BMC Gastroenterology

RESEARCH

Open Access

Development and evaluation of a predictive model of upper gastrointestinal bleeding in liver cirrhosis

Jin Peng[1†], Huiru Jin[1†], Ningxin Zhang[1†], Shiqiu Zheng[1], Chengxiao Yu[2,3], Jianzhong Yu[4*] and Longfeng Jiang[1*]

Abstract

Background Upper gastrointestinal bleeding (UGIB) is a prevalent and severe complication of cirrhosis, often resulting from esophagogastric variceal bleeding (EVB). This condition poses significant life-threatening risks. Once bleeding occurs, the risk of recurrent episodes substantially increases, further compromising liver function and worsening patient outcomes. This study aims to identify risk factors for UGIB in cirrhotic patients using clinical examination data and to develop a non-invasive predictive model to improve diagnostic precision and efficiency.

Methods Based on the inclusion and exclusion criteria, the study included 140 cirrhotic patients hospitalized at the First Affiliated Hospital of Nanjing Medical University between June 2022 and May 2023, who experienced UGIB within six months after discharge. These patients were compared with 151 cirrhotic patients hospitalized at the same hospital during the same period, who were discharged within six months without experiencing UGIB. General characteristics of the patients during hospitalisation, laboratory parameters on admission, and liver and spleen stiffness were retrospectively collected, and a retrospective case-control study was conducted. All patients were randomly assigned to the training and validation sets in a ratio of 7:3. Independent factors associated with UGIB were identified by univariate analysis, multivariate logistic regression analysis, and stepwise regression analysis, on the basis of which a predictive model was developed. The model's performance was assessed via receiver operating characteristic (ROC) curve and decision curve analysis (DCA) and was compared with established prognostic models, including the Child-Pugh and MELD scores.

Results The study analyzed 291 patients with cirrhosis, of whom 208 were allocated to the training set and 83 to the validation set. Independent predictors were identified, and predictive models were constructed using multivariate logistic regression analysis, and stepwise regression analysis in the training set, followed by validation in the validation set. The stepwise regression analysis identified ascites, spleen stiffness, albumin, fibrinogen, total cholesterol, and total bilirubin as independent predictors of UGIB *($P < 0.05$)*. These variables were incorporated into the predictive

[†]Jin Peng, Huiru Jin and Ningxin Zhang contributed equally to this article and should be regarded as co-first authors.

*Correspondence:
Jianzhong Yu
yujianzhong1981@163.com
Longfeng Jiang
longfengjiang@njmu.edu.cn

Full list of author information is available at the end of the article

© The Author(s) 2025. **Open Access** This article is licensed under a Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License, which permits any non-commercial use, sharing, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if you modified the licensed material. You do not have permission under this licence to share adapted material derived from this article or parts of it. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit http://creativecommons.org/licenses/by-nc-nd/4.0/.

model. The area under the curve (AUC) for UGIB prediction was 0.956 in the training set and 0.909 in the validation set, demonstrating strong predictive performance. Furthermore, comparative analysis using ROC and DCA demonstrated that the developed model outperformed established scoring systems, such as the Child-Pugh score and the MELD score.

Conclusion Ascites, spleen stiffness, albumin, fibrinogen, total cholesterol and total bilirubin as independent predictors of UGIB in cirrhotic patients.

Keywords Cirrhosis, Upper gastrointestinal bleeding, Prediction model, Retrospective case-control study

Introduction

Cirrhosis is a common chronic progressive disease frequently encountered in clinical practice. In its advanced stages, it is characterized by hepatic decompensation and portal hypertension, making it a significant contributor to the morbidity and mortality associated with chronic liver disease [1]. According to statistics, cirrhosis was responsible for 2.4% of all global deaths in 2019 [2]. Upper gastrointestinal bleeding (UGIB) occurs in more than 30% of patients with cirrhosis, while up to two-thirds of cirrhotic patients develop concomitant esophageal varices, both of which significantly reduce survival rates [3, 4]. Therefore, prediction of UGIB in patients with cirrhosis and accurate assessment of disease severity are crucial for improving patient prognosis. Studies indicate that laboratory parameters (e.g., total bilirubin [TBIL], serum creatinine [Scr], and total cholesterol [TC]), together with clinical indicators (e.g., liver stiffness [LS], spleen stiffness [SS], and the presence of abdominal fluid), are associated with UGIB occurrence in cirrhotic patients [5–11]. Although some studies support these findings, no comprehensive analyses or predictive models have been established, and threshold values vary considerably across studies. In this context, this study aims to develop and validate a non-invasive predictive model using multivariable analysis to assess the risk of UGIB in cirrhotic patients. Following the TRIPOD (Transparent Reporting of a multivariable prediction model for Individual Prognosis Or Diagnosis) guidelines [12], we designed the study and reported the results with strict adherence to standards. By identifying key independent predictive factors, we developed a predictive model and compared its performance with traditional scoring systems. This approach aims to enhance diagnostic accuracy and provide valuable insights to support improved patient management.

Methods

Research design

This study was approved by the Ethics Committee of the First Affiliated Hospital of Nanjing Medical University (Nanjing, Jiangsu Province, China), with approval number 2023-SR-395. Designed as a single-center retrospective case-control study, it strictly adheres to the TRIPOD guidelines for design and reporting. The primary objective of this study is to develop and validate a non-invasive predictive model for assessing the risk of UGIB in patients with liver cirrhosis, encompassing data collection, variable selection, model development, and performance validation.

Patient selection

This study retrospectively enrolled 291 patients with liver cirrhosis, including 119 men and 172 women, who met the specified inclusion and exclusion criteria, between June 2022 and May 2023. A total of 140 patients with cirrhosis hospitalized at the First Affiliated Hospital of Nanjing Medical University during the study period, who experienced UGIB within six months of discharge, were included in the study. These patients were compared with 151 patients with cirrhosis hospitalized during the same period at the same hospital, who were discharged within six months without developing UGIB. We retrospectively collected data on general characteristics (including age, sex, ascites status, and hepatic encephalopathy) as well as laboratory and instrumental findings (including complete blood count, liver and renal function markers, coagulation parameters, and liver and spleen stiffness) for all enrolled patients after hospital admission. A total of 291 patients were randomly allocated to the training and validation sets in a 7:3 proportion. A normality test confirmed that all analyzed variables deviated from a normal distribution. The chi-square test was employed to assess potential risk factors for UGIB in patients with cirrhosis. Multivariate logistic regression and stepwise regression analyses were subsequently performed on the training set to identify independent predictors of UGIB and develop a predictive model, which was validated using the validation set. Finally, the predictive model was evaluated against established scoring systems, including the Child-Pugh and MELD scores, through receiver operating characteristic (ROC) curve analysis and decision curve analysis (DCA).

