BMC Gastroenterology

RESEARCH

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Predictive role of the Albumin-Bilirubin score in ICU patients with cirrhosis and sepsis: insights from a large retrospective cohort

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Abstract

Background The albumin-bilirubin (ALBI) score is a valuable prognostic tool for diseases such as hepatocellular carcinoma, heart failure, and acute kidney injury. However, its association with the prognosis of patients with liver cirrhosis and sepsis in the intensive care unit (ICU) remains unclear.

Methods This retrospective study analyzed data from ICU patients with liver cirrhosis and sepsis admitted to the Beth Israel Deaconess Medical Center between 2008 and 2022. The primary and secondary endpoints were 28-day (short-term) and 90-day (long-term) mortality, respectively. Relationships between mortality risk and the ALBI scores were assessed by Kaplan-Meier, multivariable Cox proportional hazard, and restricted cubic spline (RCS) analyses. The receiver operating characteristic (ROC) curves were used to evaluate the predictive ability of the ALBI score for 28-day and 90-day mortality in these patients. Subgroup analyses were used to explore the associations between the ALBI scores and different patient populations.

Results The study included 2,047 ICU patients with liver cirrhosis and sepsis. Patients with higher ALBI scores had significantly higher 28-day and 90-day mortality rates than those with lower scores (Kaplan-Meier). The ALBI score was an independent predictor of short-term and long-term mortality (multivariable Cox regression). In the fully adjusted model, the hazard ratios (HRs) for the ALBI score as a continuous variable were 1.38 (95% confidence interval [CI]: 1.20–1.58, $P < 0.001$) and 1.33 (95% CI: 1.18–1.50, $P < 0.001$) for 28-day and 90-day mortality, respectively. When categorized into tertiles, the mortality risk was significantly higher for patients in the highest tertile than for those in the lowest tertile, with HRs of 1.51 (95% CI: 1.23–1.85, P for trend < 0.001) and 1.45 (95% CI: 1.21–1.73, P for trend < 0.001) for 28-day and 90-day mortality, respectively. A nonlinear relationship was identified between the ALBI score and short- and long-term mortality (RCS analysis). The results of the ROC curve analysis confirmed that the predictive ability of the ALBI score for 28-day and 90-day mortality was not inferior to that of the Sequential Organ Failure Assessment score. Subgroup analyses showed that there were no significant interactions between ALBI scores and the vast majority of subgroups.

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Conclusions Higher ALBI scores were significantly and independently associated with increased short- and long-term mortality in ICU patients with liver cirrhosis and sepsis. The ALBI score may help with risk and prognostic evaluations in this high-risk population.

Keywords Cirrhosis, Sepsis, Albumin-bilirubin score, Mortality risk, Intensive care unit

Background

Cirrhosis is a chronic progressive disease characterized by hepatic dysfunction and structural distortion caused by various etiologies, including chronic viral hepatitis, alcoholic liver disease, and nonalcoholic fatty liver disease [1–3]. When patients with cirrhosis develop sepsis, their condition often deteriorates rapidly, primarily due to the exacerbation of hepatic dysfunction, immune dysregulation, and multi-organ failure caused by sepsis [4, 5]. Studies have shown that hospitalized patients with cirrhosis are four to five times more likely to develop infections than the general population, and those who progress to sepsis experience worse outcomes with significantly higher mortality rates [6]. Thus, identifying reliable and readily available prognostic markers is critical for optimizing risk stratification and guiding clinical decision-making in this vulnerable population.

The albumin-bilirubin (ALBI) score was initially developed to evaluate liver function and stratify prognosis in patients with hepatocellular carcinoma, but in recent years, it has demonstrated unique prognostic value for various complications [7–9]. Compared with the Child-Pugh score, the ALBI score relies solely on serum albumin and bilirubin levels, offering greater simplicity and objectivity [10]. Previous studies have found that the ALBI score effectively predicts survival in patients with hepatocellular carcinoma and performs well in prognosticating outcomes in non-hepatic diseases, such as heart failure and acute kidney injury [11–13]. However, its utility in assessing the prognosis of intensive care unit (ICU) patients with cirrhosis and sepsis remains unclear. Given the focus of the ALBI score on hepatic functional parameters, its potential application in this high-risk population warrants further investigation.

Patients with cirrhosis and sepsis admitted to the ICU often present with coagulopathy, systemic inflammation, and multi-organ dysfunction, posing significant challenges to clinical management [14, 15]. Although existing prognostic tools such as the Sequential Organ Failure Assessment (SOFA) score and the Model for End-Stage Liver Disease (MELD) score are widely used in ICU settings [16], these systems rely on multiple clinical and/or laboratory parameters, which can complicate their application. In contrast, the ALBI score, with its simplicity and liver-specific focus, requires fewer laboratory parameters and may offer valuable prognostic insights in this patient population.

Therefore, this study retrospectively analyzed data from ICU patients with cirrhosis and sepsis to evaluate the associations between the ALBI score and short-term (28-day) and long-term (90-day) mortality. We hypothesized that higher ALBI scores would be independently associated with an increased mortality risk. Moreover, our research seeks to identify novel prognostic biomarkers that could complement existing scoring systems like SOFA and MELD, with the ultimate goal of improving patient prognosis by enhancing the accuracy and efficiency of current prognostication tools.

Methods

Data sources and study population

This retrospective study used data from the Medical Information Mart for Intensive Care-IV (MIMIC-IV, version 3.0), a publicly available database developed by the Laboratory for Computational Physiology at the Massachusetts Institute of Technology (Cambridge, MA, USA). The MIMIC-IV (v 3.0) includes comprehensive electronic health records of patients admitted to the Beth Israel Deaconess Medical Center between 2008 and 2022 [17]. The research team completed the Collaborative Institutional Training Initiative program and passed "Conflicts of Interest" and "Data or Specimens Only Research" examinations to gain access to the MIMIC-IV database.

Patients with cirrhosis and sepsis admitted to the ICU were identified using the International Classification of Diseases, 9th and 10th Revision (ICD-9 and – 10) codes. According to the Sepsis-3 criteria, patients with suspected infection and a SOFA score ≥ 2 were classified with sepsis [18]. The exclusion criteria were: [1] age < 18 years at the time of first admission [2], ICU length of stay < 24 h, and [3] absence of recorded albumin or bilirubin values within the first 24 h of admission. Only data from the first admission of patients with multiple ICU admissions were included. Figure 1 details the study design.

