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Original Article

Predictive value of blood coagulation and routine blood indices for rebleeding after endoscopic treatment in hepatitis B-related cirrhotic patients with esophagogastric fundal varices: a logistic regression model analysis

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Abstract: Objective: To evaluate the predictive value of blood coagulation and routine blood indices for rebleeding after endoscopic treatment of ruptured esophagogastric fundal varices (EGVB) in cirrhotic patients with hepatitis B infection. Methods: This retrospective analysis included 248 patients with hepatitis B-related cirrhosis and EGVB who received initial endoscopic treatment from October 2019 to March 2022 and were followed up for 12 months. Patients were divided into rebleeding and non-rebleeding groups. Laboratory indices were analyzed, and univariate and multivariate analyses identified predictors of rebleeding. The efficacy of a logistic regression model was evaluated using Receiver Operating Characteristic (ROC) curves, calibration curves, and decision curve analysis (DCA), and a risk factor nomogram was constructed for assessing the predictive efficiency of those risk factors. Results: Univariate analysis showed significant differences in portal vein diameters and lower Child-Pugh scores in the rebleeding group in contrast to those in the non-rebleeding group. Key laboratory markers such as platelet count (PLT), albumin (ALB), alanine aminotransferase (ALT), lymphocytes (LYM), and prognostic nutritional index (PNI) were lower, while prothrombin time (PT) and lactate levels (LN) were higher in the rebleeding group than those in the non-rebleeding group. Multivariate analysis identified portal vein diameter, PLT, ALT, PT, LYM, and PNI as significant predictors of rebleeding. The logistic model demonstrated high accuracy (AUC=0.986) and clinical value, validated by ROC curves, calibration curves (C-index =0.986), and DCA results. A risk factor predictive nomogram was successfully constructed. Conclusion: This study developed a logistic regression model with a nomogram for predicting EGVB-related rebleeding in patients with hepatitis B-related cirrhosis, achieving an AUC of 0.986, indicating high accuracy and significant clinical relevance.

Keywords: Thermocoagulation, blood count, hepatitis B, cirrhosis, esophagogastric fundus varices, endoscopic treatment, rebleeding

Introduction

Cirrhosis represents the terminal phase of chronic liver damage induced by various etiologic agents. It is characterized by widespread hepatocyte necrosis, excessive fibrous connective tissue proliferation, nodule regeneration, and pseudo-lobule formation, ultimately disrupting the typical architecture and perfusion of the liver [1-3]. Gastrointestinal cirrhosis, a prevalent condition within the digestive system, is characterized by impaired liver function and portal hypertension [4]. The causes of cirrhosis are diverse and vary widely among countries, regions, and time periods [5]. In Western countries and Japan, alcohol consumption and hep-

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atitis C virus infection are the main causes. In China, hepatitis B virus infection has historically been the leading cause, although its prevalence is gradually decreasing [6]. In addition, the incidences of autoimmune, alcoholic, and nonalcoholic fatty liver cirrhosis are growing due to increased recognition of autoimmune diseases, increased alcohol consumption, and diversified lifestyles.

Patients with cirrhosis manifest different clinical symptoms depending on the progression of the disease. Initially, symptoms may be subtle, but as cirrhosis progresses, increased liver damage and fibrosis lead to portal hypertension and associated syndromes that cause severe complications [7]. These include portal vein thrombosis, spontaneous bacterial peritonitis, gastrointestinal bleeding, hepatic encephalopathy, primary liver cancer, hepatopulmonary syndrome, and hepatorenal syndrome [8]. Esophagogastric varices are particularly common, with esophagogastric fundal variceal bleeding (EGVB) being a serious and common complication noted for its high rebleeding and mortality rates [9]. Treatments for EGVB include pharmacologic intervention, endoscopic therapy, transjugular intrahepatic portosystemic shunt (TIPSS), and surgical options [10]. Endoscopic therapy, which includes endoscopic variceal ligation (EVL), endoscopic sclerotherapy (EIS), and tissue glue injection, has emerged as the preferred method that can effectively control and prevent the occurrence of EGVB [11]. Regardless, patients still suffer from the risk of rebleeding after endoscopic treatments. Studies suggest that TIPSS, by significantly reducing portal venous pressure, results in a lower rebleeding rate than endoscopic or pharmacological methods does [12]. Identification of factors influencing rebleeding in EGVB patients is critical to assess their prognosis, allow early intervention, and reduce rebleeding and mortality.

In the management of cirrhosis, understanding the factors that contribute to rebleeding in patients is critical to improve their clinical outcomes. Although numerous studies have identified various risk factors, the combined effects of these factors have not been fully elucidated. Existing predictive tools often do not accurately reflect the pooled effects of multiple clinical and laboratory indicators and have limitations in predicting the risk of rebleeding in patients with cirrhosis, particularly hepatitis B-related cirrhosis. In addition, many existing models do not effectively incorporate new biomarkers and clinical parameters, limiting their applicability and predictive accuracy in different patient populations.

The aim of this study was to explore risk factors contributing to rebleeding in hepatitis B-related cirrhotic patients receiving endoscopic therapy for EGVB by analyzing an extensive amount of clinical and laboratory data. Our goal was to develop an accurate risk predictive model that would not only improve the quality of clinical decision-making, but also refine patient care strategies and improve their prognosis. Hopefully, the findings in this study can provide a scientific basis for designing treatment protocols tailored to hepatitis B-related cirrhotic patients complicated with EGVB, ultimately increasing their survival time and improving the quality of their life. In addition, this newly built predictive model can fill the blank that the existing tools haven't covered and demonstrate the significance of utilizing both clinical and laboratory parameters to support decision-making processes in clinical settings.

Methods and data

Ethics statement

The study was carried out with the endorsement of The Second People's Hospital of Lanzhou City Ethics Committee, ensuring adherence to ethical standards.