All patients fulfilled the diagnostic criteria established by the guidelines for the diagnosis and management of cirrhosis. The inclusion criteria were as follows: (1) diagnosis of cirrhosis confirmed by ultrasound, CT scan, liver biopsy, or liver stiffness measurement; (2) UGIB cases met the diagnostic criteria for UGIB [13]; (3) age ≥ 18

years and < 75 years; (4) adherence to prescribed medications and regular follow-ups, with complete relevant data available. The exclusion criteria were: (1) patients with a history of gastrointestinal bleeding; (2) incomplete clinical data; (3) patients with consciousness, mental disorders and severe metabolic abnormalities; (4) patients on antiplatelet, anticoagulant and lipid-lowering drugs; (5) history of splenectomy, TIPS surgery, or endoscopic variceal ligation/sclerotherapy; (6) patients with confirmed portal vein thrombosis or non-cirrhotic conditions affecting spleen stiffness (e.g., hematological disorders, splenic tumors, parasitic infections); (7) gastrointestinal bleeding during hospitalisation and presence of malignant tumours.

All patients were fully informed about the study's purpose, provided their consent to participate, and signed an informed consent form.

Liver and spleen stiffness test

The detection was performed using a FibroScan PRO® transient elastography device (Echosens, France). A qualified operator conducted the procedure following the FibroScan user manual and standard operating procedures. The patient was positioned supine with the intercostal space fully exposed. For liver stiffness measurements, the detection area was located between the 7th and 9th intercostal spaces, from the right anterior axillary line to the mid-axillary line. For spleen stiffness measurements, the detection area was positioned between the 9th and 11th intercostal spaces, along the left posterior axillary line. During the procedure, the probe was held perpendicular to the patient's skin. The median value of ten successful measurements was used to represent liver and spleen stiffness, expressed in kilopascals (kPa). A valid measurement was defined as one with a success rate above 60% and an interquartile range-to-median ratio *(IQR/M)* under 0.3.

APRI, FIB-4, ALBI calculation formulae

APRI score formulae [14] is: APRI={[AST/upper limit of normal (ULN)]/platelet count (10^9/L)} × 100.

FIB-4 index [15] is: FIB-4=(age×AST)/(platelet count×ALT^1/2), where the reference value of AST and ALT is 40 U/L.

ALBI Score [16] is: ALBI Score =(Log_{10} TBIL×0.66)+(Albumin×-0.085).

Statistical methods

Data were analyzed using IBM SPSS Statistics version 25.0. Skewed quantitative data were presented as the median *(P25, P75)*, and the chi-square test was used for between-group comparisons. Statistically significant variables from univariate analyses in the training set were subjected to multiple logistic regression and stepwise regression analyses to identify independent predictors and develop UGIB prediction models, which were subsequently validated in the validation set. Model performance was assessed using ROC and DCA, and statistical significance was defined as $\alpha = 0.05$ for a two-sided test.

Results

General characteristics

Between June 2022 and May 2023, a total of 354 patients with cirrhosis who met the inclusion criteria and were admitted to the First Affiliated Hospital of Nanjing Medical University were retrospectively reviewed. Among them, 99 patients had hepatitis B. Patients with hepatic malignancy ($n = 28$) were excluded, along with those who had undergone splenectomy or liver transplantation ($n = 20$) and those with incomplete clinical data ($n = 15$). As a result, the final study cohort comprised 291 patients, as illustrated in the flowchart in Fig. 1. Among these patients, 140 had cirrhosis complicated by UGIB, while 151 had uncomplicated cirrhosis. Baseline characteristics are presented in Table 1. The 291 patients were randomized into training and validation sets in a 7:3 ratio. The training set included 208 patients with cirrhosis, 99 of whom had UGIB, while the validation set consisted of 83 patients with cirrhosis, 41 of whom had UGIB. The baseline characteristics of the patients in the training and validation sets are summarized in Table 2. No significant differences were detected between the two groups *($P > 0.05$)*.

Predictors of UGIB and formulation of the model

Using UGIB as the dependent variable, multivariate logistic regression and stepwise regression analyses of statistically significant variables from univariate analyses in the training set identified ascites, SS, albumin (ALB), fibrinogen (FIB), TC, and TBIL as independent predictors of UGIB in cirrhotic patients ($P < 0.05$). Among them, ALB, FIB and TC were negatively associated with UGIB (Table 3). These independent predictors were incorporated into a predictive model, which exhibited excellent performance across the training, validation, and overall datasets, with area under the curve (AUC) values of 0.956, 0.909, and 0.941, respectively (Table 4).

The predictive models were compared with the Child-Pugh score, MELD score, ALBI score, and other models across the training set, validation set, and overall dataset. Figure 2A illustrates the ROC curve for UGIB prediction in cirrhotic patients in the training set, with an AUC of 0.956 [95% confidence interval (*CI*): 0.929–0.984]. The ROC curve for the validation set is depicted in Fig. 2B, with an AUC of 0.909 [95% *CI*: 0.839–0.978]. For all patients combined, the ROC curve is presented in Fig. 2C, with an AUC of 0.941 [95% *CI*: 0.914–0.968]. In all three datasets, the predictive model demonstrated

