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Association of Systemic Inflammation Response Index with Short-Term All-Cause Mortality in Decompensated Liver Cirrhosis Patients

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Background: The Systemic Inflammation Response Index (SIRI) has demonstrated predictive capabilities for clinical outcomes in various diseases. However, its prognostic utility in decompensated liver cirrhosis (DLC) remains underexplored. This study aimed to investigate the association between SIRI and the risk of short-term (3 and 6 months) all-cause mortality in DLC patients.

Methods: A total of 926 eligible patients with DLC from diverse etiologies was included in this study. In the initial cohort, the predictive accuracy of SIRI was evaluated using receiver operating characteristic (ROC) curve analysis. Patients were categorized into high- and low-SIRI groups based on the Youden index. Multivariable logistic regression analysis was employed to evaluate the independent association between SIRI and all-cause mortality. Restricted cubic spline (RCS) analysis was utilized to visualize the relationship between the continuous variable SIRI and mortality risk. These findings were validated in a validation cohort.

Results: The initial cohort had mortality rates of 8.8% and 11.6% at 3 and 6 months, respectively. The SIRI level was significantly higher in the deceased group compared to the survival group. At both time points, SIRI was an independent indicator of all-cause mortality. RCS analysis demonstrated the risk of the risk of increased with an increase in SIRI value. The Validation cohort validated the independent association between higher SIRI levels and lower short-term all-cause mortality.

Conclusion: This study's findings underscore the prognostic value of SIRI in DLC patients, indicating that higher SIRI levels are significantly associated with short-term adverse outcomes.

Keywords: decompensated liver cirrhosis, systemic inflammation response index, prognosis, all-cause mortality

Introduction

Cirrhosis, a chronic liver condition, arises from persistent inflammation and fibrosis, marking the advanced stage of liver damage.[1,2] This disease stands as the 11th leading cause of global mortality and is notably the third most common cause of death among individuals between the ages of 45 and 64.[3,4] With an annual death toll of approximately 2 million, cirrhosis poses a significant health challenge worldwide.[3,4] Decompensated liver cirrhosis (DLC) signifies a pivotal and critical phase in the progression of liver cirrhosis. It is characterized by a decline in liver function and the emergence of severe, life-threatening complications. DLC is often associated with a grim prognosis and imposes a substantial burden on healthcare systems.[5,6] The short-term mortality rate among patients with DLC can soar to 15%.[7,8] underscoring the imperative need for early detection of high-risk individuals and the swift implementation of therapeutic interventions to ameliorate patient outcomes.

Inflammation is a pivotal factor in the prognosis of liver cirrhosis. It can trigger a cascade of complications, such as ascites and hepatic encephalopathy, which in turn accelerate the progression of the disease.[9] Furthermore, inflammation contributes to the development of portal hypertension, a condition that can lead to devastating cirrhosis-related complications like variceal bleeding.[10] The onset of these complications is often a harbinger of poor short-term survival

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rates for patients. Systemic inflammation also heightens the risk of infections, which can intensify organ damage, playing a critical role in the outcomes of patients with DLC.[11]

The Systemic Inflammation Response Index (SIRI) serves as a comprehensive indicator of inflammation, based on the counts of monocytes, neutrophils, and lymphocytes.[12] Recent research has revealed that SIRI is independently correlated with the prognosis of patients suffering from a variety of conditions, including different types of tumors, autoimmune rheumatic diseases, cardiovascular diseases, cerebral hemorrhage, and pneumonia.[12–19] However, the relationship between SIRI and the short-term prognosis in patients with decompensated cirrhosis (DLC) remains unexplored. Our research aims to elucidate this connection, potentially offering new insights for the management of DLC.