Research subjects

This is a retrospective study involving 248 patients diagnosed with hepatitis B cirrhosis and EGVB undergoing their initial endoscopic treatment at The Lanzhou Petrochemical General Hospital and The Second People's Hospital of Lanzhou City between October 2019 and March 2022. These patients were divided into the rebleeding group (n=86) and the non-rebleeding group (n=162).

Inclusion exclusion criteria

Inclusion criteria: (1) Patients diagnosed with HBV cirrhosis. (2) Patients who met the diagnostic criteria for liver cirrhosis as described in *The 2015 Clinical Practice Guidelines* of the Japanese Society of Gastroenterology [13]. (3)

Patients who were admitted to the hospital for symptoms including vomiting blood and black stool after endoscopy for EGVB. (4) Patients whose postoperative follow-up and outcome records were available. (5) Patients whose clinical data were available.

Exclusion criteria: (1) Patients who had previous endoscopic experiences at another medical facility. (2) Patients who had gastrointestinal bleeding from digestive diseases other than cirrhosis. (3) Patients who had known or suspected comorbid hepatocellular carcinoma or other malignancies. (4) Patients who had severe heart failure, respiratory failure, uremia, or severe hepatic encephalopathy.

Diagnostic criteria for EGVB

Under endoscopic observation, patients were confirmed with EGVB if they presented any of the following conditions: (1) active bleeding with varicose veins; (2) "white papilla" on varicose veins; (3) blood clot or varicose vein bleeding without other potential causes. Such patients were targeted for treatments including angioactive drugs, vasopressin and endoscopic therapy.

Clinical data collection

Patients' data were collected from their clinical examination records and laboratory test records. The clinical examination parameters included age, sex, body mass index (BMI), internal portal vein diameter, Child-Pugh score [14], hospitalization times, surgical duration, intraoperative bleeding, presence of ascites, and history of diabetes mellitus, hypertension, and smoking. The laboratory parameters included hemoglobin (Hb), platelet count (PLT), total bilirubin (TBil), albumin (ALB), alanine aminotransferase (ALT), prothrombin time (PT), activated partial thromboplastin time (APTT), D-dimer (D-D), lipoprotein (a) (LN), haptoglobin (HA), procollagen type III N-terminal peptide (PCIII), sodium (NA), lymphocyte count (LYM), and prognostic nutrition index (PNI), calculated as PNI = 10ALB + 0.05LYM. Medical instruments used for detection included a Hyson Micron XT-1800i instrument for Hb, PLT, and LYM, a Beckman Coulter AU5800 automated biochemistry analyzer for TBil, ALB, ALT, and D-D, Elisa assay for LN and HA, and an automated coagulation analyzer (Coatron3000 et al.) for PT and APTT (Coatron 3000, TECO, Germany). An ultrasonic diagnostic device (Philips Medical [Suzhou] Co., LTD., model CX50) was used to determine the internal diameter of the portal vein. The frequency of the probe was 3.5-5.5 MHz, and the internal diameter of the portal vein was obtained by fasting for 8-12 h before the examination and measured when the sampling volume was 1/3 of the internal diameter of the lumen. Note: All laboratory indicators were tested before and 7 days after treatment (**Figure 1**).

Study objectives

1. To compare the differences in clinical data and laboratory parameters of patients between the rebleeding group and the non-rebleeding group. 2. To dichotomize meaningful measures using the cut-off values of the receiver operating characteristic (ROC) curves. 3. To find out independent risk factors resulting in rebleeding in patients using univariate and multivariate logistic regression analysis. 4. To determine the accuracy of the logistic regression model in predicting rebleeding using the ROC curve, calibration curve, and decision curve analysis (DCA). 5. To construct a risk factor prediction nomogram model and evaluate its accuracy, calibration ability, and clinical value of the model in predicting rebleeding.

Statistical analysis

SPSS 26.0 statistical software was used for data analysis. Counting data were expressed as the number of cases or percentages, with between-group comparisons made using the χ^2 test. Measurement data conforming to normal distribution were expressed as the mean ± standard deviation (mean ± SD), with between-group comparisons for independent samples carried out using the t-test, which was expressed as t; measurement data not conforming to normal distribution were analyzed using the Mann-Whitney U test, which was expressed as Z. ROC curves were plotted to analyze the efficiencies of the indicators in predicting the occurrence of rebleeding. AUC (area under the curve) was used to measure the overall recognition ability of the model. The closer the AUC value was to 1, the better the predictive performance of the model was. Logistics regression