ALBI score calculation, grouping and clinical outcomes

The ALBI score was calculated based on the first recorded serum albumin and total bilirubin levels after ICU admission. The ALBI score was calculated using the formula: ALBI score = (log10 bilirubin [μmol/L] × 0.66) + (albumin [g/L] × −0.085) [7]. In this study, we employed two grouping methods to assess the relationship between ALBI score and mortality risk. The first

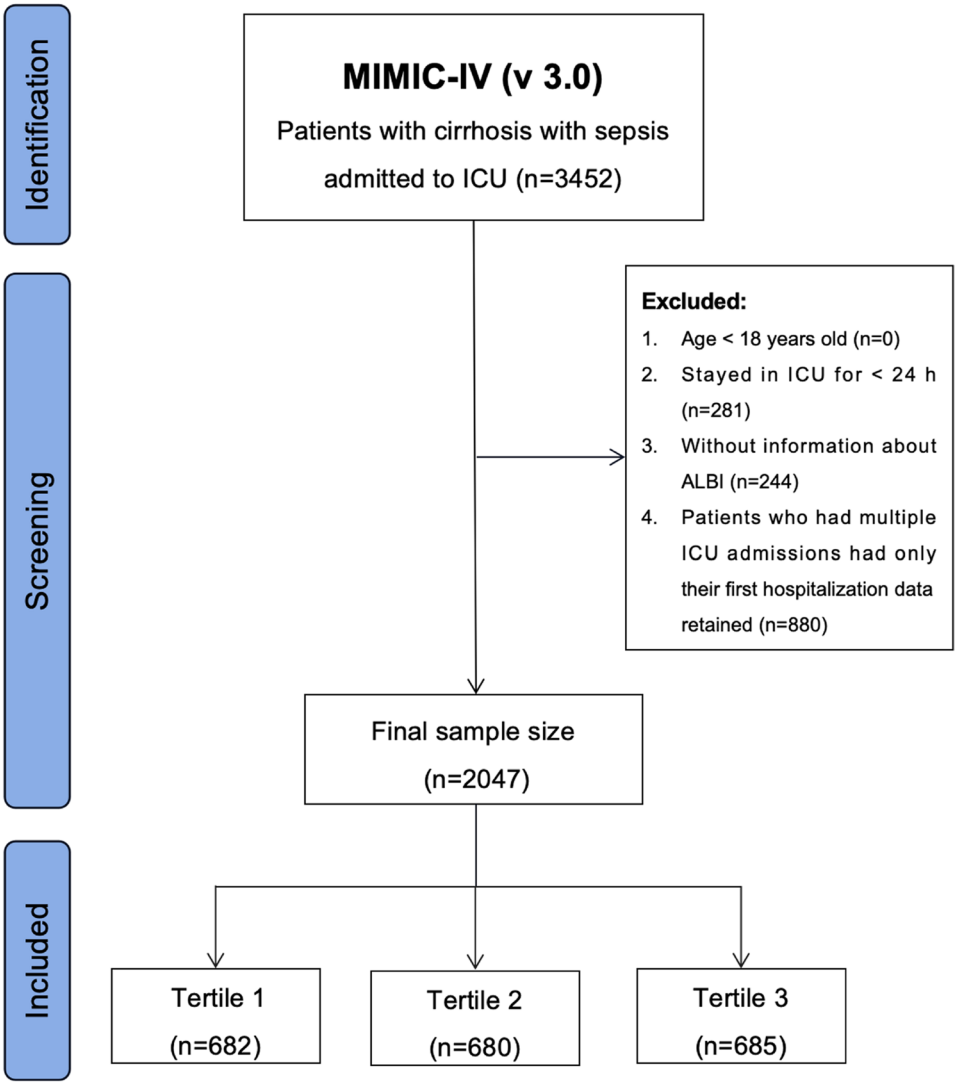

Fig. 1 CONSORT diagram for participants from MIMIC-IV (v 3.0). MIMIC-IV (v 3.0): Medical Information Mart for Intensive Care IV (version 3.0)

method was based on tertiles of the ALBI score, stratifying patients into three groups: the lowest tertile (T1) consisting of 682 patients, the middle tertile (T2) consisting of 680 patients, and the highest tertile (T3) consisting of 685 patients. The second method involved stratification based on the median ALBI score, dividing patients into two groups: those with ALBI scores above and below the median.

The primary and secondary outcomes were 28-day and 90-day mortality, respectively, defined as all-cause mortality occurring within 28 and 90 days from the date of ICU admission. Mortality data were extracted from the "date of death" field in the MIMIC-IV database, which is linked to the Social Security Death Index.

Data extraction

Data were extracted using PostgresSQL (version 13.7.2) and Navicate Premium (version 16.0) software utilizing Structured Query Language (SQL). Table 1 details the extracted variables, including demographic characteristics (such as age and sex), vital signs, comorbidities (such as hepatic failure, and hepatic failure was identified using ICD-9/10 codes, specifically including K704, K7040, K7041, K72, K720, K7200, K7201, K721, K7210, K7211, K729, K7290, K7291, and K9182), etiology of cirrhosis, laboratory results (such as white blood cell and platelet counts), clinical interventions (such as vasopressor use and continuous renal replacement therapy), survival data, microbiological results, and severity scores (such as SOFA). In addition, cardiovascular comorbidities, including heart failure diagnoses, were included. Given the retrospective nature of the study and the absence of echocardiographic and diastolic functional data, specific identification of cirrhotic cardiomyopathy was not feasible and thus was not separately assessed.

Table 1 Covariates extracted in detail from MIMIC-IV (v 3.0)

Items	Composition
Demographic variables	Age, Sex, Race
Comorbidities	Hypertension, Diabetes, Chronic obstructive pulmonary disease, Myocardial infarction, Malignancy, Atrial fibrillation, Heart failure, Renal failure
Complications of liver disease	Hepatic encephalopathy, Esophageal varices with hemorrhage, Hepatorenal syndrome, Ascites
Vital Signs	Heart rate, Systolic blood pressure, Diastolic blood pressure, Mean arterial pressure, Respiratory rate, SPO_2, Body temperature
Laboratory parameters	Neutrophil cells, Lymphocyte cells, Red blood cells, White blood cells, Erythrocyte distribution width, Platelet, Hemoglobin, Lymphocyte percentage, Hematocrit, Creatinine, Blood urea nitrogen, Albumin, Total bilirubin, Direct bilirubin, Aspartate aminotransferase, Alanine aminotransferase, Glucose, Triglyceride, Total cholesterol, High density lipoprotein cholesterol, Low density lipoprotein cholesterol, Prothrombin time, International normalized ratio, Potassium, Sodium, Calcium, Anion gap, Lactate, PH, FiO_2, PCO_2, PaO_2
Clinical Treatments	Urinary catheter, Vasopressin, Ventilation, Continuous Renal Replacement Therapy, Norepinephrine
Clinical Outcomes	Length of ICU stay, Length of hospitalization, ICU mortality, Hospital mortality, 28-day all-cause mortality, 90-day all-cause mortality
Scores	Sequential Organ Failure Assessment, Model for End-Stage Liver Disease score
Others	Causes of liver cirrhosis, Infections positions, Microculture

MIMIC-IV (v 3.0): Medical Information Mart for Intensive Care-IV (MIMIC-IV) database (version 3.0); ICU, intensive care unit

Management of abnormal and missing values

Outliers were managed using the winsorization method at the 1st and 99th percentiles via the STATA winsor2 command. Missing data were handled using multiple imputation by chained equations (MICE). Variables with >15% missingness were excluded to avoid potential bias [19].

The imputation model included all covariates used in the regression analysis. Five imputations were performed, and results were pooled using Rubin's rules. Diagnostic checks, including comparisons of variable distributions before and after imputation, showed good consistency without systematic distortion. The algorithm exhibited stable convergence across iterations. Missingness proportions are detailed in Supplementary Table 2.

Statistical analyses

Continuous variables are expressed as means ± standard deviations for normally distributed data or medians (interquartile ranges) for skewed data. Continuous variables were compared using t-tests or one-way analyses of variance. Categorical variables are presented as frequencies and percentages, and group comparisons were performed using the chi-square test or Fisher's exact test. Kaplan-Meier survival analysis and log-rank tests were used to compare the 28-day and 90-day mortality distributions among the ALBI score groups.