Materials and Methods

Patients

Patients diagnosed with DLC and admitted to the Second Affiliated Hospital of Wannan Medical College between March 2016 and March 2023 were retrospectively assembled to form the initial cohort for this investigation. DLC was characterized by biochemical, clinical, endoscopic manifestations, imaging indicators, and complications such as ascites, gastrointestinal bleeding, hepatorenal syndrome, or hepatic encephalopathy.[20] Exclusion criteria encompassed: (1) non-initial admissions, (2) malignancies, (3) autoimmune disorders, (4) primary renal diseases, (5) cardio-cerebrovascular diseases, (6) infectious diseases, (7) incomplete data, and (8) loss to follow-up. Utilizing identical exclusion criteria, patients with DLC admitted to the Yijishan Hospital of Wannan Medical College from January 2018 to March 2023 constituted the validation cohort. A detailed patient selection process is depicted in Figure 1.

Data Collection

Patient outcomes at 3 and 6 months post-admission were evaluated through review of medical records or via direct communication with patients or their relatives. Data collected at the time of admission included gender, age, etiology of cirrhosis, presence of ascites (yes/no), variceal bleeding (yes/no), hepatorenal syndrome (yes/no), hepatic encephalopathy (yes/no), and laboratory findings. The SIRI was calculated using the formula: neutrophil count ($\times 10^9$/L) × monocyte count ($\times 10^9$/L) / lymphocyte count ($\times 10^9$/L).[17] The neutrophil-to-lymphocyte ratio (NLR), monocyte-to-lymphocyte ratio (MLR) and platelet-to-lymphocyte ratio (PLR) were calculated as neutrophil count ($\times 10^9$/L) / lymphocyte count ($\times 10^9$/L), monocyte count ($\times 10^9$/L) / lymphocyte count ($\times 10^9$/L), and platelet count ($\times 10^9$/L) / lymphocyte count ($\times 10^9$/L), respectively.

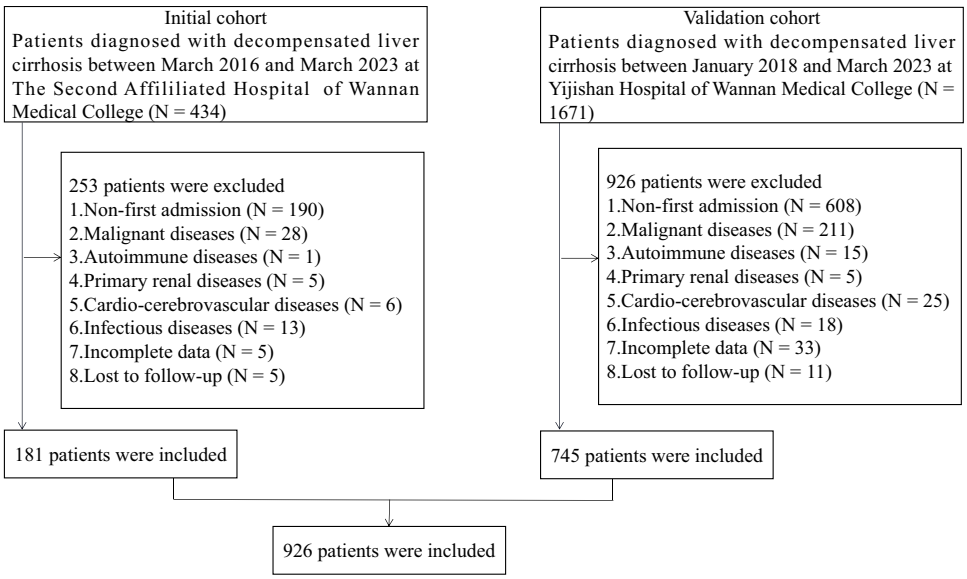

Figure 1 Flowchart of the patients selection process.