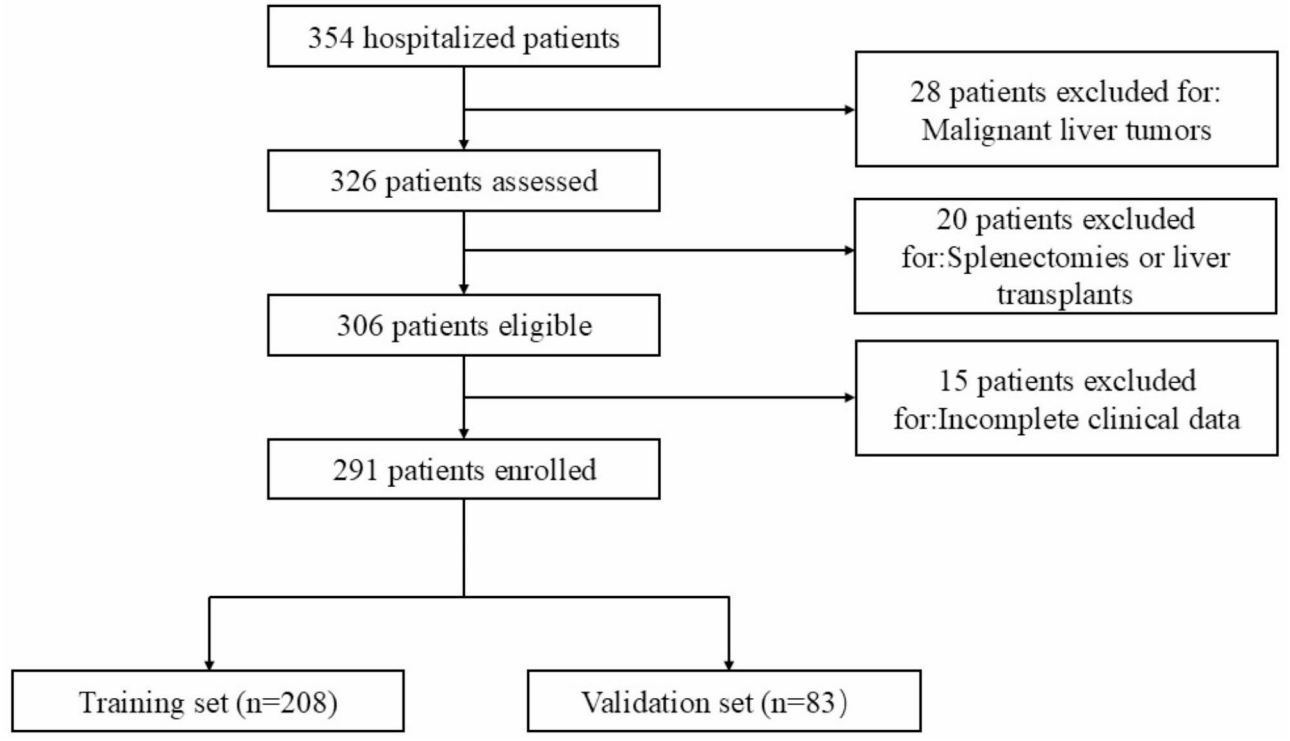

Fig. 1 Flow diagram depicting the participant selection process

Table 1 Characteristics of patients in the UGIB and non-UGIB sets at baseline

Variable	UGIB set(*n* = 140)	non-UGIB set(*n* = 151)	*P* value
Age (year)	54(45,64)	51(41,61)	0.071
Male sex (%)	54(38.6%)	65(43.0%)	0.438
Ascites (%)	91(65.0%)	45(29.8%)	0.000
Hepatic Encephalopathy (%)	72(51.4%)	35(23.2%)	0.000
Viral hepatitis B (%)	40(28.6%)	59(39.1%)	0.059
LS (kPa)	40.6(34.9,50.7)	25.5(17.8,29.9)	0.006
SS (kPa)	72.8(59.3,81.1)	46.0(27.9,55.2)	0.001
PLT (10^9/L)	90.8(85.7,98.1)	106.6(75.0,166.0)	0.000
ALT (U/L)	59.3(45.6,71.8)	57.3(47.3,73.4)	0.941
AST (U/L)	78.6(70.9,98.5)	51.9(40.6,63.5)	0.006
APRI	2.29(1.65,2.89)	1.08(0.75,1.87)	0.000
FIB-4	5.71(4.31,7.66)	3.06(2.20,5.34)	0.000
Hb (g/L)	69.1(58.0,78.8)	94.8(86.0,102.8)	0.227
ALB (g/L)	28.6(24.3,31.9)	36.3(34.1,40.1)	0.000
TBIL (umol/L)	46.5(35.3,60.5)	26.1(19.8,34.8)	0.000
Scr (umol/L)	66.2(54.7,77.0)	44.7(39.3,53.1)	0.000
FIB (g/L)	1.50(1.03,1.68)	2.19(1.82,2.55)	0.000
TC (mmol/L)	3.13(2.95,3.19)	3.26(2.94,3.36)	0.000
PT (s)	16.5(15.5,17.8)	13.5(12.5,15.0)	0.000

Quantitative variables are reported as the median *(IQR: 25th–75th percentile).*

Categorical variables are expressed as numbers (percentages)

LS Liver stiffness; *SS* Spleen stiffness; *PLT* Platelet; *ALT* Alanine aminotransferase; *AST* Aspartate aminotransferase; *Hb* Hemoglobin; *ALB* Albumin; *TBIL* Total bilirubin; *Scr* Serum creatinine; *FIB* Fibrinogen; *TC* Total cholesterol; *PT* Prothrombin time

Table 2 Characteristics of patients in the training and validation sets at baseline

Variable	Training set(*n* = 208)	Validation set(*n* = 83)	*P* value
Age (year)	52(44,62)	55(44,64)	0.897
Male sex (%)	84(40.4%)	35(42.2%)	0.780
Ascites (%)	98(47.1%)	38(45.8%)	0.837
Esophagogastric Varices (%)	100(48.1%)	33(39.8%)	0.240
Hepatic Encephalopathy (%)	83(39.9%)	24(28.9%)	0.082
Viral hepatitis B (%)	75(36.1%)	24(28.9%)	0.246
LS (kPa)	30.6(20.4,41.7)	30.8(19.1,41.0)	0.821
SS (kPa)	55.2(39.0,73.0)	54.0(38.8,72.4)	0.746
PLT (10^9/L)	93.0(77.2,144.2)	95.5(79.3,140.0)	0.579
ALT (U/L)	57.6(45.9,71.2)	60.0(46.8,73.6)	0.979
AST (U/L)	64.0(44.4,83.0)	63.5(43.9,81.5)	0.834
APRI	1.80(0.90,2.48)	1.70(0.89,2.43)	0.864
FIB-4	4.65(2.73,6.43)	4.60(2.75,6.47)	0.572
Hb (g/L)	85.6(67.0,100.0)	84.3(64.9,101.0)	0.921
ALB (g/L)	33.9(27.6,38.3)	33.9(27.7,37.9)	0.794
TBIL (umol/L)	34.9(24.1,53.2)	34.8(22.8,50.1)	0.617
Scr (umol/L)	53.7(41.1,70.8)	54.4(41.1,74.4)	0.952
FIB (g/L)	1.82(1.39,2.40)	1.78(1.34,2.43)	0.614
TC (mmol/L)	3.18(2.96,3.31)	3.19(2.89,3.42)	0.515
PT (s)	15.1(12.8,16.7)	14.8(12.7,16.8)	0.642