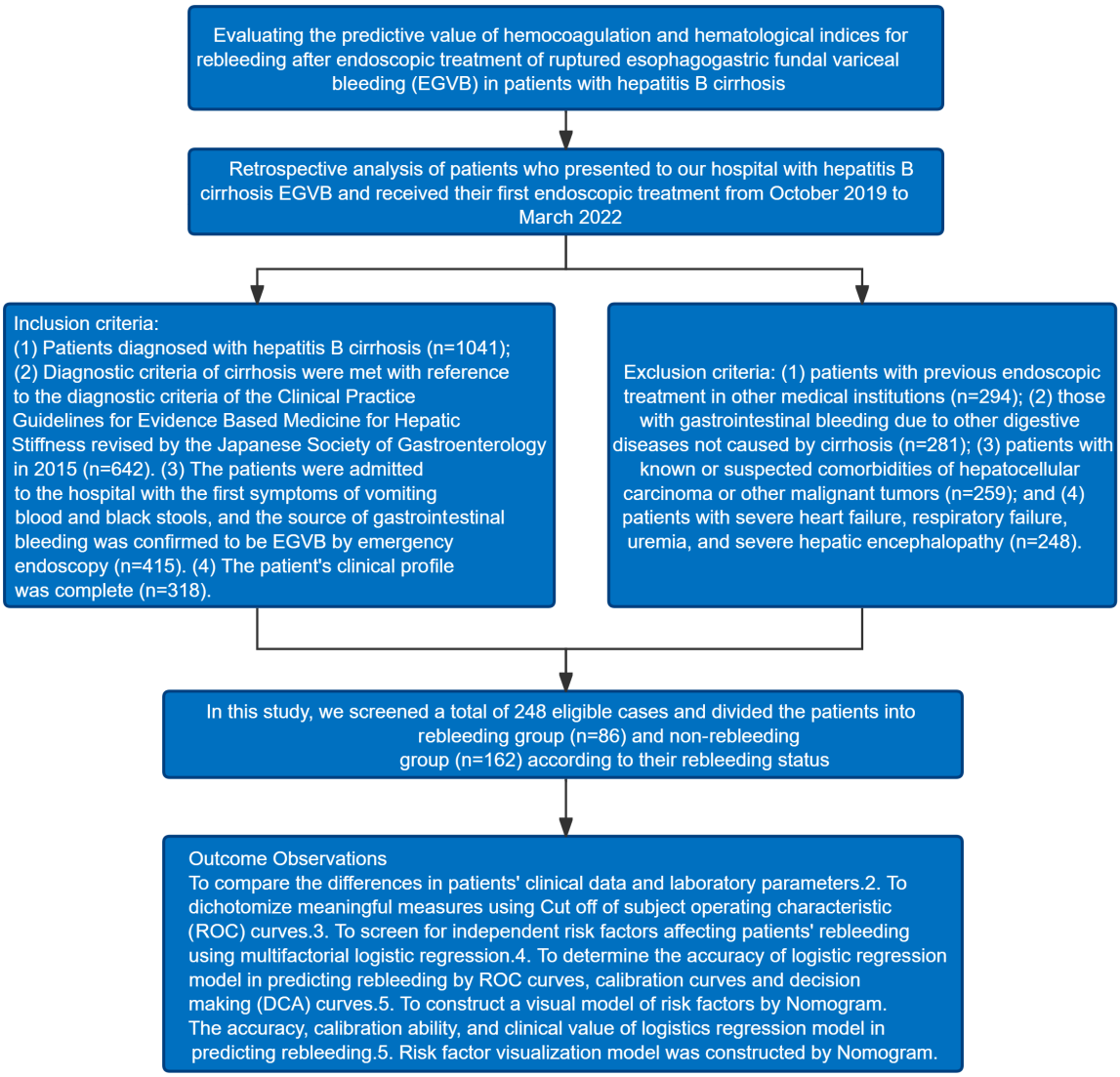

Figure 1. Flowchart of the study.

was carried out to analyze risk factors of rebleeding in hepatitis B-related cirrhotic patients undergoing endoscopic therapy for EGVB. Quasi-curve and DCA analyses and Nomogram construction were performed using the R software (4.3.2). Calibration curves were used to assess the consistency between the predicted probabilities of the model and the actual probabilities of the occurrence of rebleeding. C-index was employed to measure the predictive accuracy of the model, with a value closer to 1 indicating more accurate prediction. DCA was used to assess the predictive value of the model in clinical settings. By comparing the net benefit at different thresholds, DCA can help clinicians decide under what circumstances the use of a particular predictive model will provide the greatest health benefit. Differences were considered statistically significant at $P<0.05$.

Results

Baseline data

The baseline data of patients enrolled in this study were compared between the rebleeding group and the non-rebleeding group. It was observed that the internal diameters of the portal vein in patients were significantly larger in the rebleeding group than those in the non-rebleeding group ($P<0.05$). The Child-Pugh scores were significantly lower in the rebleeding group than those in the non-rebleeding

Table 1. Comparison of baseline data between the two groups

Marker	Rebleeding group (n=86)	Non-rebleeding group (n=162)	χ^2/t/Z value	*P*-value
Age				
≥65 years	60 (69.77%)	78 (48.15%)	10.638	0.001
<65 years	26 (30.23%)	84 (51.85%)		
Gender				
Male	52 (60.47%)	84 (51.85%)	1.683	0.195
Women	34 (39.53%)	78 (48.15%)		
Body mass index (kg/m^2)	23.15±3.14	23.25±3.74	-0.227	0.820
Portal vein internal diameter (cm)	1.42±0.44	1.21±0.30	4.13	<0.001
Child-Pugh Rating	11.00 (9.00, 12.00)	8.00 (7.00, 9.00)	7.914	<0.001
Surgical time (min)	19.00 (16.00, 21.00)	18.00 (16.00, 20.00)	1.387	0.164
Intraoperative bleeding (min)	41.24±10.14	39.86±8.36	1.087	0.279
Ascitic fluid				
Yes	22 (25.29%)	52 (32.1%)	1.257	0.262
No	65 (74.71%)	110 (67.9%)		
History of diabetes				
Yes	22 (25.29%)	32 (19.75%)	1.021	0.312
No	65 (74.71%)	130 (80.25%)		
History of hypertension				
Yes	19 (22.09%)	45 (27.78%)	0.948	0.330
No	67 (77.91%)	117 (72.22%)		
Smoking history				
Yes	56 (65.12%)	89 (54.94%)	2.397	0.122
No	30 (34.88%)	73 (45.06%)		

group (P<0.05). Except for the aforementioned indicators, the others did not show significant differences (P>0.05). See **Table 1** for details.

Laboratory indicators

Comparison of the laboratory parameters of patients between the two groups showed that PLT, ALB, ALT, LYM, and PNI were significantly lower in the rebleeding group than those in the non-rebleeding group (all P<0.001). In addition, patients in the rebleeding group had higher PT (P=0.003) and LN (P=0.004) levels than those in the non-rebleeding group. See **Table 2** for details.