Cox proportional hazards regression models were employed to evaluate the association between ALBI score and mortality. Three models were developed: Model 1 was unadjusted; Model 2 was adjusted for age, sex, and race; and Model 3 was further adjusted for clinical and laboratory covariates. Covariate selection was based on established prognostic relevance in critically ill patients with cirrhosis and sepsis, incorporating inflammatory markers (white blood cell count), organ dysfunction indicators (SOFA score), prevalent comorbidities (hypertension, diabetes mellitus, heart failure, respiratory failure), and critical care interventions (vasopressor administration, continuous renal replacement therapy). Lactate, a marker of tissue hypoperfusion, was included in sensitivity analyses to assess robustness. Hazard ratios (HRs) were calculated for each tertile, using the lowest tertile as the reference.

A restricted cubic spline (RCS) analysis was used to evaluate the nonlinear relationship between the ALBI score and mortality. Receiver operating characteristic (ROC) analysis was used to evaluate the predictive ability of the ALBI score for 28-day and 90-day mortality after ICU admission, including its sensitivity and specificity, as well as to calculate the area under the curve (AUC). Subgroup analyses were conducted to explore the consistency of the ALBI score performance across age, sex, and comorbidity subgroups. All statistical analyses were performed using R (version 4.2.2; R Core Team, Vienna, Austria), STATA (version 16.0; StataCorp LLC, College Station, TX, USA), and SPSS (version 22.0; IBM Corp., Armonk, NY, USA), with statistical significance defined as a two-sided P-value of < 0.05.

Results

Participant baseline characteristics

Table 2 summarizes the baseline characteristics of 2,047 patients with liver cirrhosis and sepsis stratified into three groups (T1, T2, and T3) based on the ALBI score. The primary etiology of cirrhosis in all groups of patients was alcohol consumption, followed by hepatitis virus infection. As the ALBI scores increased, patient age progressively decreased, with a median age of 55 years in the T3 group compared to 59 years in the T1 group ($P < 0.001$). Patients in the T3 group exhibited more severe liver dysfunction, as indicated by higher total bilirubin (median: 112.86 μmol/L) and lower albumin (median, 23 g/dL) levels ($P < 0.001$) (Table 3). Additionally, the prevalence of complications, such as ascites (61.73%) and hepatic failure (38.12%), was significantly higher in the T3 group ($P < 0.001$). The severity of illness also increased across

Table 2 Baseline characteristics of participants

Variable	Overall (*n* = 2,047)	T1 (*n* = 682)	T2 (*n* = 680)	T3 (*n* = 685)	*P* value
ALBI	−1.29 (−1.74 to −0.86)	−1.93 (−2.22 to −1.74)	−1.29 (−1.43 to −1.15)	−0.70 (−0.86 to −0.45)	< 0.001
Demographics					
Age, years	57 (50–65)	59 (52–67)	58 (50–65)	55 (47–62)	< 0.001
Men, n (%)	1320 (64.48)	432 (63.53)	454 (66.28)	434 (63.64)	0.480
Ethnicity, n (%)					
Asian populations	52 (2.54)	17 (2.50)	21 (3.07)	14 (2.05)	0.550
White populations	1318 (64.39)	452 (66.47)	442 (64.53)	424 (62.17)	
Black populations	139 (6.79)	42 (6.18)	47 (6.86)	50 (7.33)	
Others	538 (26.28)	169 (24.85)	175 (25.55)	194 (28.45)	
Causes of liver cirrhosis, n (%)					
Alcohol	907 (44.31)	255 (37.50)	292 (42.63)	360 (52.79)	< 0.001
Viral	575 (28.09)	194 (28.53)	212 (30.95)	169 (24.78)	
Biliary	43 (2.10)	19 (2.79)	12 (1.75)	12 (1.76)	
Others	522 (25.50)	212 (31.18)	169 (24.67)	141 (20.67)	
Comorbidities					
Hypertension, n (%)	1384 (67.61)	437 (64.26)	473 (69.05)	474 (69.50)	0.070
Diabetes mellitus, n (%)	627 (30.63)	262 (38.53)	192 (28.03)	173 (25.37)	< 0.001
Chronic obstructive pulmonary disease, n (%)	133 (6.50)	65 (9.56)	34 (4.96)	34 (4.98)	< 0.001
Heart failure, n (%)	299 (14.61)	146 (21.47)	90 (13.14)	63 (9.24)	< 0.001
Renal failure, n (%)	376 (18.37)	111 (16.32)	116 (16.93)	149 (21.85)	0.010
Myocardial infarction, n (%)	236 (11.53)	95 (13.97)	76 (11.09)	65 (9.53)	0.030
Malignancy, n (%)	377 (18.42)	130 (19.12)	137 (20.00)	110 (16.13)	0.150
Respiratory failure, n (%)	953 (46.56)	288 (42.35)	318 (46.42)	347 (50.88)	0.007
Atrial fibrillation, n (%)	378 (18.47)	161 (23.68)	122 (17.81)	95 (13.93)	< 0.001
Septic shock, n (%)	613 (29.95)	181 (26.62)	183 (26.72)	249 (36.51)	< 0.001
Complications of liver disease					
Ascites, n (%)	1110 (54.23)	320 (47.06)	369 (53.87)	421 (61.73)	< 0.001
Hepatorenal syndrome, n (%)	349 (17.05)	109 (16.03)	108 (15.77)	132 (19.35)	0.140
Hepatic encephalopathy, n (%)	229 (11.19)	66 (9.71)	72 (10.51)	91 (13.34)	0.080
Esophageal varices with hemorrhage, n (%)	271 (13.24)	82 (12.06)	88 (12.85)	101 (14.81)	0.300
Hepatic failure, n (%)	646 (31.56)	168 (24.71)	218 (31.82)	260 (38.12)	< 0.001
Infections position					
Blood, n (%)	84 (4.10)	15 (2.21)	36 (5.26)	33 (4.84)	0.009
Lung, n (%)	626 (30.58)	203 (29.85)	207 (30.22)	216 (31.67)	0.740
Abdomen, n (%)	384 (18.76)	112 (16.47)	112 (16.35)	160 (23.46)	< 0.001
Urinary, n (%)	356 (17.39)	112 (16.47)	116 (16.93)	128 (18.77)	0.500
Skin, n (%)	90 (4.40)	26 (3.82)	29 (4.23)	35 (5.13)	0.480
Microculture					
Fungal, n (%)	373 (18.22)	133 (19.56)	106 (15.47)	134 (19.65)	0.070
Bacterial, n (%)	1128 (55.11)	362 (53.24)	365 (53.28)	401 (58.80)	0.060
Bacterial and fungal, n (%)	236 (11.53)	83 (12.21)	64 (9.34)	89 (13.05)	0.080
Vital sign					
Heart rate, beats/min	93 (80–107)	90 (76–103)	93 (79–107)	97 (84–109)	< 0.001
Systolic blood pressure, mmHg	114 (100–132)	117 (101–137)	115 (101–131)	112 (98–128)	0.001
Diastolic blood pressure, mmHg	63 (54–75)	64 (54–77)	63 (55–74)	62 (53–73)	0.110
Mean arterial pressure, mmHg	80.67 (70.67–92.67)	82.33 (70.67–94.67)	81 (71.67-92)	78.67 (70-90.33)	0.009
Respiratory rate, times/min	19 (16–23)	19 (16–23)	19 (16–23)	20 (16–24)	0.030
SPO_2, %	98 (95–100)	97.5 (95–100)	98 (96–100)	98 (95–100)	0.008
Body temperature, ℃	36.72 (36.44–37.06)	36.72 (36.44-37)	36.78 (36.5-37.11)	36.72 (36.44–37.06)	0.100
Scores					
SOFA	3 (1–6)	3 (0–6)	3 (1–6)	4 (1–7)	< 0.001
MELD	24 (17–32)	21 (14–29)	22 (16–29)	28 (21–36)	< 0.001