Statistical Analysis

Continuous variables were presented as mean ± standard deviation or median (first quartile, third quartile), while categorical variables were expressed as counts (percentages). Independent sample t-tests or Mann–Whitney *U*-tests were employed to compare continuous variables that were normally distributed or not, respectively. Categorical data were compared using chi-square tests. Receiver operating characteristic (ROC) curves were generated to ascertain the area under the curve (AUC), and patients were stratified into high and low SIRI groups based on the Youden index derived from the ROC curve. The Delong test was used to compare the AUC values.[21] Univariate analysis was conducted to assess the correlation between various variables and all-cause mortality, with variables yielding a p-value less than 0.05 being selected for inclusion in the multivariable analysis. Multivariable logistic regression analysis was then performed to ascertain the independent relationship between SIRI and all-cause mortality. Based on multivariable analysis, restricted cubic splines (RCS) analysis was utilized to graphically represent the association between SIRI (as a continuous variable) and the risk of all-cause mortality. All statistical procedures were carried out using SPSS (version 27.0), R (version 4.0.2), and MedCalc (Version 15.2). All statistical tests were two-tailed, with a p-value of less than 0.05 considered indicative of statistical significance.

Results

Baseline Characteristics

The present study enrolled a total of 926 patients with DLC who met the inclusion criteria. Within the initial cohort, the mean age of the patients was 64 years, comprising 82 females (45.3%) and 99 males (54.7%). Chronic hepatitis B virus (HBV) infection was identified as the predominant cause of cirrhosis in 119 cases (65.7%). Complications included ascites in 135 cases (74.6%), esophagogastric variceal bleeding in 35 cases (19.3%), hepatic encephalopathy in 11 cases (6.1%), and hepatorenal syndrome in 4 cases (2.2%). The all-cause mortality rates at the 3- and 6-month endpoints were 8.8% and 11.6%, respectively. Detailed characteristics of the initial and validation cohorts are summarized in Table 1.

Clinical Features and Laboratory Results Between Survival and Deceased Groups

In the initial cohort, values of neutrophils (Neut), monocytes (Mono), total bilirubin (Tbil), creatinine (Cr), prothrombin time (PT), and SIRI were markedly elevated in the deceased group compared to the survival group at both the 3- and 6-month follow-up endpoints. At the 6-month mark, lymphocyte (LYM) counts were significantly reduced in the deceased group relative to the survival group; no significant inter-group differences were observed at the 3-month mark. Hemoglobin (HGB), platelet (PLT) counts, albumin (Alb), alanine aminotransferase (ALT), gamma-glutamyl transferase (GGT), and gender remained consistent between the two groups across both follow-up endpoints. Comprehensive details for the survival and deceased groups in the initial and validation cohorts are delineated in Table 1.

Clinical Characteristics and Laboratory Results Between High and Low SIRI Groups

In the initial cohort, ROC analysis revealed AUC values for SIRI at 3 and 6 months to be 0.841 and 0.807, respectively (Figure 2A and B). Participants were categorized into high and low SIRI groups based on the Youden index from the ROC curve. The optimal cutoff points for 3 and 6 months were established at 2.227 and 0.961, respectively. Within the high SIRI group, elevated values of Neut, Mono, Tbil, PT, and SIRI, alongside a higher all-cause mortality rate, were observed, with a concurrent significant decrease in Alb compared to the low SIRI group. At the 3-month mark, HGB values were notably lower in the high SIRI group; this difference was not apparent at the 6-month mark. Further details regarding the high and low SIRI groups in the validation cohort are presented in Table 2.

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Table 1 Clinical and Laboratory Characteristics of Patients with Decompensated Liver Cirrhosis in the Initial and Validation Cohort at the 3-Month, and 6-Month Follow-Ups