Quantitative variables are expressed as median *(25th percentile; 75th percentile)*

Categorical variables are expressed as numbers (percentages)

Table 3 Results of multivariable binary logistic stepwise regression analysis for UGIB in cirrhotic patients

Variable	Regression Coefficient (B)	Standard Error (SE)	Standardized Coefficient (β)	t value	*P* value
ALB	-0.051	0.007	-0.684	-7.263	0.000
TC (mmol/L)	-0.212	0.033	-0.282	-6.365	0.000
SS (kPa)	0.007	0.001	0.344	5.799	0.000
TBIL (umol/L)	0.007	0.001	0.305	5.203	0.000
FIB (g/L)	-0.411	0.071	-0.610	-5.767	0.000
Ascites	0.123	0.045	0.123	2.738	0.007

ALB Albumin; *TC* Total cholesterol; *SS* Spleen stiffness; *TBIL* Total Bilirubin; *FIB* Fibrinogen

the highest AUC when compared to the other models (Fig. 2).

To enhance clinical applicability, this study visualized the predictive model by constructing a nomogram (Fig. 3A), which intuitively represents the relationships among the six variables included in the model. Calibration curves for the training and validation sets are shown in Fig. 3B and C, respectively, demonstrating that the predicted risk closely aligns with the observed risk. Additionally, DCA were conducted for both the training and validation sets to evaluate the clinical utility of the model, with comparisons made against the Child-Pugh score, MELD score, ALBI score, and others (Fig. 3D, E). The results indicated that the predictive model provided substantial net benefits, highlighting its high clinical value and suitability for guiding clinical decision-making.

Discussion

Cirrhosis is a pathological condition characterized by diffuse liver fibrosis, the formation of pseudolobules, and the proliferation of intrahepatic and extrahepatic blood vessels [17]. Cirrhosis may remains asymptomatic in the compensated stage; however, as the disease progresses to the decompensated stage, complications such as gastrointestinal bleeding, hepatic encephalopathy, hepatorenal syndrome, portal vein thrombosis, and ascites commonly develop [18]. Among these complications, upper gastrointestinal hemorrhage is the second most prevalent condition in cirrhotic patients, following ascites, and continues to be a major cause of mortality [19]. Therefore, understanding the risk factors for UGIB in cirrhotic patients and enhancing its prediction and diagnosis are crucial for effective clinical management and reducing patient mortality.

Upper gastrointestinal bleeding is a life-threatening complication with a high mortality rate among critically ill patients with liver cirrhosis. This study aimed to develop a diagnostic model for UGIB prediction using a retrospective case-control study of cirrhotic patients. Data on general characteristics—including gender, age, ascites, hepatic encephalopathy, complete blood count, liver and renal function markers, coagulation parameters, as well as liver and spleen stiffness during hospitalization—were collected. As the disease progresses, portal hypertension leads to splenic congestion and enlargement, accompanied by tissue hyperplasia, which manifests as increased liver and spleen stiffness values [19]. Semmler et al. demonstrated that monitoring liver stiffness in patients with progressive chronic liver disease

Table 4 The diagnostic accuracy of the model for the prediction of UGIB

	AUR	*P* Value	Cutoff values	95%CI	Se%	Sp%
Training set	0.956	<0.001	0.404	0.929–0.984	92.9	89.9
Validation set	0.909	<0.001	0.416	0.839–0.978	87.8	85.7
All patients	0.941	<0.001	0.408	0.914–0.968	90.7	86.8

Se sensitivity, *Sp* specificity

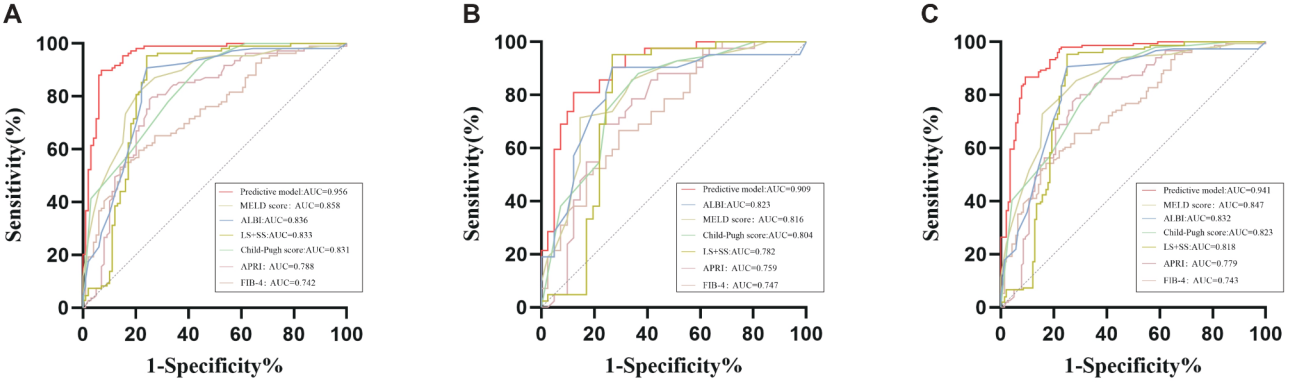

Fig. 2 Comparison between the predictive model and clinical models across training, validation, and overall datasets