Table 2 (continued)

Variable	Overall (*n* = 2,047)	T1 (*n* = 682)	T2 (*n* = 680)	T3 (*n* = 685)	*P* value
Treatment					
Urinary catheter, n (%)	567 (27.70)	162 (23.82)	182 (26.57)	223 (32.70)	< 0.001
Vasopressin, n (%)	411 (20.08)	115 (16.91)	126 (18.39)	170 (24.93)	< 0.001
Ventilation, n (%)	1799 (87.88)	589 (86.62)	617 (90.07)	593 (86.95)	0.100
Continuous Renal Replacement Therapy, n (%)	387 (18.91)	122 (17.94)	125 (18.25)	140 (20.53)	0.410
Norepinephrine, n (%)	835 (40.79)	263 (38.68)	258 (37.66)	314 (46.04)	0.003
Clinical Outcomes					
LOS ICU, day	3.88 (2.09–7.90)	3.89 (2.01–7.78)	3.70 (2.07–7.83)	4.00 (2.16–8.31)	0.020
LOS Hospital, day	12.50 (6.79–22.79)	11.92 (6.42–21.69)	12.08 (6.79–22.50)	13.23 (7.67–25.04)	0.290
ICU mortality, n (%)	376 (18.37)	111 (16.32)	116 (16.93)	149 (21.85)	0.020
Hospital mortality, n (%)	585 (28.58)	158 (23.24)	184 (26.86)	243 (35.63)	< 0.001
28-day mortality, n (%)	622 (30.39)	168 (24.71)	191 (27.88)	263 (38.56)	< 0.001
90-day mortality, n (%)	832 (40.64)	240 (35.29)	259 (37.81)	333 (48.83)	< 0.001

ALBI albumin-bilirubin, *SOFA* sequential organ failure assessment, *MELD* Model for End-Stage Liver Disease score, *ICU* intensive care unit

Table 3 Laboratory parameters

Variable	Overall (*n* = 2,047)	T1 (*n* = 682)	T2 (*n* = 680)	T3 (*n* = 685)	*P* value
ALBI	−1.29 (−1.74 to −0.86)	−1.93 (−2.22 to −1.74)	−1.29 (−1.43 to −1.15)	−0.70 (−0.86 to −0.45)	< 0.001
Laboratory parameters					
Neutrophil cells, 10^9/L	5.64 (3.38–9.82)	5.12 (3.05–9.05)	5.14 (3.26–9.38)	6.55 (3.6-11.53)	< 0.001
Lymphocyte cells, 10^9/L	1.1 (0.69–1.69)	1.06 (0.63–1.69)	1.13 (0.71–1.69)	1.13 (0.74–1.67)	0.330
Red blood cells, 10^9/L	10.3 (6.5–15.9)	9.55 (6.3–13.7)	10.3 (6.1–15.7)	11.4 (7.2–18.5)	< 0.001
White blood cells, 10^9/L	2.96 (2.52–3.47)	3.09 (2.6–3.67)	2.96 (2.53–3.39)	2.85 (2.43–3.35)	< 0.001
Erythrocyte distribution width, %	17 (15.3–19.1)	16.3 (14.7–18.3)	17 (15.3-18.85)	17.7 (15.9–19.9)	< 0.001
Platelets, 10^9/L	100 (65–151)	113.5 (74.5–158)	95 (63–145)	91 (59–146)	< 0.001
Hemoglobin, g/dL	9.3 (8-10.7)	9.4 (8.1-11.05)	9.4 (8-10.6)	9.2 (7.9–10.7)	0.100
Hematocrit, %	27.9 (24.2–32.5)	28.3 (24.9–33.5)	28.1 (24.4–32.1)	27.4 (23.7–31.8)	< 0.001
Creatinine, mg/dL	1.3 (0.8–2.3)	1.5 (0.9–2.6)	1.2 (0.8–1.9)	1.3 (0.8–2.5)	< 0.001
Blood urea nitrogen, mg/dL	28 (16–49)	30 (16.5–56)	25 (15–41)	29 (17–49)	< 0.001
Albumin, g/dL	29 (25–33)	34.5 (32–38)	29 (26–31)	23 (21–26)	< 0.001
Total bilirubin, μmol/L	56.43 (25.65–136.8)	29.07 (15.39–58.14)	53.01 (27.36-116.28)	112.86 (58.14-251.37)	< 0.001
Direct bilirubin, mg/dL	1.7 (0.7–4.7)	1 (0.4–2.2)	1.6 (0.7–4.5)	3.3 (1.2–8.1)	< 0.001
Aspartate aminotransferase, IU/L	76 (42–177)	54.5 (33–110)	82 (43–198)	109 (56–248)	< 0.001
Alanine aminotransferase, IU/L	35 (21–82)	30 (17–58)	35 (21–93)	42.5 (25-103.5)	< 0.001
Glucose, mg/dL	127 (102–167)	129 (106-171.5)	127 (101–171)	123 (98–162)	0.006
Prothrombin time, s	19 (15.8–24.1)	17.1 (14.4–22.1)	18.6 (15.8–22.9)	21.05 (17.8–26.8)	< 0.001
International normalized ratio	1.7 (1.4–2.2)	1.6 (1.3-2)	1.7 (1.4–2.1)	2 (1.6–2.5)	< 0.001
Potassium, mEq/L	4.2 (3.7–4.8)	4.2 (3.8–4.8)	4.1 (3.7–4.7)	4.15 (3.7–4.8)	0.030
Sodium, mEq/L	137 (132–140)	137 (134–141)	138 (133–141)	135 (130–139)	< 0.001
Calcium, mg/dL	8.2 (7.6–8.8)	8.5 (8–9)	8.2 (7.6–8.8)	7.9 (7.3–8.5)	< 0.001
Anion gap, mEq/L	15 (12–19)	16 (13–20)	15 (12–18)	15 (12–19)	< 0.001
Lactate, mmol/L	2.4 (1.7–4.1)	2.2 (1.5–3.6)	2.4 (1.6-4)	2.7 (1.9–4.5)	< 0.001
PH	7.36 (7.30–7.42)	7.36 (7.29–7.42)	7.37 (7.31–7.42)	7.36 (7.29–7.42)	0.100
FiO2	50 (50–100)	50 (49–80)	50 (40–96)	53 (50–100)	0.530
PCO2	38 (33–44)	39 (33-45.5)	39 (34–45)	37 (32–43)	< 0.001
PaO2	81 (49–153)	79 (47–150)	86.5 (51–167)	79 (48–138)	0.080

ALBI albumin-bilirubin

the groups, with progressively higher SOFA and MELD scores in the T3 group, indicating worse disease status. The hospital length of stay increased as the ALBI score increased, with a median of 13.23 days in the T3 group compared with 11.92 days in the T1 group, although this difference was statistically insignificant ($P = 0.29$). However, mortality rates were significantly higher in the T3 group. The 28-day mortality rate in the T3 group was 38.56% versus 24.71% in the T1 group, and the 90-day mortality rate was 48.83% in the T3 group versus 35.29% in the T1 group (both $P < 0.001$). Additionally, in the T3 and T1 groups, the ICU mortality rates were 21.85% and 16.32%, respectively, and the hospital mortality rates were 35.63% and 23.24%, respectively (all $P < 0.05$). Overall, patients with higher ALBI scores had more severe disease states, longer hospital stays, and markedly worse short- and long-term outcomes. In addition, we regrouped participants by the median of ALBI scores, refer to Supplementary Table 1 for more details.