Determination of the optimal cut-off value using ROC curves

Up to 10 risk factors were identified that were probably in association with rebleeding in hepatitis B-related patients undergoing endoscopic therapy for EGBV via analysis of variance. Of the 10 risk factors, all were measurable except for the age factor. ROC curves were employed to determine the optimal cut-off values for portal vein internal diameter, Child-Pugh score, PLT, ALB, ALT, PT, LN, LYM, and PNI. See **Figure 2** and **Table 3** for details.

Risk factors of rebleeding in hepatitis B-related patients undergoing endoscopic therapy for EVGB by multivariate logistic regression analysis

The measured data were categorized according to the cut-off value of the ROC curves. See **Table 4** for details. Subsequently, portal vein internal diameter (OR=8.717, P=0.013), PLT (OR=0.006, P=0.001), ALT (OR=0.003, P<0.001), PT (OR=8.671, P=0.011), LYM (OR=0.108, P=0.005), and PNI (OR=0.140, P=0.012) were identified as independent risk factors for rebleeding in hepatitis B-related patients undergoing endoscopic therapy for

Table 2. Comparison of laboratory indicators between the two groups

Marker	Rebleeding group (n=86)	Non-rebleeding group (n=162)	t/Z value	*P*-value
HB (g/L)	71.71±13.00	69.07±15.38	1.429	0.155
PLT (*10^9/L)	55.09±24.38	122.07±50.01	-14.167	<0.001
TBil (μmol/L)	24.92±6.89	23.59±9.21	1.284	0.201
ALB (g/L)	28.95±3.19	32.49±3.88	-7.704	<0.001
ALT (μ/L)	20.70 (11.18, 28.91)	53.70 (41.16, 64.16)	-11.249	<0.001
PT (s)	14.00 (13.00, 15.00)	13.00 (12.00, 15.00)	2.936	0.003
APTT (s)	32.29±7.03	31.91±5.31	0.443	0.659
D-D (mg/L)	1.10 (0.74, 1.37)	1.12 (0.76, 1.38)	0.06	0.953
LN (μg/L)	149.35±60.53	127.29±47.77	2.93	0.004
HA (μg/L)	710.19±174.07	696.62±122.49	0.643	0.521
PCIII (μg/L)	48.44±16.28	52.30±15.12	-1.824	0.07
NA (mmol/L)	145.17 (140.63, 149.54)	143.77 (138.45, 147.81)	1.408	0.159
LYM (*10^9/L)	1.00±0.36	1.19±0.42	-3.667	<0.001
PNI	289.55±31.88	324.95±38.76	-7.707	<0.001

Note: Hb: Hemoglobin; PLT: Platelet count; TBil: Total bilirubin; ALB: Albumin; ALT: Alanine aminotransferase; PT: Prothrombin time; APTT: Activated Partial Thromboplastin Time; D_D: D-Dimer; LN: Lipoprotein (a); HA: Haptoglobin; PCIII: Procollagen Type III N-Terminal Peptide; NA: Sodium; LYM: Lymphocyte count; PNI: Prognostic Nutritional Index.

EGVB via multivariate logistic regression analysis. See **Table 5** for details.

Construction and validation of the logistic prediction model

To demonstrate the value of the logistic prediction model, we compared the risk scores of patients in the rebleeding group with those in the non-rebleeding group. We verified the accuracy, calibration, and clinical application of the model using ROC curves, calibration curves, and DCA curves. To begin with, we calculated the risk score of each patient using the formula: Risk score = (portal vein internal diameter × 2.165) + (PLT × -5.1) + (ALT × -5.99) + (PT × 2.16) + (LYM × -2.224) + (PNI × -1.966) + 0.493. We found that patients in the rebleeding group had significantly higher risk scores than those in the non-rebleeding group (**Figure 3A**, P< 0.05). ROC curve analysis showed that the area under the curve of the logistic model for predicting patients' rebleeding was 0.986, indicating a high predictive value of the model (**Figure 3B**). Calibration curve analysis revealed a C-index of 0.986 (95% CI: 0.976-0.997), indicating excellent discriminatory power of the model. Furthermore, the Hosmer-Lemeshow test with a *P*-value of 0.997 indicated no significant difference between the predicted and observed values of the model, indicating good calibration (**Figure 3C**). Finally, the DCA curve analysis showed that the Akaike Information Criterion (AIC) of the model was 71.427, indicating a good fit of the model, and the net return of the model was 65.32%, suggesting that the model could achieve a high return in practical applications (**Figure 3D**).

Visualization of the risk factor prediction model by a nomogram

A nomogram was employed in the study for the visualization of the risk factor prediction model. It was observed from the visualized risk factor model that PLT and ALT were strongly associated with the occurrence of rebleeding in patients with hepatitis-B relayed cirrhosis and EVGB. And the association was observed between portal vein internal diameter, PT, LYM and PNI and the occurrence of rebleeding, as well. The model realizes the assessment of rebleeding risks by analyzing data extracted from patients to obtain corresponding values. For example, a patient who experienced rebleeding had the following data: portal vein internal diameter of 1.02 cm, PLT=50.34 (× 10^9/L), ALT=13.23 (μ/L), PT=13 (s), LYM=1.45 (× 10^9/L), and PNI=344.87. By retrieving the corresponding values, the score was calculated as 41 + 81 + 100 + 0 + 0 + 0 + 0=222. The 222 was the final risk score of the patients. The probability of rebleeding for this patient was approximately 60% (**Figure 4A**). ROC curve analysis showed