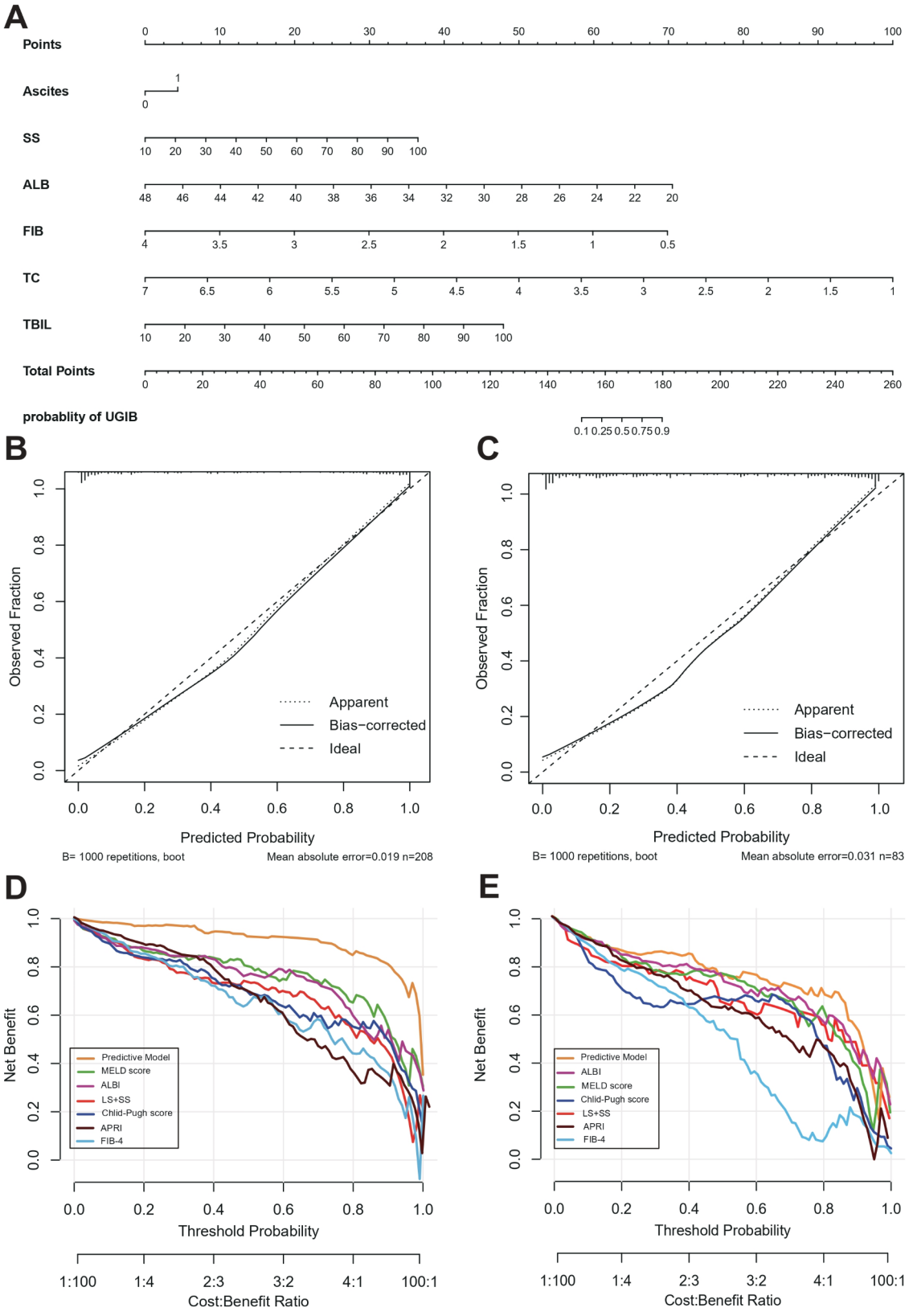

Fig. 3 Nomogram, Calibration, and Decision Curve Analysis for UGIB Prediction **A** Nomogram for predicting the probability of UGIB based on variables including ascites, SS, ALB, FIB, TC, and TBIL. **B**, **C** Calibration curves for the predictive model in the training set (**B**) and validation set (**C**), demonstrating good agreement between predicted and observed probabilities. **D**, **E** Decision curve analysis (DCA) comparing the predictive model with a traditional models in the training set (**D**) and validation set (**E**) shows superior net benefits of the predictive model

allows for real-time assessment of the risk of cirrhotic decompensation events [20]. A meta-analysis further suggested that splenic stiffness testing can help patients with chronic liver disease avoid unnecessary invasive procedures by identifying those at low risk of esophageal varices [21]. In this study, liver and spleen stiffness values were significantly higher in cirrhotic patients with UGIB compared to those without UGIB, and the differences were statistically significant.

Total bilirubin is widely used in clinical practice to assess liver function, as its levels reflect the liver's synthetic and excretory capacities. Prognostic models, such as the Child-Pugh score and MELD score, incorporate TBIL as a key parameter for evaluating clinical outcomes in patients. Additionally, Huttakan et al. highlighted the significant clinical value of the albumin-bilirubin (ALBI) score in identifying patients with decompensated cirrhosis [22]. Labenz et al. observed that targeting patients with significantly elevated AST or ALT levels during initial screening and follow-up examinations can significantly enhance the detection rate of advanced liver fibrosis and early cirrhosis. This approach enables early preventive diagnosis and treatment, ultimately improving patient outcomes [23]. This indicates that changes in liver function directly affect AST levels. Moreover, during the decompensated phase of cirrhosis, renal vasoconstriction and a reduction in glomerular filtration rate occur as a result of portal hypertension, significant disruptions in arterial circulation, and overactivation of the endogenous vasoactive system [24]. Both Giusepp et al. and Tomasz et al. demonstrated that serum creatinine levels vary significantly in patients with advanced liver disease. These fluctuations are closely associated with mortality and serve as reliable predictors of short- and medium-term survival in patients with end-stage liver disease [25, 26]. Although these parameters have been shown to increase in patients with cirrhosis, their predictive value for UGIB has not been extensively studied in this population. To address this gap, we conducted a retrospective study in cirrhotic patients to develop a predictive model for identifying UGIB.

This study, following TRIPOD guidelines, developed a non-invasive prediction model for UGIB in cirrhotic patients, incorporating six independent factors: ascites, SS, ALB, FIB, TC, and TBIL. The Baveno VI guidelines recommend using a combination of LS and PLT count to evaluate the presence of clinically significant portal hypertension in cirrhotic patients. Furthermore, the Baveno VII guidelines suggest that a spleen stiffness value of <40 kPa can reliably exclude high-risk varices based on the Baveno VI criteria, with a missed diagnosis rate of less than 5% in patients with esophageal varices [27]. Liver stiffness is the most effective non-invasive method for quantifying portal hypertension in patients with compensated progressive chronic liver disease [28]. Spleen stiffness provides additional insights into the severity of portal hypertension, the presence of esophageal varices, and the associated risk of hemorrhage [29]. Yang LB et al. developed a non-invasive predictive model incorporating SS and LS metrics to evaluate the severity of esophageal and gastric varices and the risk of UGIB. The model demonstrated excellent performance and strong diagnostic efficacy.

Similar to the prediction model developed by Yang LB et al., the prediction model established in this study demonstrates a higher AUC value (0.956 vs. 0.833) [10]. Furthermore, compared to the AST-to-Platelet Ratio Index (APRI) and FIB-4 scores, the new model exhibits superior diagnostic performance.