Kaplan-Meier survival curves

Figure 2 illustrates the survival probabilities of patients with liver cirrhosis and sepsis stratified into tertiles based on the ALBI score. Significant differences in survival were observed across tertiles for 28-day and 90-day mortality (overall log-rank test $P < 0.0001$). At 28 days, the mortality rates were 24.71% for T1, 27.88% for T2, and significantly higher at 38.56% for T3 (Table 2). Correspondingly, Fig. 2A shows a clear separation in the survival curves, with T3 patients having the poorest survival probabilities, followed by T2 and T1 patients. Pairwise comparisons revealed statistically significant differences between T3 and both T1 ($P < 0.001$) and T2 ($P = 0.003$), while the difference between T1 and T2 was not statistically significant ($P = 0.145$).

At 90 days, the mortality rate increased to 35.29% for T1, 37.81% for T2, and 48.83% for T3 (Table 2). This trend is further reflected in Fig. 2B, where the survival probability for patients in T3 continued to decline markedly compared with the other groups. Pairwise comparisons again showed that T3 had significantly higher mortality than both T1 ($P < 0.001$) and T2 ($P = 0.005$), while T1 and T2 remained statistically similar ($P = 0.203$).

These results highlight the strong prognostic value of the ALBI score in predicting both short-term (28-day) and long-term (90-day) mortality. Patients in the highest ALBI tertile (T3) consistently exhibited significantly worse survival outcomes than those in lower tertiles, underscoring the association between higher ALBI scores, more severe liver dysfunction, and poor prognosis.

Supplementary Fig. 1 presents the survival curves of patients stratified by the median ALBI score. The results also showed that patients with higher ALBI scores had significantly higher 28-day and 90-day mortality rates than those with lower scores.

Relationships between ALBI scores and clinical outcomes

Table 4 presents the results of the Cox proportional hazards regression analyses for 28-day and 90-day all-cause mortality in patients with liver cirrhosis and sepsis; three models were constructed. For 28-day mortality, the ALBI score as a continuous variable was significantly associated with increased risk in all models, with HRs ranging from 1.38 (95% confidence interval [CI]: 1.20–1.58) in Model 3 to 1.64 (95% CI: 1.44–1.88) in Model 2 ($P < 0.001$ for all). When stratified by tertiles, the highest tertile (T3) demonstrated a significantly increased risk compared to the reference group (T1), with HRs of 1.72 (95% CI: 1.42–2.09) in Model 1, 1.90 (95% CI: 1.56–2.32) in Model 2, and 1.51 (95% CI: 1.23–1.85) in Model 3 (P for trend < 0.001 in all models).

For 90-day mortality, a similar trend was observed. The ALBI score as a continuous variable was independently

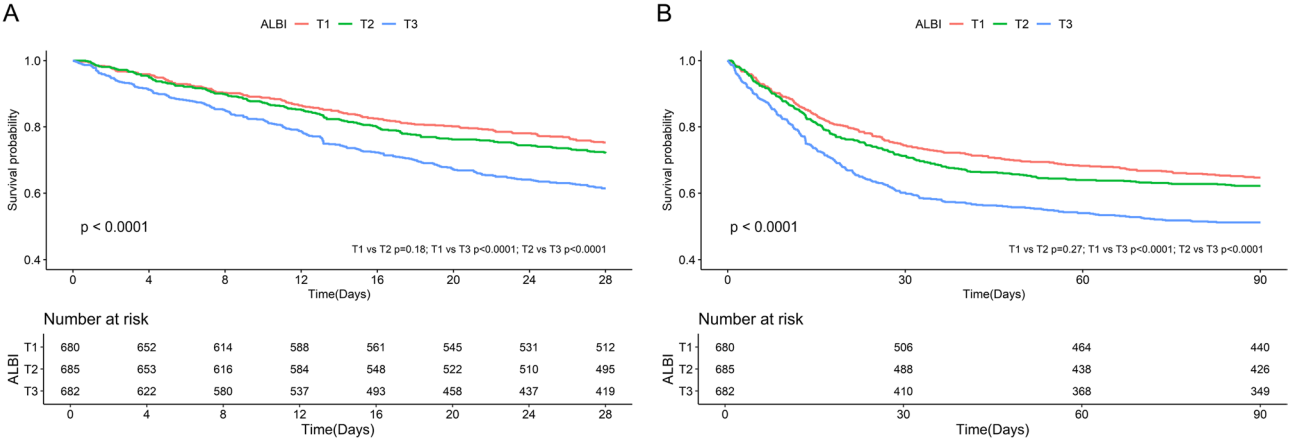

Fig. 2 Kaplan-Meier survival analysis curves for all-cause mortality. Kaplan-Meier curves and cumulative incidence of 28-day (**A**), and 90-day (**B**) all-cause mortality stratified by ALBI score tertiles.

Table 4 Cox proportional hazard ratios (HR) for all-cause mortality

	Model 1		Model 2		Model 3	
	HR (95% CI)	***P* value**	**HR (95% CI)**	***P* value**	**HR (95% CI)**	***P* value**
28-day mortality						
ALBI (Continuous)	1.50 (1.32-1.71)	<0.001	1.64 (1.44-1.88)	<0.001	1.31 (1.14-1.50)	<0.001
ALBI (Tertiles)						
T1	Reference		Reference		Reference	
T2	1.15 (0.94-1.42)	0.18	1.21 (0.98-1.49)	0.07	1.09 (0.88-1.35)	0.42
T3	1.72 (1.42-2.09)	<0.001	1.90 (1.56-2.32)	<0.001	1.42 (1.15-1.74)	<0.001
P for trend	<0.001		<0.001		<0.001	
ALBI (< -1.29)	1.48 (1.26-1.74)	<0.001	1.59 (1.36-1.87)	<0.001	1.32 (1.12-1.55)	0.001
90-day mortality						
ALBI (Continuous)	1.41 (1.26-1.58)	<0.001	1.55 (1.38-1.74)	<0.001	1.27 (1.13-1.44)	<0.001
ALBI (Tertiles)						
T1	Reference		Reference		Reference	
T2	1.10 (0.93-1.32)	0.27	1.16 (0.97-1.38)	0.10	1.07 (0.90-1.28)	0.45
T3	1.58 (1.34-1.86)	<0.001	1.76 (1.48-2.08)	<0.001	1.36 (1.13-1.62)	<0.001
P for trend	<0.001		<0.001		<0.001	
ALBI (< -1.29)	1.40 (1.22-1.61)	<0.001	1.52 (1.33-1.75)	<0.001	1.23 (1.07-1.42)	<0.001

