 (29%)
Other	312 (38%)	262 (37%)	50 (45%)
Regular antiviral therapy	55 (17.9%)	49 (17.6%)	6 (20.7%)
WBC ($\times 10^9$ /L)	4.24 (3.1)	4.17 (3.1)	4.56 (3.3)
Hemoglobin (g/L)	100 \pm 29	102 \pm 19	90 \pm 27
Platelet ($\times 10^9$ /L)	81 (53)	80 (53)	91 (56)
PT (s)	3.2 (3.3)	3.1 (3.1)	4.2 (4.7)
Fibrinogen (g/L)	14.00 (3.1)	14.00 (3.1)	14.05 (3.3)
Albumin (g/L)	1.72 (0.9)	1.72 (0.8)	1.71 (1.1)
TBIL (mol/L)	26 (28)	25 (27)	30 (36)
ALT (U/L)	29 (28)	29 (28)	25 (21)
TBA (mol/L)	31 (50)	31 (50)	33 (52)
BUN (mol/L)	5.7 (3.8)	5.6 (3.5)	7.2 (7.5)
Serum Na (mmol/L)	140 (5)	140 (5)	138 (5)
Diabetes (n, %)	591 (73%)	511 (73%)	80 (71%)
Ascites (n, %)	221 (27%)	189 (27%)	32 (29%)
Moderate to severe Hepatic en- cephalopathy (n, %)	359 (44%)	322 (46%)	37 (33%)
None/Grade 0	204 (25%)	322 (26%)	25 (22%)
Grades 1-2	249 (31%)	199 (28%)	50 (45%)
Grades 3-4	16 (2%)	9 (1.3%)	7 (6%)
Child-Pugh score (n, %)			
Grade A	525 (65%)	467 (67%)	58 (52%)
Grade B	230 (28%)	184 (26%)	46 (41%)
Grade C	57 (7%)	49 (7%)	8 (7%)
Portal vein thrombosis (n, %)	734 (90%)	635 (91%)	99 (88%)

Characteristic	Total (n=812)	Survival Group (n=700)	Death Group (n=112)
Bleeding history (n, %)	78 (10%)	65 (9%)	13 (12%)

Note: NLR = neutrophil-to-lymphocyte ratio.

2.2 Variable Screening To identify risk factors for 1-year mortality in cirrhosis patients with and without EGVB and reduce multicollinearity, univariate logistic regression analysis was performed with 1-year mortality (assignment: yes = 1, no = 0) as the dependent variable and all variables in Table 1 as independent variables: age (actual value), sex (female = 0, male = 1), etiology (viral = 1, alcoholic = 2, other = 3), regular antiviral therapy in viral cirrhosis (no = 0, yes = 1), WBC, hemoglobin, platelet, NLR, PT, fibrinogen, albumin, TBIL, ALT, TBA, BUN, serum sodium (all actual values), diabetes (no = 0, yes = 1), ascites (none = 0, mild = 1, moderate to severe = 2), hepatic encephalopathy (none = 0, grades 1-2 = 1, grades 3-4 = 2), Child-Pugh score (A = 1, B = 2, C = 3), portal vein thrombosis (no = 0, yes = 1), and bleeding history (no = 0, yes = 1). Variables with $P < 0.1$ from univariate analysis and variables potentially affecting 1-year mortality (PT, portal vein thrombosis) were included in multivariate logistic regression.

The results showed that albumin (OR = 0.95, 95% CI: 0.91-0.99) and serum sodium (OR = 0.95, 95% CI: 0.90-0.99) were protective factors, while age (OR = 1.04, 95% CI: 1.02-1.06) and hepatic encephalopathy (grades 3-4) (OR = 3.72, 95% CI: 1.21-11.37) were risk factors for 1-year mortality ($P < 0.05$) (see Table 2).

Table 2 Logistic Regression Analysis

Variable	Univariate Analysis	Multivariate Analysis
	Wald ²	OR
Age	<0.001	1.04
Sex (male vs. female)	0.69	-
Etiology (alcoholic vs. viral)	-	-
Etiology (other vs. viral)	2.74	-
Regular antiviral therapy (yes vs. no)	<0.001	-0.01
PT	0.00	5.11
Fibrinogen	<0.001	-0.05
ALT	<0.001	0.04
Diabetes (yes vs. no)	4.18	-0.22
Ascites (mild vs. none)	0.78	0.28
Ascites (moderate to severe vs. none)	<0.001	0.67
Hepatic encephalopathy (grades 1-2 vs. none)	0.06	-