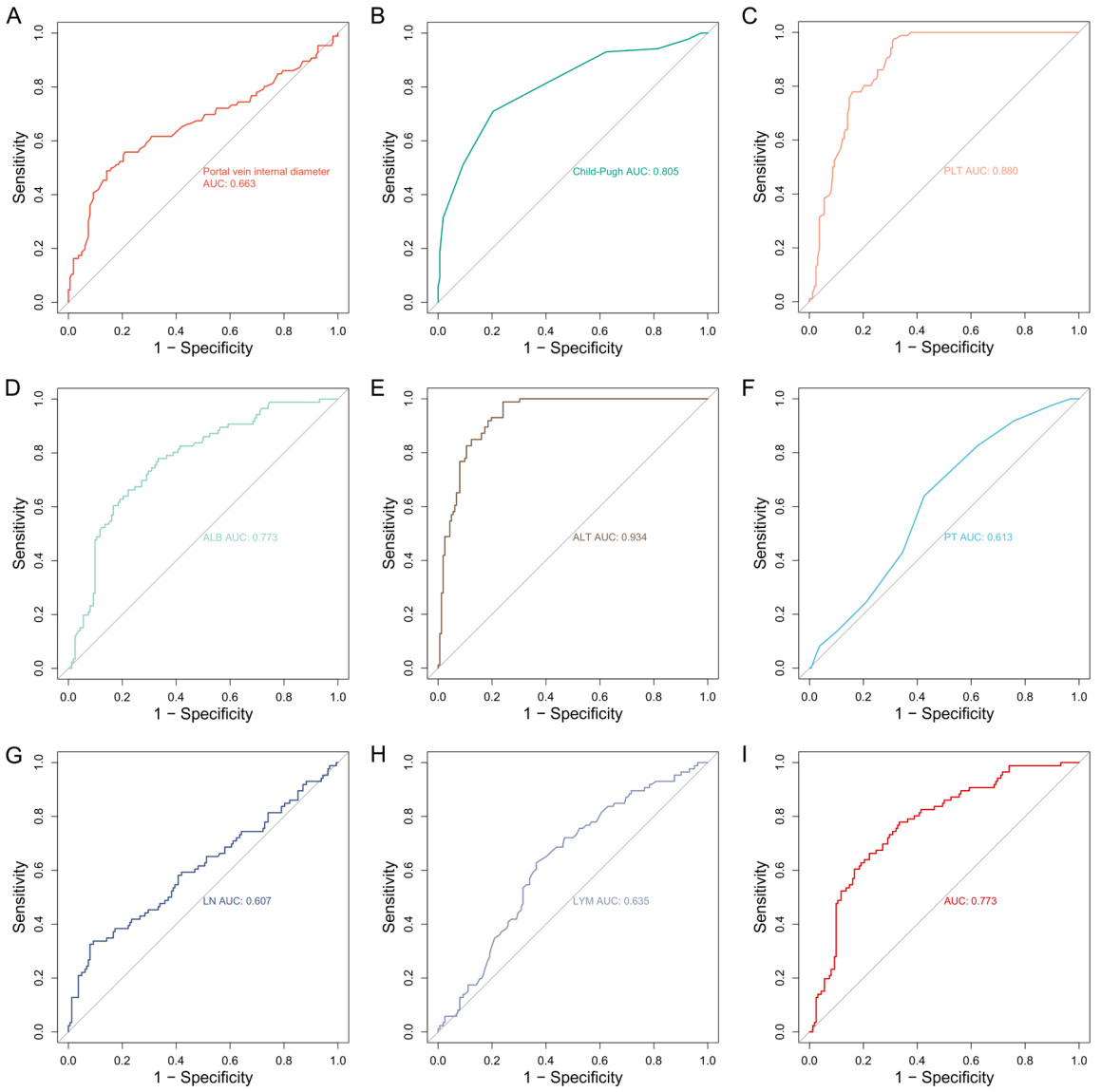

Figure 2. ROC curves of measurement data. A. The ROC curve of portal vein internal diameter. B. The ROC curve of Child-Pugh score. C. The ROC curve of PLT. D. The ROC curve of ALB. E. The ROC curve of ALT. F. The ROC curve of PT. G. The ROC curve of LN. H. The ROC curve of LYM. I. The ROC curve of PNI. Note: PLT: Platelet count; ALB: Albumin; ALT: Alanine aminotransferase; PT: Prothrombin time; LN: Lipoprotein (a); LYM: Lymphocyte count; PNI: Prognostic Nutritional Index.

that the area under the curve of the model for predicting the risk of rebleeding in patients was 0.985, indicating that the model had a high predictive value (**Figure 4B**). Calibration curve analysis showed a C-index of 0.985 (0.974-0.996), indicating that the model had excellent discriminatory power. In addition, the *P*-value of the Hosmer-Lemeshow test was 0.997, indicating that there was no significant difference between the predicted and observed values of the model, suggesting that the calibration was good (**Figure 4C**). Finally, the DCA curve analysis showed that the AIC of the model was 71.791, indicating that the model was well-fitted, and the net return of the model was 65.32%, suggesting that the model could achieve a high rate of return in practical applications (**Figure 4D**).

Discussion

Portal hypertension and the formation of portal collateral circulation due to cirrhosis can cause EGVB, which occurs in approximately 80-90%

Table 3. Predictive efficacies of the risk factors for rebleeding in EGVB patients by ROC curve analysis

Marker	AUC	95% CI	Specificity	Sensitivity	Youden index	Cut off
Portal vein internal diameter (cm)	0.663	0.586-0.663	79.01%	55.81%	34.83%	1.405
Child-Pugh Rating	0.805	0.746-0.805	79.63%	70.93%	50.56%	9.5
PLT (*10^9/L)	0.88	0.839-0.880	68.52%	97.67%	66.19%	98
ALB (g/L)	0.773	0.712-0.773	66.67%	77.91%	44.57%	31.02
ALT (μ/L)	0.934	0.905-0.934	75.93%	98.84%	74.76%	40.075
PT (s)	0.613	0.543-0.613	57.41%	63.95%	21.36%	13.5
LN (μg/L)	0.607	0.529-0.607	91.98%	32.56%	24.53%	187.995
LYM (*10^9/L)	0.635	0.564-0.635	63.58%	62.79%	26.37%	1.07
PNI	0.773	0.712-0.773	66.67%	77.91%	44.57%	310.256

Note: PLT: Platelet count; ALB: Albumin; ALT: Alanine aminotransferase; PT: Prothrombin time; LN: Lipoprotein (a); LYM: Lymphocyte count; PNI: Prognostic Nutritional Index.