The clinical significance and predictive value of ascites, SS, ALB, FIB, TC, and TBIL for predicting UGIB can be summarized as follows. First, portal hypertension induces splenic congestion, hematoma formation, and tissue proliferation, leading to increased stiffness in both the liver and spleen. The hyperdynamic circulation in the spleen is more pronounced than in the liver, making spleen stiffness a particularly accurate marker for predicting portal hypertension [30–32]. Additionally, the presence of ascites often signifies advanced liver disease and increased portal hypertension, which elevate the risk of variceal rupture and worsen the prognosis [33–35]. In this study, we identified spleen stiffness and ascites as predictors of UGIB, consistent with the aforementioned findings.

Secondly, ALB is synthesized by hepatocytes and secreted into the bloodstream. In addition to maintaining plasma colloid osmotic pressure, ALB plays a crucial role in substance binding and transport, immune regulation, mitigating inflammatory damage, and protecting vascular endothelial cells [36]. Patients with cirrhosis often develop hypoalbuminemia due to severely impaired liver function. TBIL not only serves as a key indicator of liver dysfunction but is also closely associated with the occurrence and prognosis of UGIB. Elevated bilirubin levels indicate more severe disease and an increased risk of UGIB [37]. Combining total bilirubin with other liver function indicators can provide a more comprehensive approach to clinical assessment and intervention. In a study by Oikonomou et al., ALB was combined with bilirubin and platelet count to develop models such as the Albumin-Bilirubin (ALBI) score and the Platelet-ALBI (PALBI) score. Both models demonstrated strong predictive value for assessing the prognosis of patients with stable cirrhosis in the decompensated stage [38]. In this study, low albumin and high bilirubin levels were identified as independent risk factors for UGIB. Low albumin levels may increase the risk of infection and systemic inflammation, potentially leading to organ dysfunction

in patients with decompensated cirrhosis. Additionally, hypoalbuminemia can impair vascular endothelial cell function and increase capillary permeability, further contributing to the risk of UGIB [39]. Additionally, elevated total bilirubin (TBIL) exacerbates hepatic dysfunction, aggravates portal hypertension, and impairs coagulation, all of which contribute to UGIB and increase the risk of variceal rupture and mucosal injury [40].

Thirdly, fibrinogen is a glycoprotein synthesized and secreted by hepatocytes, playing a pivotal role in coagulation and hemostasis processes. Desborough et al. were the first to establish a direct relationship between FIB levels and the clinical prognosis of patients with cirrhosis, showing that for every 1 g/L decrease in FIB, the mortality rate increased by 29%. Consequently, FIB serves as an independent predictor of mortality outcomes in these patients [41]. In this study, we compared the fibrinogen levels of cirrhotic patients with UGIB to those without UGIB and found that the former had significantly lower FIB levels. This finding reinforces the conclusion that low FIB is an independent risk factor for cirrhosis complicated by upper gastrointestinal bleeding.

Finally, total cholesterol, as a sterol compound, plays a crucial role in the construction of cellular membranes. Low TC levels can increase the fragility of erythrocytes and vascular endothelial cells, leading to thinning of vessel walls and reduced elasticity. These changes make blood vessels more prone to rupture and bleeding due to vasculopathy [41]. Low TC levels have been shown to be closely associated with the occurrence of decompensation events and decreased survival rates in patients with liver cirrhosis [42]. In this study, we observed lower TC levels in the cirrhosis group with UGIB compared to the group without UGIB, low TC levels were found to independently influence patients' clinical outcomes. This finding is consistent with the conclusions of Stefanutti et al., who demonstrated that low lipid levels contribute to complications such as liver and kidney damage, as well as gastrointestinal bleeding [43].

This study has several limitations. First, as a single-center case-control study, the relatively homogeneous patient population resulted in a limited dataset, potentially introducing bias. Second, only internal validation was performed, highlighting the need for future prospective studies with larger sample sizes to confirm the model's reliability and generalizability. Lastly, stratified analyses of antiviral therapy and non-selective beta-blockers (NSBB) were not conducted, as the study included only patients with hepatitis B and those regularly taking NSBB. Future research incorporating these factors could enhance risk prediction and improve the model's clinical applicability.

Conclusion

In this study, ascites, SS, ALB, FIB, TC, and TBIL were identified as independent predictors of upper gastrointestinal bleeding in patients with cirrhosis through stepwise regression analysis. Using these clinical indicators, a nomogram diagnostic model was developed, offering a simple, efficient, and personalized approach to diagnosing UGIB with promising potential for clinical application. However, despite the innovative contributions of this study, further multicenter research with larger and more diverse sample sizes is required to validate these findings and improve the diagnostic accuracy and clinical applicability of the nomogram.

Abbreviations

ROC	Receiver operating characteristic
AUC	Area under the curve
DCA	Decision curve analysis
EVB	Esophagogastric variceal bleeding
UGIB	Upper gastrointestinal bleeding
LSPS	Liver stiffness prediction score
LS	Liver stiffness
SS	Spleen stiffness
PLT	Platelet
ALT	Alanine aminotransferase
AST	Aspartate aminotransferase
Hb	Hemoglobin
ALB	Albumin
TBIL	Total bilirubin
Scr	Serum creatinine
FIB	Fibrinogen
TC	Total cholesterol
PT	Prothrombin time
APRI	AST to platelet ratio index
ALBI	Albumin-bilirubin
PALBI	Platelet-ALBI
NSBB	Non-selective beta-blockers
TRIPOD	Transparent Reporting of a multivariable prediction model for Individual Prognosis Or Diagnosis

Diagnostic codes (ICD-10 codes)

K74.5	Biliary cirrhosis, unspecified
K70.3	Alcoholic cirrhosis of liver
K71.7	Toxic liver disease with fibrosis and cirrhosis of liver
K74.6	Other and unspecified cirrhosis
K76.6	Portal hypertension
I85.0	Oesophageal varices with bleeding
I85.9	Oesophageal varices without bleeding
R18	Ascites
K72.91	Liver failure with hepatic encephalopathy

Acknowledgements

We sincerely thank the study participants and their families for their contributions to this study.

Author contributions

J.P.,H-R.J.andN-X.Z.was responsible for the study design, and the initial draft of the manuscript. S-Q. Z. and C-X.Y. undertaken data collection, statistical analyses. J-Z.Y. and L-F.J. contributed to revising the manuscript critically for important intellectual content and approved the final version for publication. All authors reviewed the manuscript critically for important intellectual content and have read and approved the final manuscript.