Variable	Univariate Analysis	Multivariate Analysis
Hepatic encephalopathy (grades 3-4 vs. none)	1.64	5.13
Child-Pugh B vs. A	<0.001	1.31
Child-Pugh C vs. A	-	-
Portal vein thrombosis (yes vs. no)	-	-
Bleeding history (yes vs. no)	-	-

2.3 Comparison of Baseline Characteristics Before and After Matching Before matching, patients were divided into a control group without bleeding (n = 654) and an EGVB group (n = 158). The mortality rate was 13.3% in the EGVB group and 13.9% in the control group, with no statistically significant difference. Significant differences between groups were observed in age, WBC, hemoglobin, NLR, albumin, BUN, presence of ascites, and presence of portal vein thrombosis (P < 0.05).

To reduce confounding effects on outcomes, 1:2 propensity score matching was performed based on logistic regression results (caliper value = 0.1). After matching, baseline characteristics and laboratory parameters were well balanced between groups. Following exclusion of unmatched cases, the final cohort consisted of 290 control patients and 145 EGVB patients, both with a mortality rate of 12.4%. No significant differences remained in age, albumin, serum sodium, or hepatic encephalopathy between groups (P > 0.05) (see Table 3).

Table 3 Baseline Characteristics Before and After Matching

Characteristic	Before Matching (n=812)	After Matching (n=435)
	Control (n=654)	EGVB (n=158)
1-year survival outcome		
Survival (n, %)	563 (86.1%)	137 (86.7%)
Death (n, %)	91 (13.9%)	21 (13.3%)
Age (years)	63 ± 11	58 ± 11
Etiology (n, %)		
Viral	248 (38%)	60 (38%)
Alcoholic	260 (40%)	46 (29%)
Other	46 (7%)	52 (33%)
WBC ($\times 10^9$ /L)	3.93 (2.7)	5.93 (4.1)
Hemoglobin (g/L)	105 ± 27	81 ± 29
NLR	3.2 (3.1)	3.6 (3.1)
PT (s)	14.00 (3.2)	13.85 (2.9)
Albumin (g/L)	31.2 ± 6.5	32.1 ± 5.4
BUN (mol/L)	5.2 (3.0)	8.7 (6.0)
Serum Na (mmol/L)	140.0 (5.0)	139.3 (4.8)
Ascites (n, %)		
Moderate to severe	265 (41%)	94 (59.5%)

Characteristic	Before Matching (n=812)	After Matching (n=435)
Hepatic encephalopathy (n, %)		
None/Grade 0	607 (92.8%)	153 (96.9%)
Grades 1-2	32 (4.9%)	4 (2.5%)
Grades 3-4	15 (2.3%)	1 (0.6%)
Portal vein thrombosis	599 (92%)	135 (85%)

2.4 Analysis of Factors Affecting 1-Year Mortality After Matching

In the EGVB group, univariate logistic analysis showed that prothrombin time (OR = 1.18, 95% CI: 0.99-1.41) and blood urea nitrogen (OR = 1.16, 95% CI: 1.03-1.29) were risk factors for 1-year mortality. Multivariate logistic regression including factors with $P < 0.1$ from univariate analysis identified BUN (OR = 1.15, 95% CI: 1.02-1.29) as an independent risk factor in the EGVB group (see Table 4).

In the control group, univariate logistic regression showed that age (OR = 1.07, 95% CI: 1.03-1.12), alcoholic etiology (OR = 2.45, 95% CI: 1.07-5.59), hemoglobin (OR = 0.98, 95% CI: 0.97-1.00), NLR (OR = 1.11, 95% CI: 1.05-1.19), BUN (OR = 1.09, 95% CI: 1.03-1.17), serum sodium (OR = 0.91, 95% CI: 0.85-0.97), mild ascites (OR = 2.38, 95% CI: 0.19-6.21), and moderate to severe ascites (OR = 3.47, 95% CI: 1.42-8.46) were risk factors, while albumin (OR = 0.92, 95% CI: 0.87-0.98) was protective. Multivariate analysis including factors with $P < 0.1$ identified age (OR = 1.09, 95% CI: 1.04-1.14) and NLR (OR = 1.09, 95% CI: 1.00-1.18) as independent risk factors in the control group ($P < 0.05$) (see Table 5).