Model 1: Unadjusted

Model 2: Adjusted age, gender, and ethnicity

Model 3: Adjusted age, gender, ethnicity, white blood cells, hypertension, heart failure, respiratory failure, diabetes, vasopressin, continuous renal replacement therapy, international normalized ratio, lactate, and Sequential Organ Failure Assessment

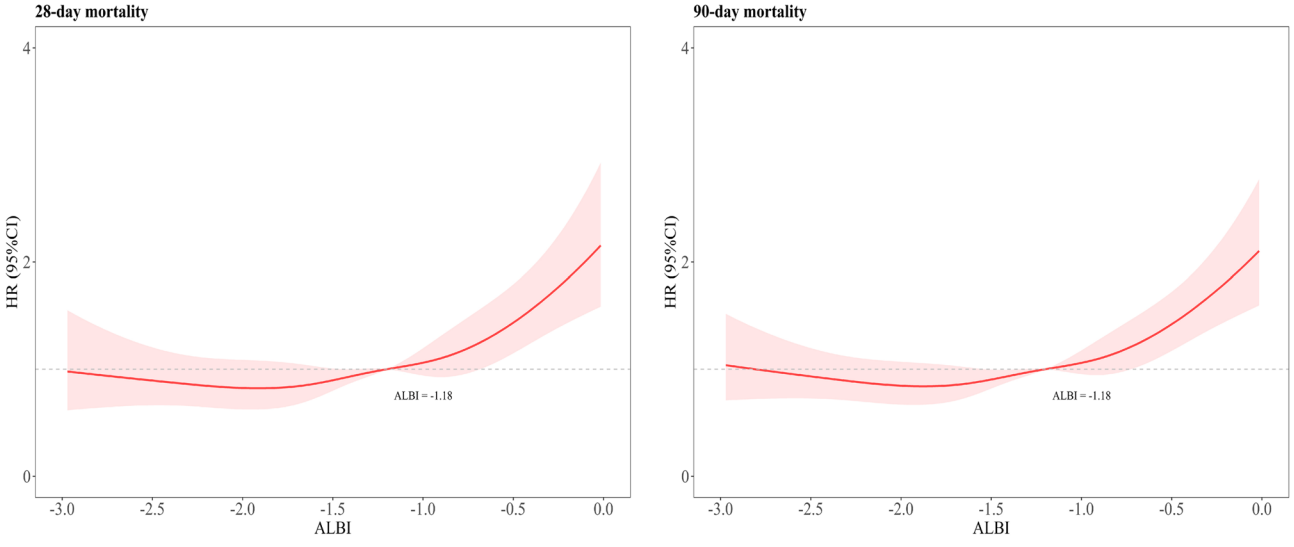

Fig. 3 Restricted cubic spline regression analysis of ALBI score with all-cause mortality. Restricted cubic spline regression analysis of ALBI score with 28-day (**A**), and 90-day (**B**) all-cause mortality. 28-day all-cause mortality: *P* for nonlinearity = 0.01. 90-day all-cause mortality: *P* for nonlinearity = 0.002. ALBI: albumin-bilirubin

associated with higher mortality risk, with HRs ranging from 1.33 (95% CI: 1.18–1.50) in Model 3 to 1.55 (95% CI: 1.38–1.74) in Model 2 ($P < 0.001$ for all). Patients in the highest tertile (T3) exhibited a significantly elevated risk compared to T1, with HRs of 1.58 (95% CI: 1.34–1.86) in Model 1, 1.76 (95% CI: 1.48–2.08) in Model 2, and 1.45 (95% CI: 1.21–1.73) in Model 3 (P for trend < 0.001 in all models). These findings suggest that a higher ALBI score is strongly and independently associated with increased short-term (28-day) and long-term (90-day) mortality risk in patients with liver cirrhosis and sepsis, particularly in those within the highest tertile.

RCS analysis

Figure 3 illustrates the results of the RCS analysis for 28-day and 90-day mortality, as measured by HR and

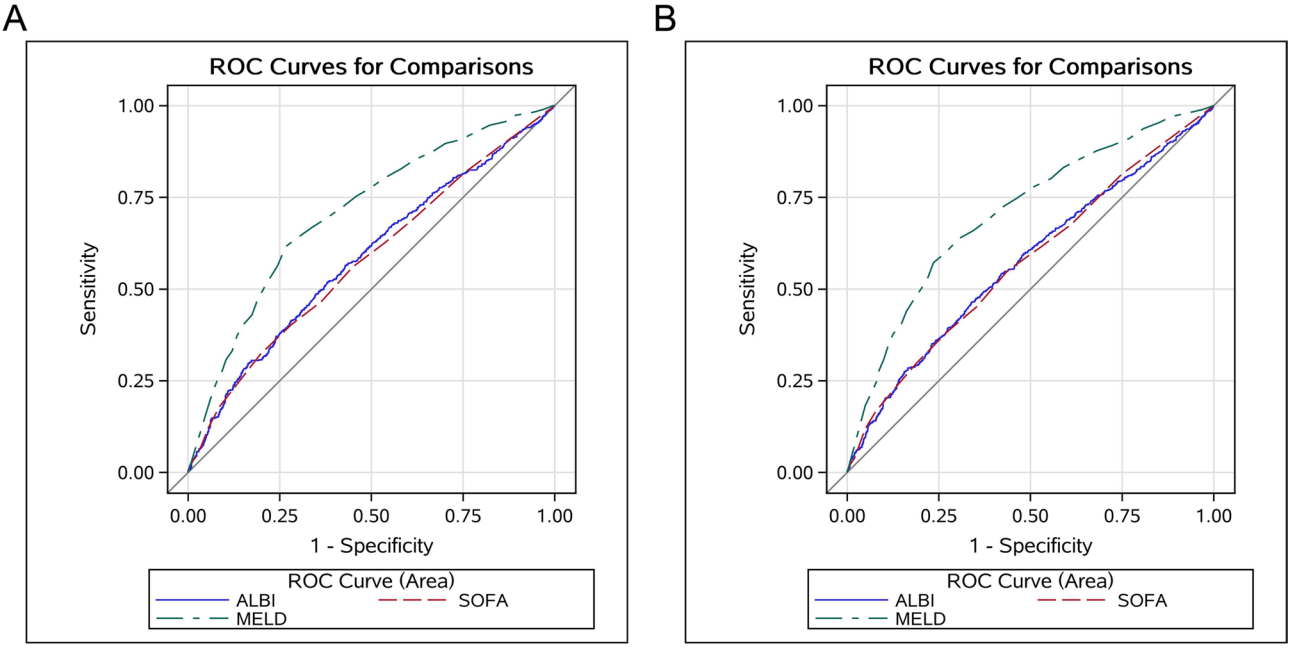

Fig. 4 ROC curve assesses the predictive capability of the ALBI score for 28-day (**A**), and 90-day (**B**) all-cause mortality. ALBI: albumin-bilirubin

Table 5 Information of ROC curves in Fig. 4

Variables	AUC (%)	95% CI (%)	Threshold	Sensitivity	Specificity
28-day mortality					
ALBI	60.02	55.79–61.27	−1.16	0.62	0.52
SOFA	56.21	55.08–60.52	27.50	0.73	0.62
MELD	69.81	68.37–73.25	6.50	0.80	0.32
90-day mortality					
ALBI	58.17	54.82–59.92	−1.09	0.66	0.46
SOFA	55.37	54.85–59.89	27.50	0.76	0.57
MELD	68.70	68.41–72.99	3.50	0.56	0.55

ALBI albumin-bilirubin, *SOFA* Sequential Organ Failure Assessment, Model for End-Stage Liver Disease

their corresponding 95% CIs across different values of the ALBI score. The analysis reveals a nonlinear relationship between ALBI score and mortality risk. As depicted in the graph, below a certain threshold of the ALBI score, the HR remains relatively stable or even shows a slight decrease, suggesting that slight increases in the ALBI score do not significantly elevate the risk of death within this range. Once the ALBI score surpasses this threshold, the risk of mortality increases sharply, with HR values rising markedly beyond this point.