Table 4. Values of predictors related to rebleeding

Marker	Value assignment
Portal vein internal diameter (cm)	≥1.405=1, <1.405=0
Child-Pugh Rating	≥9.5=1, <9.5=0
PLT (*10^9/L)	≥98=1, <98=0
ALB (g/L)	≥31.02=1, <31.02=0
ALT (μ/L)	≥40.075=1, <40.075=0
PT (s)	≥13.5=1, <13.5=0
LN (μg/L)	≥187.995=1, <187.995=0
LYM (*10^9/L)	≥1.07=1, <1.07=0
PNI	≥310.256=1, <310.256=0
Age	≥65 years =1, <65 years =0
Bleeding	Rebleeding group =1, non-rebleeding group =0

Note: PLT: Platelet count; ALB: Albumin; ALT: Alanine aminotransferase; PT: Prothrombin time; LN: Lipoprotein (a); LYM: Lymphocyte count; PNI: Prognostic Nutritional Index.

Table 5. Multivariate logistic regression analysis results

Marker	β	Standard error	Chi-square value	*P*-value	OR value	95% CI	
						Lower limit	Limit
Age	1.287	0.784	2.693	0.101	3.623	0.779	16.853
Portal vein internal diameter	2.165	0.868	6.226	0.013	8.717	1.591	47.759
Child_Pugh	1.472	0.789	3.478	0.062	4.360	0.928	20.487
PLT	-5.100	1.273	16.058	<0.001	0.006	0.001	0.074
ALT	-5.990	1.742	11.828	0.001	0.003	<0.001	0.076
PT	2.160	0.853	6.417	0.011	8.671	1.630	46.118
LN	0.568	1.027	0.306	0.580	1.764	0.236	13.196
LYM	-2.224	0.796	7.804	0.005	0.108	0.023	0.515
PNI	-1.966	0.783	6.310	0.012	0.140	0.030	0.649

Note: PLT: Platelet count; ALT: Alanine aminotransferase; PT: Prothrombin time; LN: Lipoprotein (a); LYM: Lymphocyte count; PNI: Prognostic Nutritional Index. Because of the covariance between ALB and PIN, we selected PIN but excluded ALB for the analysis.

of patients with end-stage cirrhosis. These patients typically have higher rates of morbidity, major bleeding, rebleeding, and mortality [15]. Increased or obstructed blood flow in the portal vein increases pressure in the portal vein and its branches, resulting in collateral circulation