Variables	Initial cohort							Validation cohort						
	All patients (n = 181)	3 months		P	6 months		P	All patients (n = 745)	3 months		P	6 months		P
		Survivors (n = 165)	Deaths (n = 16)		Survivors (n = 160)	Deaths (n = 21)			Survivors (n = 673)	Deaths (n = 72)		Survivors (n = 649)	Deaths (n = 96)	
Gender (n, %)[#]				0.087			0.101				0.885			0.727
Male	99 (54.7%)	87 (52.7%)	12 (75.0%)		84 (52.5%)	6 (28.6%)		439 (58.9%)	396 (58.8%)	43 (59.7%)		384 (59.2%)	55 (57.3%)	
Female	82 (45.3%)	78 (47.3%)	4 (25.0%)		76 (47.5%)	15 (71.4%)		306 (41.1%)	277 (41.2%)	29 (40.3%)		265 (40.8%)	41 (42.7%)	
Age (years)*	64.0 (53.0–74.0)	64.0 (53.0–74.0)	68.0 (63.0–74.0)	0.076	64.0 (53.0–74.0)	71.0 (63.0–74.0)	0.049	61.0 (52.0–70.0)	59.0 (51.0–70.0)	64.7 ± 12.0	0.006	59.0 (51.0–70.0)	64.4 ± 12.7	0.003
Neut (10^9/L)[#]	2.3 (1.6–3.7)	2.2 (1.6–3.4)	3.8 (2.8–4.9)	<0.001	2.2 (1.6–3.4)	3.6 (2.5–4.8)	0.001	2.3 (1.5–3.8)	2.1 (1.5–3.5)	4.2 (2.6–6.8)	<0.001	2.1 (1.5–3.5)	3.9 (2.3–6.4)	<0.001
LYM (10^9/L)[#]	0.8 (0.6–1.2)	0.8 (0.6–1.3)	0.6 (0.4–1.1)	0.088	0.8 (0.6–1.3)	0.6 (0.3–1.1)	0.026	0.9 (0.6–1.3)	0.9 (0.6–1.3)	0.9 (0.6–1.4)	0.799	0.9 (0.6–1.3)	0.9 (0.6–1.3)	0.813
Mono (10^9/L)*	0.3 (0.2–0.5)	0.3 (0.2–0.5)	0.5 (0.3–0.7)	0.020	0.3 (0.2–0.5)	0.4 (0.3–0.6)	0.035	0.3 (0.2–0.5)	0.3 (0.2–0.4)	0.4 (0.3–0.7)	<0.001	0.3 (0.2–0.4)	0.4 (0.3–0.7)	<0.001
HGB (g/L)[#]	100.3 ± 27.0	100.7 ± 27.1	96.7 ± 25.7	0.574	101.0 ± 27.0	96.0 ± 27.5	0.436	99.0 (78.5–116.0)	100.0 (81.0–116.0)	86.6 ± 34.4	0.002	100 0.0 (80.0–116.5)	88.0 ± 29.8	0.002
PLT (10^9/L)*	74.0 (51.0–118.5)	72.0 (50.0–111.5)	97.5 (70.3–177.0)	0.051	72.0 (50.0–114.8)	87.0 (67.5–145.0)	0.134	65.0 (45.0–97.5)	64.0 (44.0–96.0)	77.0 (56.0–123.8)	0.001	63.0 (44.0–95.5)	77.0 (54.3–114.5)	0.001
Alb (g/L)*	32.2 ± 6.6	32.5 ± 6.8	30.0 ± 5.0	0.160	32.6 ± 6.8	29.7 ± 4.5	0.065	29.8 ± 5.9	30.2 ± 5.8	26.0 ± 5.6	<0.001	29.8 (26.4–34.2)	25.9 ± 5.6	<0.001
Tbil (umol/L)*	20.3 (12.4–34.9)	18.9 (12.2–31.3)	56.8 (16.7–242.5)	0.003	18.9 (12.1–31.0)	36.1 (14.4–179.0)	0.006	27.8 (18.0–45.7)	26.5 (17.9–42.8)	49.9 (26.3–104.2)	<0.001	26.6 (17.9–42.7)	44.6 (20.0–82.7)	<0.001