Table 4 Univariate and Multivariate Logistic Regression Analysis of EGVB Group After Matching

Variable	Univariate Analysis	Multivariate Analysis
	Wald ²	OR
Age	-	-
Etiology (alcoholic vs. viral)	-	-
Etiology (other vs. viral)	-	-
PT	-	1.18
BUN	-	1.16
Ascites (mild vs. none)	-	-
Ascites (moderate to severe vs. none)	-	-
Hepatic encephalopathy (grades 1-2 vs. none)	-	-
Hepatic encephalopathy (grades 3-4 vs. none)	-	-
Portal vein thrombosis (yes vs. no)	-	-

Table 5 Univariate and Multivariate Logistic Regression Analysis of Control Group After Matching

Variable	Univariate Analysis	Multivariate Analysis
	Wald ²	OR
Age	<0.001	1.07
Etiology (alcoholic vs. viral)	0.08	2.45
Etiology (other vs. viral)	0.17	-
Hemoglobin	<0.001	0.98
NLR	<0.001	1.11
BUN	<0.001	1.09
Serum Na	<0.001	0.91
Albumin	<0.001	0.92
Ascites (mild vs. none)	-	2.38
Ascites (moderate to severe vs. none)	-	3.47
Hepatic encephalopathy (grades 1-2 vs. none)	-	-
Hepatic encephalopathy (grades 3-4 vs. none)	-	-
Portal vein thrombosis (yes vs. no)	-	-

Discussion

Over the past 30 years, prognosis for cirrhosis patients with EGVB has improved significantly, though mortality remains high. Identifying risk factors affecting prognosis in this population is crucial for guiding follow-up and treatment strategies. This study collected clinical data from cirrhosis patients with and without EGVB, applied propensity score matching to reduce confounding, and used logistic regression to compare factors influencing 1-year mortality between groups, aiming to investigate the impact of EGVB on mortality outcomes.

This study showed an overall 1-year mortality rate of 13.8% in cirrhosis patients. Before matching, the EGVB group had a 1-year mortality of 13.3% compared to 13.9% in the non-bleeding group, consistent with recent studies reporting rates of 8-15%. After matching, both groups had a mortality rate of 12.4%, suggesting similar 1-year mortality between EGVB and control patients.

To further identify prognostic factors affecting 1-year mortality, we performed univariate and multivariate logistic regression. Age, albumin, serum sodium, and hepatic encephalopathy were identified as risk factors for 1-year mortality. Advanced age may reflect longer disease duration and more severe complications, associated with lower survival rates. Albumin reflects not only synthetic liver function but also modulates immune function, inflammatory responses, and vascular endothelial function, serving as a reliable prognostic indicator. Cirrhosis patients develop splanchnic vasodilation, triggering compensatory activation of sympathetic nervous system, renin-angiotensin-aldosterone system, and antidiuretic hormone, leading to progressive sodium retention and hyponatremia. Serum sodium level is an important indicator of disease severity and an independent mortality predictor. Hepatic encephalopathy is a common complica-

tion, with studies showing 1-year mortality up to 40% in affected patients, far exceeding the average.

To enhance credibility, we applied PSM to balance confounding factors (age, albumin, serum sodium, hepatic encephalopathy). After matching, logistic analysis of the EGVB group identified BUN as an independent risk factor. Following EGVB, hemoglobin breakdown and absorption in the intestine, along with stress responses, can cause enterogenous azotemia. Additionally, blood loss reduces renal perfusion, making BUN a marker of renal function. Research on BUN for predicting prognosis in EGVB patients is limited and warrants further investigation to validate its predictive utility and potentially incorporate it into existing models.

In the matched control group, multivariate analysis identified age and NLR as independent risk factors. Inflammation is a key driver of cirrhosis progression and closely linked to prognosis. NLR, an inflammation-based marker, has been shown to be an independent mortality predictor in cirrhosis patients.

This study is innovative in its use of non-invasive clinical data and propensity score matching to investigate the impact of EGVB on 1-year mortality and compare prognostic factors between groups, offering valuable clinical insights. However, limitations exist. First, this single-center retrospective study may have selection bias; larger multicenter prospective studies are needed for validation. Second, we only examined 1-year mortality without incorporating time-to-event variables; future Cox regression analysis would be valuable. Third, we did not collect data on variceal severity to assess its impact on outcomes.

In conclusion, EGVB occurrence did not significantly affect 1-year mortality in cirrhosis patients, but risk factors for mortality differed between groups, providing new references for clinical follow-up and management.

Conflict of Interest Statement: The authors declare no conflicts of interest.

Author Contributions: Yu Xueke contributed to study conception, data collection, and manuscript writing. Li Mengling, Peng Siyuan, and Shen Yueming contributed to study design, data collection, and manuscript revision. Liang Lunxi contributed to study design, statistical analysis, and critical revision. Zeng Ya contributed to study conception, quality control, and final approval.

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Note: Figure translations are in progress. See original paper for figures.

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