ROC curve analysis

We plotted ROC curves for the ALBI, SOFA, and MELD scores to assess their ability to predict 28-day and 90-day mortality in patients. The results showed that although the AUC of the ALBI score was lower than that of the MELD score, it was not inferior to the AUC of the SOFA score for both 28-day and 90-day mortality prediction. Further details are provided in Fig. 4; Table 5, and Supplementary Table 3.

Subgroup analyses

Figure 5 displays the subgroup analysis results exploring the associations between the ALBI score tertiles (T2 and T3 versus T1) and 28-day and 90-day mortality in patients with liver cirrhosis and sepsis while focusing on the interaction effects between the ALBI score and the subgroup variables.

For 28-day mortality, the interaction P-values across subgroup variables, such as age, sex, hypertension, and respiratory failure, were consistently non-significant ($P > 0.05$). This result indicated that these variables failed to modify the association between the ALBI score and 28-day mortality. For example, the interaction P-values for age (<60 years vs. ≥60 years) and hypertension status (yes vs. no) were 0.90 and 0.38, respectively, demonstrating that the increased risk associated with higher ALBI scores was consistent regardless of these stratifying factors.

A similar pattern was observed across all subgroups for 90-day mortality, with P-values for interaction remaining

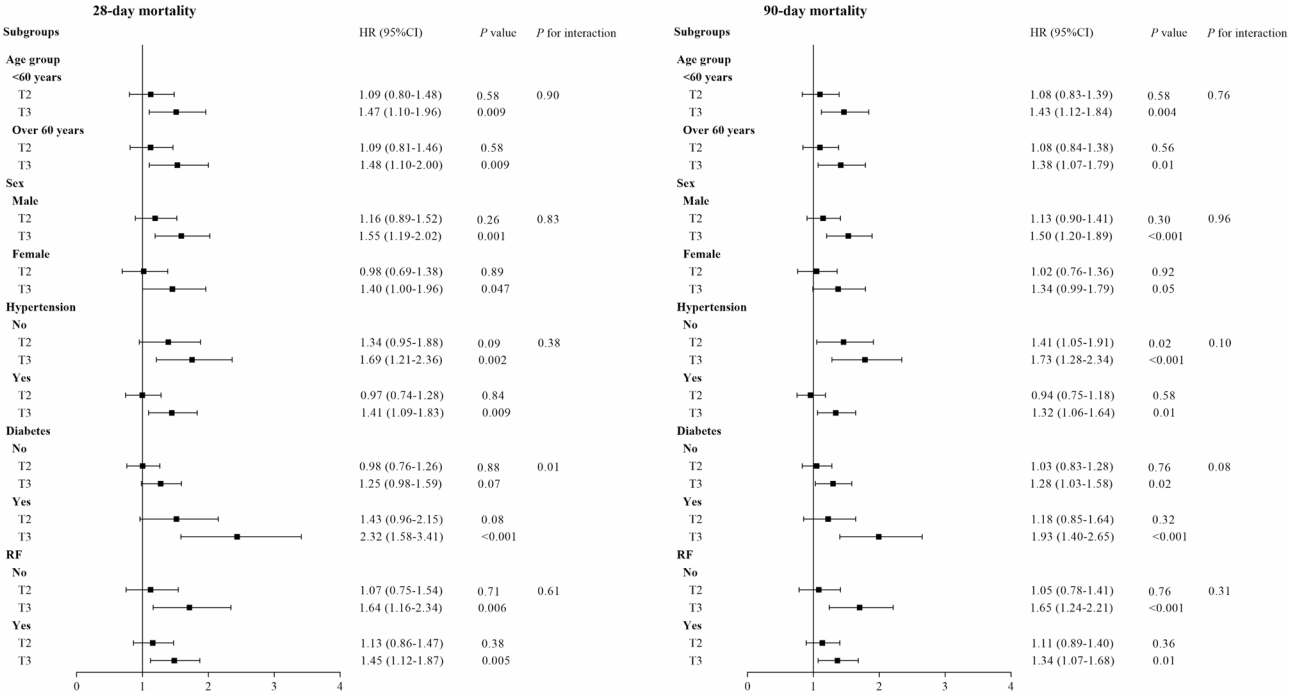

Fig. 5 Forest plots of stratified analyses of ALBI score and 28-day (**A**), and 90-day (**B**) all-cause mortality. ALBI: albumin-bilirubin

above 0.05 in all subgroups. For instance, the interaction P-values for sex (male vs. female) and diabetes status (yes vs. no) were 0.96 and 0.08, respectively. These findings indicate that demographic or clinical factors, such as age, sex, or comorbidities, do not influence the prognostic value of the ALBI score for 90-day mortality. The absence of significant interaction effects across all subgroup variables highlights the robustness and consistency of the ALBI score as a predictor of mortality in patients with liver cirrhosis and sepsis. This uniform association supports the broad applicability of the ALBI score in diverse patient populations, reinforcing its clinical utility as an independent prognostic marker.

Discussion

To the best of our knowledge, this study is the first to retrospectively evaluate the prognostic value of the ALBI score in ICU patients with cirrhosis and sepsis. We found that higher ALBI scores were significantly associated with increased 28- and 90-day mortality, and this association remained robust after adjustment for key demographic and clinical covariates. This trend persisted across both tertile and median-based stratifications, indicating a clear, dose–response relationship.

Mechanistically, the ALBI score is derived from serum albumin and bilirubin levels, reflecting both hepatic synthetic and excretory functions [20]. Albumin, a major hepatic protein, is a negative acute-phase reactant whose levels decrease during systemic inflammation, acute illness, and stress [21, 22]. In cirrhosis, hypoalbuminemia indicates impaired liver function and systemic inflammation driven by cytokines such as TNF-α and IL-6, which reduce albumin synthesis and increase catabolism [22]. This cascade contributes to vascular permeability, immune dysregulation, and multi-organ dysfunction [23, 24]. Conversely, elevated bilirubin reflects hepatic metabolic dysfunction and is often associated with cholestasis and severe liver injury. Moreover, hyperbilirubinemia may aggravate systemic inflammation through oxidative stress mechanisms [25]. Thus, the ALBI score effectively captures both hepatic reserve and inflammatory burden in critically ill patients with cirrhosis and sepsis.