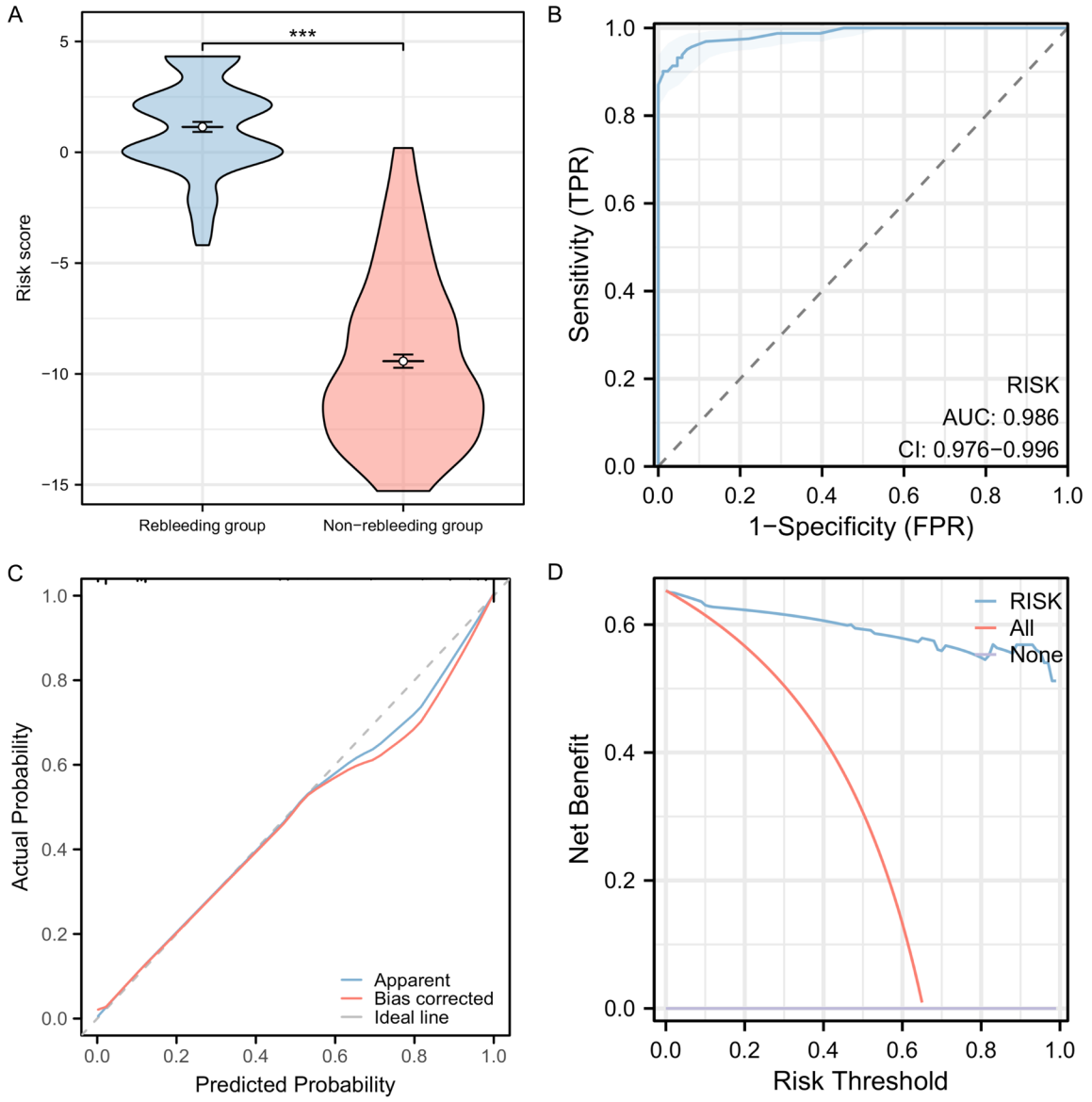

Figure 3. Assessment of the predictive value of the logistic regression model. A. Comparison of logistic regression risk scores of patients between the rebleeding group and the non-bleeding group. B. ROC curves of risk scores for predicting rebleeding in patients. C. Assessment of the accuracy of the calibration curves for the logistic regression prediction models. D. DCA curve for clinical value assessment of logistic regression prediction models. Note: ***P<0.001.

[16]. Although collateral circulation is a compensatory response, it is ineffective in relieving portal hypertension. Endoscopic sclerotherapy combined with tissue glue injection is a standard treatment for EGVB [17]. However, rebleeding is still a serious condition in this type of patients, which poses challenges to their health and prognostic outcomes, despite the successful examples of endoscopic treatment for EGVB [18]. Endoscopic therapy related-rebleeding has been tackled in some studies to a certain extent. Limitations of the therapy still exist.

This study found that portal vein internal diameter, PLT, ALT, PT, LYM, and PNI were independent risk factors of rebleeding in hepatitis B related cirrhosis patients with EVGB following endoscopic therapy. These risk factors were analyzed in three perspectives: vascular characteristics, hematological parameters, and the indicators of liver function and nutritional status.

Vascular characteristics: The increase in the internal diameter of the portal vein reflects the

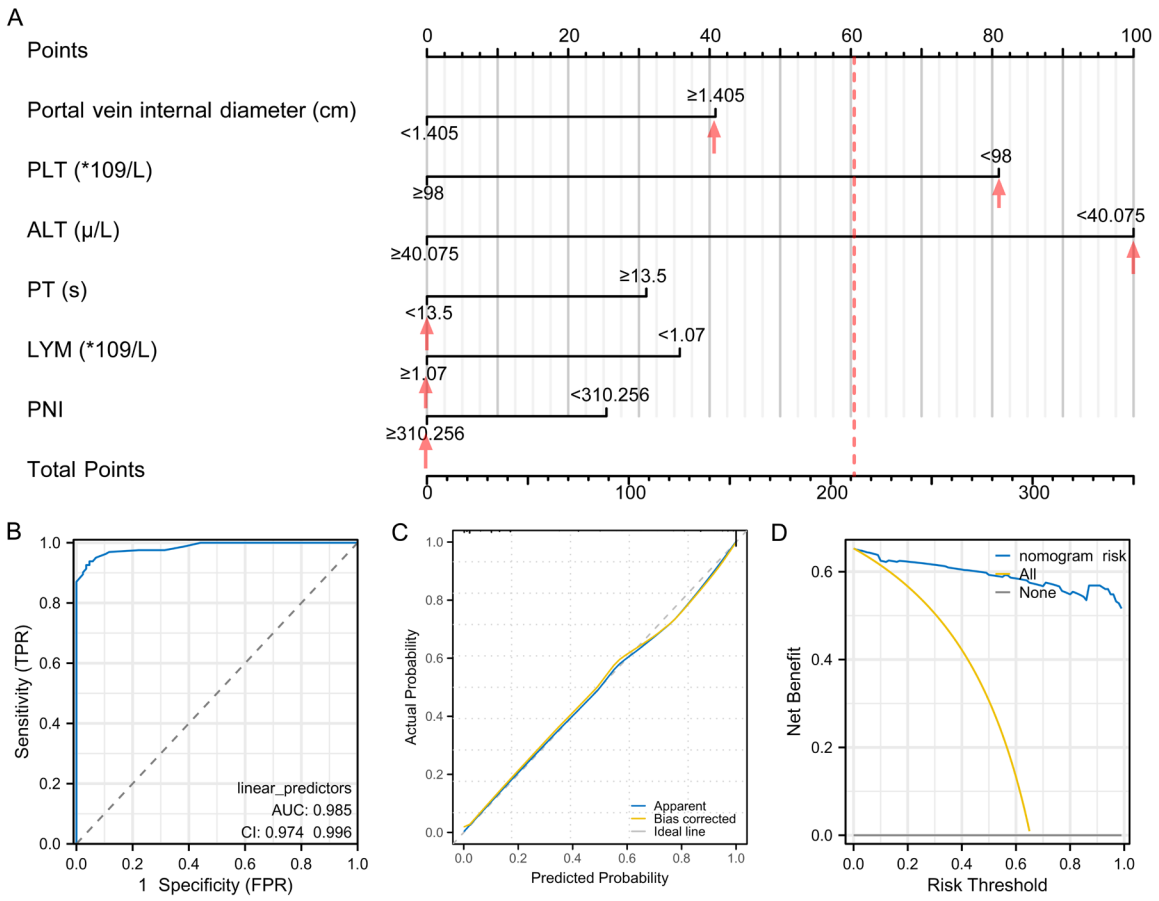

Figure 4. The risk factor nomogram model. A. Visualized nomogram of risk factors. B. The ROC curves of risk scores for predicting rebleeding in patients. C. Assessment of the accuracy of the calibration curves for the nomogram prediction model. D. The DCA curves for clinical value assessment of the nomogram prediction model. Note: The red markers are the corresponding scores of the patients' indicators, and the dotted line is the total score of the patients with the probability of incidence.