ALT (U/L)*	21.0 (16.0–36.0)	21.0 (16.0–34.0)	29.5 (10.5–140.8)	0.459	21.0 (16.0–34.0)	25.0 (15.0–98.5)	0.569	26.0 (18.0–48.0)	26.0 (18.0–48.0)	26.0 (15.0–57.8)	0.847	27.0 (18.0–48.5)	26.0 (15.0–44.0)	0.228
GGT (U/L)[#]	42.0 (25.0–124.5)	42.0 (24.5–119.0)	49.5 (27.8–157.5)	0.595	41.5 (24.0–112.8)	53.0 (28.5–153.0)	0.294	47.0 (22.0–107.0)	48.0 (23.0–107.5)	38.5 (18.0–98.5)	0.084	49.0 (24.0–107.5)	37.5 (15.5–98.5)	0.018
Cr (umol/L)*	82.3 (69.8–102.1)	81.2 (68.6–98.6)	103.6 (83.2–143.8)	0.013	81.3 (69.2–98.3)	1101.0 (74.5–143.5)	0.043	65.9 (53.2–84.4)	65.5 (53.2–82.6)	75.6 (52.7–112.6)	0.012	65.4 (53.1–82.8)	69.3 (54.6–108.1)	0.021
PT (s)*	13.2 (12.0–15.0)	13.2 (12.0–14.7)	16.0 (12.7–23.8)	0.023	13.2 (11.9–14.7)	15.3 (12.7–22.0)	0.018	14.9 (13.5–16.6)	14.8 (13.4–16.5)	16.5 (14.7–22.2)	<0.001	14.8 (13.4–16.4)	16.0 (14.3–20.8)	<0.001
SIRI*	0.8 (0.5–1.9)	0.8 (0.5–1.7)	2.8 (1.9–5.0)	<0.001	0.7 (0.4–1.7)	2.5 (1.3–4.8)	<0.001	0.7 (0.4–1.7)	0.65 (0.4–1.4)	2.0 (1.1–4.0)	<0.001	0.6 (0.4–1.3)	1.9 (0.9–3.5)	<0.001
Etiology (n, %)														
HBV	119 (65.7%)	107 (64.8%)	12 (75.0%)		103 (64.4%)	16 (76.2%)		447 (60.0%)	403 (59.9%)	44 (61.1%)		387 (59.6%)	60 (62.5%)	
HCV	12 (6.6%)	12 (7.3%)	0		12 (7.5%)	0		46 (6.2%)	42 (6.2%)	4 (5.6%)		40 (6.2%)	6 (6.3%)	
Alcoholism	13 (7.2%)	11 (6.7%)	2 (12.5%)		10 (6.3%)	3 (14.3%)		38 (5.1%)	34 (5.1%)	4 (5.6%)		32 (4.9%)	6 (6.3%)	
Others	37 (20.4%)	35 (21.2%)	2 (12.5%)		35 (21.9%)	2 (9.5%)		214 (28.7%)	194 (28.8%)	20 (27.8%)		190 (29.3%)	24 (25.0%)	
Modes of decompensation (n, %)														
Ascites	135 (74.6%)	121 (73.3%)	14 (87.5%)		118 (73.8%)	17 (81.0%)		536 (71.9%)	479 (71.2%)	57 (79.2%)		460 (70.9%)	76 (79.2%)	
Variceal bleeding	35 (19.3%)	31 (18.8%)	4 (25.0%)		31 (19.4%)	4 (19.0%)		208 (27.9)	188 (27.9%)	20 (27.8%)		179 (27.6%)	29 (30.2%)	
HE	11 (6.1%)	9 (5.5%)	2 (12.5%)		8 (5.0%)	3 (14.3%)		37 (4.7%)	19 (2.8%)	18 (25.0%)		19 (2.9%)	18 (18.8%)	
HRS	4 (2.2%)	1 (0.6%)	3 (18.8%)		1 (0.6%)	3 (14.3%)		15 (2.0%)	4 (0.6%)	11 (15.3%)		3 (0.5%)	12 (12.5%)	