Additionally, the gut-liver axis plays a critical role in the progression of both cirrhosis and sepsis [26, 27]. Increased intestinal permeability promotes bacterial translocation and endotoxemia, initiating systemic inflammatory response syndrome and subsequent multi-organ dysfunction [5, 28]. In our study, the ALBI score enabled risk stratification by dynamically reflecting this complex hepatic-infectious interplay.

Our RCS analysis demonstrated a nonlinear relationship between the ALBI score and mortality, with a marked increase in risk observed above specific threshold values. This data-driven pattern suggests that the ALBI score may serve as a useful early warning indicator for poor prognosis in ICU patients with cirrhosis and sepsis. While we proposed a preliminary inflection-based threshold derived from tertile stratification and RCS findings, we emphasize that this cutoff is exploratory and should be interpreted with caution until externally

validated in prospective cohorts.Nevertheless, this preliminary threshold may help identify high-risk patients who could benefit from closer monitoring, more intensive supportive therapies, or expedited ICU admission.

To enhance clinical utility, we propose several potential pathways for integrating the ALBI score into practice. First, as a pre-ICU triage tool, the ALBI score could assist emergency department or general ward clinicians in identifying patients with liver dysfunction and systemic inflammation who are at elevated risk and may require early transfer to intensive care.Second, the ALBI score could be incorporated as a complementary parameter into existing risk models—such as SOFA or MELD—to improve liver-specific prognostic precision, especially in patients with sepsis-related hepatic impairment.Lastly, the ALBI score may support early treatment escalation decisions in ICU settings by serving as a simple, objective measure of hepatic reserve. Future research should aim to determine optimal ALBI thresholds for guiding clinical interventions, define appropriate time points for reassessment, and evaluate whether ALBI-based risk stratification translates into improved outcomes. These steps will be crucial in transitioning the ALBI score from a statistical prognostic marker to a clinically actionable tool.

Compared to traditional ICU scores such as SOFA and MELD, ALBI offers a simpler and more liver-specific assessment. The SOFA score includes only bilirubin for hepatic function and omits synthetic capacity. MELD, originally designed to prioritize liver transplant candidates, incorporates INR, which may be affected by anticoagulation and not fully reflect sepsis-induced hepatic dysfunction [29, 30]. In contrast, the ALBI score focuses on two fundamental aspects of liver function and performed comparably or better than SOFA in predicting short- and long-term mortality.

In subgroup analysis, we observed a statistically significant interaction between diabetes mellitus and ALBI score. The association between ALBI and mortality was stronger in diabetic patients, potentially due to mechanisms such as hepatic steatosis, oxidative stress, and insulin resistance [31], along with hyperglycemia-induced inflammasome activation and elevated proinflammatory cytokines [32]. Diabetes-related immune dysfunction, including impaired neutrophil chemotaxis and macrophage phagocytosis [33], may further amplify vulnerability in this population. These processes could interact with cirrhosis-related immune impairment, exacerbating clinical outcomes in sepsis.

To validate robustness, we applied a median-based dichotomization in sensitivity analyses. This approach, while clinically intuitive, supported our main findings—higher ALBI scores were consistently associated with worse outcomes.

Despite the strengths of our study, several limitations must be acknowledged. First, this was a retrospective study based on data from a single tertiary care center, which may limit the generalizability of our findings to other healthcare settings or populations. Although we employed rigorous inclusion criteria, multivariable adjustments, sensitivity analyses, and subgroup stratifications to enhance internal validity, the absence of external validation remains a notable limitation. Future prospective and multicenter studies, as well as analyses based on other publicly available critical care databases (e.g., eICU or HiRID), are warranted to confirm the applicability of our findings across broader clinical contexts. Second, patients with ICU stays shorter than 24 h were excluded, which might have led to an underestimation of early mortality risk, especially among patients who died shortly after admission. Third, ALBI scores were calculated based on laboratory parameters obtained within the first 24 h of ICU admission, without accounting for subsequent dynamic changes in liver function, which may also carry prognostic significance. Finally, although renal dysfunction was incorporated into the multivariate models, the neurological component of organ dysfunction could not be included due to substantial missing or inconsistent Glasgow Coma Scale data within the MIMIC-IV database. As the SOFA score already includes a neurologic assessment, we chose not to impute or supplement this domain separately to avoid potential multicollinearity. Nevertheless, this exclusion may have resulted in incomplete adjustment for overall disease severity.

In conclusion, the ALBI score is a simple, objective, and effective tool for early risk stratification in ICU patients with cirrhosis and sepsis. Its integration into ICU workflows and dynamic risk models warrants further exploration through prospective multicenter studies.

Conclusion

Higher ALBI scores were significantly and independently associated with increased short-term and long-term mortality risk in ICU patients with cirrhosis and sepsis. Owing to its simplicity and potential prognostic value, the ALBI score could complement existing clinical tools for managing critically ill patients with cirrhosis and sepsis.

Abbreviations

ALBI	albumin-bilirubin
CI	confidence interval
HR	hazard ratio
ICU	intensive care unit
MIMIC-IV	Medical Information Mart for Intensive Care-IV
RCS	restricted cubic spline
SOFA	Sequential Organ Failure Assessment
MELD	Model for End-Stage Liver Disease
ROC	Receiver operating characteristic

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12876-025-04111-7.

Supplementary Material 1.

Supplementary Material 2.

Supplementary Material 3.

Supplementary Material 4.

Acknowledgements
We are appreciative of the MIMIC-IV (v 3.0) participants and staff. We thank all reviewers who participated in the review.

Authors' contributions
(I) Conception and design: Jianjun Wang, Pei Yang, Chuan Qin, Yongwei Huang, Zhaohui Hu, Ruizi Shi, Sirui Chen; (II) Administrative support: Sirui Chen, Xi Chen, Hua Luo, Jianping Gong, Xintao Zeng, Decai Wang; (III) Provision of study material: All authors; (IV) Collection and assembly of data: All authors; (V) Data analysis and interpretation: Jianjun Wang, Pei Yang, Chuan Qin; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors. Jianjun Wang, Pei Yang, and Chuan Qin contributed equally to this work and share the first authorship. Jianping Gong, Xintao Zeng, and Decai Wang contributed equally to this work and share the corresponding authorship.

Funding
This study was supported by National Natural Science Foundation of China (NSFC) (Grant no.82400758), NHC Key Laboratory of Nuclear Technology Medical Transformation (Mianyang Central Hospital) (Grant no.2023HYX032), Health Commission of Sichuan Province Medical Science and Technology Program (Grant no.24QNMP028), Scientifc Research Project of Mianyang Health Commission (Grant no.201926), Clinical Special Project of Mianyang Central Hospital (Grant no.2024LC007), and Medical Research Youth Innovation Project of Sichuan Province, China (Grant no.Q23046).

Data availability
Raw data supporting the conclusions of this paper will be made available by the authors without reservation and may be requested from the corresponding author.

Declarations

Ethics approval and consent to participate
This study used the publicly available MIMIC-IV (v. 3.0) database, which contains deidentified data. Therefore, additional approval from the institutional review board was not required. All study methods adhered to the relevant ethical guidelines and regulations, ensuring the protection of patient privacy and data confidentiality.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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Received: 24 March 2025 / Accepted: 23 June 2025
Published online: 15 July 2025

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