Funding

This research was supported by Natural Science Foundation of Jiangsu Province (BK20161059).

Data availability
The final results of this study are included in the figures, tables and supplementary materials. Raw data are not publicly available due to privacy and ethical restrictions. For inquiries, contact the corresponding author.

Declarations

Ethics approval and consent to participate
The study was approved by the Ethics Committee of The First Affiliated Hospital of Nanjing Medical University (Approval No.: 2023-SR-395) and conducted in accordance with the Declaration of Helsinki and relevant regulations. All patients were fully informed about the study, provided their consent to participate, and signed an informed consent form.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

TRIPOD guidelines
This study adheres to the TRIPOD reporting guidelines to ensure transparency and rigor in the development of the prediction model.

Author details
[1]Department of Infectious Diseases, The First Affiliated Hospital of Nanjing Medical University, Nanjing, Jiangsu, China
[2]Health Management Center, The First Affiliated Hospital of Nanjing Medical University, Nanjing, Jiangsu, China
[3]Department of Health Management, School of Public Health, Nanjing Medical University, Nanjing, Jiangsu, China
[4]Department of Nephrology, Haian Hospital of Traditional Chinese Medicine Affiliated to Nanjing University of Chinese Medicine, Nantong, Jiangsu, China

Received: 8 October 2024 / Accepted: 11 February 2025
Published online: 06 March 2025

References

1. Ginès P, Krag A, Abraldes JG, Solà E, Fabrellas N, Kamath PS. Liver cirrhosis. Lancet (London England). 2021;398(10308):1359–76.
2. Global health estimates. Leading causes of death. [https://www.who.int/data/gho/data/themes/mortality-and-global-health-estimates/ghe-leading-causes-of-death.]
3. Alqahtani SA, Jang S. Pathophysiology and management of Variceal Bleeding. Drugs. 2021;81(6):647–67.
4. Fouad TR, Abdelsameea E, Abdel-Razek W, Attia A, Mohamed A, Metwally K, Naguib M, Waked I. Upper gastrointestinal bleeding in Egyptian patients with cirrhosis: post-therapeutic outcome and prognostic indicators. J Gastroenterol Hepatol. 2019;34(9):1604–10.
5. Zhou YF, Xu Y, Ding YF, Yu XJ, Wu YL, Chen P, Zou DW. Novel nomogram model for predicting 6-week mortality in liver cirrhosis patients with acute upper gastrointestinal bleeding. J Dig Dis. 2022;23(8–9):516–26.
6. Hsieh YC, Lee KC, Chen PH, Su CW, Hou MC, Lin HC. Acute kidney injury predicts mortality in cirrhotic patients with gastric variceal bleeding. J Gastroenterol Hepatol. 2017;32(11):1859–66.
7. Mandal AK, Paudel MS, Kc S, Chaudhary S, Paudel BN, Poudyal NS, Shrestha B, Karki B, Thapa S, Khadka D, et al. Factors Predicting Mortality of Acute Variceal bleeding in liver cirrhosis. JNMA. 2018;56(209):493–6.
8. Yamuna J, Akila A, Muruganandam VU, Sivakumar K, Natarajan K, Muruganathan A. Lipid Profile as an Indicator of Severity in cirrhosis of liver: hospital based cross-sectional study. J Assoc Phys India. 2023;71(3):11–2.
9. Wong GLH, Kwok R, Hui AJ, Tse YK, Ho KT, Lo AOS, Lam KLY, Chan HCH, Lui RA, Au KHD, et al. A new screening strategy for varices by liver and spleen stiffness measurement (LSSM) in cirrhotic patients: a randomized trial. Liver Int. 2018;38(4):636–44.
10. Yang LB, Gao X, Li H, Tantai XX, Chen FR, Dong L, Dang XS, Wei ZC, Liu CY, Wang Y. Non-invasive model for predicting high-risk esophageal varices based on liver and spleen stiffness. World J Gastroenterol. 2023;29(25):4072–84.
11. Peng YJ, Liu X, Liu Y, Tang X, Zhao QP, Du Y. Computed tomography-based multi-organ radiomics nomogram model for predicting the risk of esophagogastric variceal bleeding in cirrhosis. World J Gastroenterol. 2024;30(36):4044–56.
12. Collins GS, Reitsma JB, Altman DG, Moons KG. Transparent reporting of a multivariable prediction model for individual prognosis or diagnosis (TRIPOD): the TRIPOD statement. BMJ (Clinical Res ed). 2015;350:g7594.
13. [Guidelines on the management of. Esophagogastric variceal bleeding in cirrhotic portal hypertension]. Zhonghua Gan Zang Bing Za Zhi. 2022;30(10):1029–43.
14. Wai CT, Greenson JK, Fontana RJ, Kalbfleisch JD, Marrero JA, Conjeevaram HS, Lok AS. A simple noninvasive index can predict both significant fibrosis and cirrhosis in patients with chronic hepatitis C. Hepatology. 2003;38(2):518–26.
15. Sterling RK, Lissen E, Clumeck N, Sola R, Correa MC, Montaner J, Torriani MSS, Dieterich FJ, Thomas DT. Development of a simple noninvasive index to predict significant fibrosis in patients with HIV/HCV coinfection. Hepatology. 2006;43(6):1317–25.
16. Johnson PJ, Berhane S, Kagebayashi C, Satomura S, Teng M, Reeves HL, O'Beirne J, Fox R, Skowronska A, Palmer D, et al. Assessment of liver function in patients with hepatocellular carcinoma: a new evidence-based approach-the ALBI grade. J Clin Oncology: Official J Am Soc Clin Oncol. 2015;33(6):550–8.
17. [Chinese guidelines on the management of liver cirrhosis]. Zhonghua Gan Zang Bing Za Zhi. 2019;27(11):846–65.
18. Huang DQ, Terrault NA, Tacke F, Gluud LL, Arrese M, Bugianesi E, Loomba R. Global epidemiology of cirrhosis - aetiology, trends and predictions. Nat Rev Gastroenterol Hepatol. 2023;20(6):388–98.
19. Khan YBH, Lakhani RS, Khan DA, Jannat AY, Khan RU, Naqvi AA, Obeng SF, Kupec G, Singal JT. Antibiotic Prophylaxis for Upper Gastrointestinal Bleed in Liver cirrhosis; less may be more. Dig Dis Sci. 2023;68(1):284–90.
20. Semmler G, Yang Z, Fritz L, Köck F, Hofer BS, Balcar L, Hartl L, Jachs M, Stopfer K, Schedlbauer A, et al. Dynamics in Liver stiffness measurements predict outcomes in Advanced Chronic Liver Disease. Gastroenterology. 2023;165(4):1041–52.
21. Hu X, Huang X, Hou J, Ding L, Su C, Meng F. Diagnostic accuracy of spleen stiffness to evaluate portal hypertension and esophageal varices in chronic liver disease: a systematic review and meta-analysis. Eur Radiol. 2021;31(4):2392–404.
22. Navadurong H, Thanapirom K, Wejnaruemarn S, Prasoppokakorn T, Chaiteerakij R, Komolmit P, Treeprasertsuk S. Validation of the albumin-bilirubin score for identifying decompensation risk in patients with compensated cirrhosis. World J Gastroenterol. 2023;29(32):4873–82.
23. Labenz C, Arslanow A, Nguyen-Tat M, Nagel M, Wörns MA, Reichert MC, Heil FJ, Mainz D, Zimper G, Römer B, et al. Structured early detection of asymptomatic liver cirrhosis: results of the population-based liver screening program SEAL. J Hepatol. 2022;77(3):695–701.
24. Angeli P, Garcia-Tsao G, Nadim MK, Parikh CR. News in pathophysiology, definition and classification of hepatorenal syndrome: a step beyond the International Club of ascites (ICA) consensus document. J Hepatol. 2019;71(4):811–22.
25. Cullaro G, Hsu CY, Lai JC. Variability in serum creatinine is associated with waitlist and post-liver transplant mortality in patients with cirrhosis. Hepatology. 2022;76(4):1069–78.
26. Dziodzio T, Öllinger R, Schöning W, Rothkäppel A, Nikolov R, Juraszek A, Ritschl PV, Stockmann M, Pratschke J, Jara M. Validation of a new prognostic model to predict short and medium-term survival in patients with liver cirrhosis. BMC Gastroenterol. 2020;20(1):265.
27. de Franchis R, Bosch J, Garcia-Tsao G, Reiberger T, Ripoll C. Baveno VII - renewing consensus in portal hypertension. J Hepatol. 2022;76(4):959–74.
28. Anstee QM, Castera L, Loomba R. Impact of non-invasive biomarkers on hepatology practice: past, present and future. J Hepatol. 2022;76(6):1362–78.
29. Buechter M, Kahraman A, Manka P, Gerken G, Jochum C, Canbay A, Dechêne A. Spleen and liver stiffness is positively correlated with the risk of esophageal variceal bleeding. Digestion. 2016;94(3):138–44.
30. Riva MA, Ferraina F, Paleari A, Lenti MV, Di Sabatino A. From sadness to stiffness: the spleen's progress. Intern Emerg Med. 2019;14(5):739–43.
31. Wang H, Wen B, Chang X, Wu Q, Wen W, Zhou F, Guo Y, Ji Y, Gu Y, Lai Q, et al. Baveno VI criteria and spleen stiffness measurement rule out high-risk varices in virally suppressed HBV-related cirrhosis. J Hepatol. 2021;74(3):584–92.