presence and worsening of portal hypertension, which is a direct manifestation of cirrhosis progression [19]. Portal hypertension leads to blood flow to low-pressure collateral circulation, including the esophagogastric fundus vein, increasing its risk of rupture and bleeding. Increased internal diameter of the portal vein can be considered as a surrogate for increased portal pressure and is therefore a significant risk factor for rebleeding in EGVB. Previously, Wu et al. [20] found that hepatic venous pressure gradient was significantly higher in patients in the rebleeding group before endoscopic treatment than those in the non-bleeding group. Logistic regression analysis showed that high hepatic venous pressure gradient (HVPG) was the only risk factor for failure of combined endoscopic treatment. In the context of cirrhosis, an increase in HVPG reflects an increase in hepatic resistance to blood flow, and this increase in resistance leads to increased pressure in the portal venous system, which in turn leads to dilatation of the internal diameter of the portal vein. The study by Wu et al. [20] highlighted the importance of high HVPG as an independent predictor of endoscopic treatment failure. This finding supports the use of the internal diameter of the portal vein as an essential parameter in assessing the risk of rebleeding in EGVB.

Hematological parameters: PLT plays a critical role in blood coagulation and hemostasis [21]. Low PLT count (thrombocytopenia) is one of the common complications of cirrhosis, attributing from excessive removal of PLT due to decreased hepatic ability to synthesize clotting factors and hypersplenism [22]. A low PLT count reduc-

es the hematological ability to clot and increases the risk of bleeding, making it a risk factor for rebleeding in EGVB. In their study, Iijima et al. [23] proposed thrombocytopenia as a risk factor for bleeding in atrial fibrillation and coronary artery disease. In addition, Zhuang et al. [24] found that decreased PLT count was an independent risk factor for rebleeding in patients with acute upper gastrointestinal bleeding. These findings have covered multiple clinical scenarios and highlighted the importance of PLT levels in the assessment and management of bleeding risks in patients. Comprehensive assessment of PLT levels and timely intervention are necessary to minimize bleeding-associated complications and improve patients' prognosis.

Indicators of liver function and nutritional status: Elevated Alanine aminotransferase (ALT) indicates the presence of liver injury or inflammation, which may lead to increased portal hypertension and EGVB [25]. Prolonged PT indicates impaired coagulation mechanisms, increasing the likelihood of bleeding. Decreased LYM may reflect decreased immune function, which increases the risk of complications, for instance infection, indirectly affecting the treatment and prognosis of EGVB patients. Previously, the study by Liang et al. [26] found that PT>18 s was an independent risk factor for early variceal rebleeding after endoscopic variceal ligation. Low PNI, an indicator of malnutrition, suggests that patient's overall health is poor, which may exacerbate disease progression and increase the risk of rebleeding. Together, these factors increase the risk of rebleeding in hepatitis B-related patients with EGVB after endoscopic therapy, emphasizing the importance of comprehensive assessment and early intervention of patients' liver function, coagulation status, immunity, and nutritional status.

Lastly, we constructed a prediction model based on logistic regression coefficients. With the constructed logistic regression model and its visualized risk factor prediction model (nomogram), this study significantly improved the predictive accuracy of the prediction models for rebleeding risks from EGVB following endoscopic treatment in hepatitis B related cirrhotic patients and extended their clinical applications. These tools not only demonstrated a high degree of efficacy in predicting the risk of rebleeding in patients with an AUC value of 0.986 by integrating multiple vital factors such as portal vein internal diameter, PLT, ALT, PT, LYM and PNI, but also proved the utility of the models in supporting clinical decision-makings as well as the high net benefit through the calibration curve and DCA curve analyses. Previously, the study by He et al. [27] found that the ROC curve of a model constructed by Cox regression for rebleeding after endoscopic treatment of EGVB in patients with cirrhosis was 0.773. In addition, Tantai et al. [28] found that Child-Turcotte-Pugh score and clinical Rockall score had AUCs of 0.717 and 0.716, respectively, in predicting the rate of in-hospital rebleeding. Furthermore, Rao et al. [29] showed that the C-index of the predictive model constructed with computed tomography imaging features reached 0.854 in predicting rebleeding in patients. The AUC and C-index of our constructed risk factor prediction model were significantly higher than those in the previous study, demonstrating high feasibility and practical value of our model in clinical settings. As an intuitive risk factor visualization tool, the nomogram allows clinicians to quickly assess patients' risk of rebleeding, enabling personalized risk management and optimization of therapeutic strategies, significantly improving the accuracy and efficiency of medical decision-making. Therefore, at the end of the study, we constructed a nomogram that provides clinicians with a powerful tool to assess and manage the risk of EGVB rebleeding in cirrhotic patients. By integrating key variables such as portal vein internal diameter, PLT, ALT, PT, LYM and PNI, this nomogram not only allows for a quick and intuitive prediction of a patient's likelihood of rebleeding, but also enables physicians to develop a more personalized treatment plan based on the specifics of each patient.

The limitations of this study, such as the small sample size and retrospective design, may have affected the generalizability of the prediction model and the accuracy of the results. To address these limitations and refine our conclusions, we plan to expand the sample size in future studies to include patient populations from different regions, ethnicities, and cirrhosis disease courses, and to adopt a multicenter collaborative approach to improve the generalizability and applicability of the model. In the

meantime, a prospective study design will be taken into consideration to accurately document and evaluate the factors that influence the risk of EGVB rebleeding.

Conclusion

In this study, we have successfully constructed a logistic regression model and its risk factor visualized nomogram to predict the risk of rebleeding in hepatitis B-related patients with EGVB after endoscopic treatment, with an AUC value of 0.986, demonstrating very high predictive accuracy and clinical application value. This finding has supported the implementation of personalized risk management and the optimization of therapeutic strategies.

Disclosure of conflict of interest

None.

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