32. Bolognesi M, Merkel C, Sacerdoti D, Nava V, Gatta A. Role of spleen enlargement in cirrhosis with portal hypertension. Dig Liver Dis. 2002;34(2):144–50.
33. Liu L, Ye S, Nie Y, Zhu X. Comparative efficacy of endoscopic variceal ligation versus non-selective beta-blockers in primary prevention of gastroesophageal varix type 2: an IPTW-adjusted study. Surg Endosc 2024.
34. Oppong B, Amponsah GM, Gyabaah S, Nicholas MK, Boateng S, Ameyaw PA, Asamoah DO, Nkum BC. Upper Gastrointestinal endoscopic findings and their clinical correlates in patients with liver cirrhosis in Northern Ghana. Cureus. 2024;16(8):e67725.
35. Hu K, Sedki M, Kwong A, Kesselman A, Kolli KP, Morelli G, Spengler E, Said A, Lai J, Desai A, et al. Portal hypertensive gastropathy and MELD-Na score predict recurrent gastrointestinal bleeding after TIPSS: an ALTA Group Study. Alimentary pharmacology & therapeutics; 2024.
36. Pompili E, Zaccherini G, Baldassarre M, Iannone G, Caraceni P. Albumin administration in internal medicine: a journey between effectiveness and futility. Eur J Intern Med. 2023;117:28–37.
37. Huang XQ, Ai YJ, Li F, Ye ST, Wang JH, Zhang R, Zhang W, Zhu YL, Chen SY. Impact of rifaximin on cirrhosis complications and gastric microbiota in patients with gastroesophageal variceal bleeding: a pilot randomized controlled trial. J Dig Dis. 2024;25(8):504–16.
38. Oikonomou T, Goulis L, Doumtsis P, Tzoumari T, Akriviadis E, Cholongitas E. ALBI and PALBI grades are Associated with the outcome of patients with stable decompensated cirrhosis. Ann Hepatol. 2019;18(1):126–36.
39. Wang G, Ding T, Ai L. Editorial: effects and mechanisms of probiotics, prebiotics, synbiotics and postbiotics on intestinal health and disease. Front Cell Infect Microbiol. 2024;14:1430312.
40. Li J, Qi X, Deng H, Peng Y, Shao L, Ma J, Sun X, Li H, Guo X. Association of conventional haemostasis and coagulation tests with the risk of acute upper gastrointestinal bleeding in liver cirrhosis: a retrospective study. Gastroenterol Rep. 2016;4(4):315–9.
41. Desborough MJ, Kahan BC, Stanworth SJ, Jairath V. Fibrinogen as an independent predictor of mortality in decompensated cirrhosis and bleeding. Hepatology. 2017;65(3):1079–80.
42. Feng R, Guo X, Kou Y, Xu X, Hong C, Zhang W, An Y, Philips CA, Mancuso A, Qi X. Association of lipid profile with decompensation, liver dysfunction, and mortality in patients with liver cirrhosis. Postgrad Med. 2021;133(6):626–38.
43. Stefanutti C, Julius U, Watts GF, Harada-Shiba M, Cossu M, Schettler VJ, De Silvestro G, Soran H, Van Lennep JR, Pisciotta L, et al. Toward an international consensus-integrating lipoprotein apheresis and new lipid-lowering drugs. J Clin Lipidol. 2017;11(4):858–e871853.

Publisher's note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.