Note: Data are expressed as number, mean ± standard deviation, median (25th–75th percentiles), or frequency [percentage (%)]. *Significant differences (P < 0.05) were observed between the initial group and validation group. [#]No significant differences (P > 0.05) were observed between the initial group and validation group.

Abbreviations: Neut, neutrophils; LYM, lymphocyte; Mono, monocytes; HGB, hemoglobin; PLT, platelet; Alb, albumin; Tbil, total bilirubin; ALT, alanine aminotransferase; GGT, γ–glutamyl transpeptidase; Cr, creatinine; PT, prothrombin time; SIRI, Systemic Inflammation Response Index; HBV, hepatitis B virus; HCV, hepatitis C virus; HE, hepatic encephalopathy; HRS, hepatorenal syndrome.

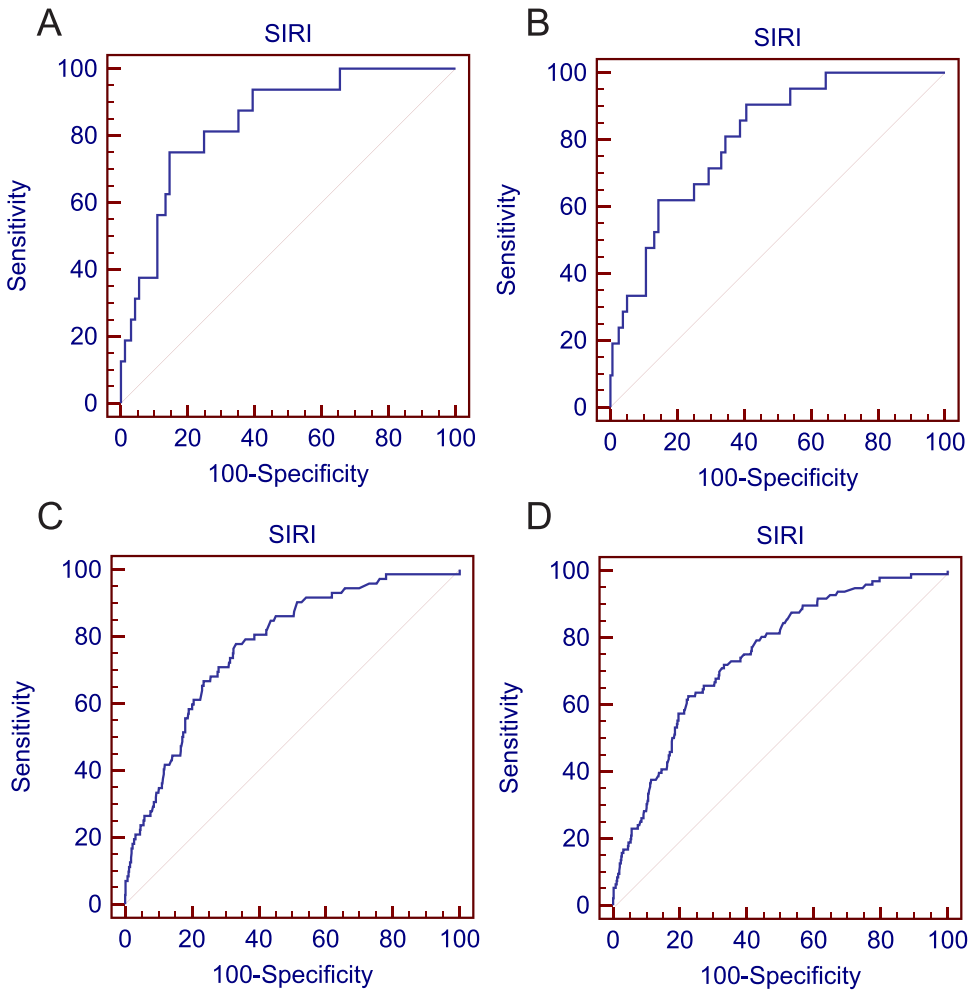

Figure 2 Receiver operating characteristic curve for the prognosis prediction of patients with decompensated cirrhosis by SIRI. (**A**) 3 months of initial cohort; (**B**) 6 months of initial cohort; (**C**) 3 months of validation cohort; (**D**) 6 months of validation cohort.

High SIRI Levels are Independently Associated with All-Cause Mortality in Patients with DLC

Univariate analysis was conducted to identify variables significantly linked to patient outcomes ($P < 0.05$), which were subsequently included in the multivariable analysis. The findings from the multivariable analysis indicated that elevated SIRI levels are independently correlated with all-cause mortality at both 3- and 6-month follow-up endpoints (Table 3). The RCS analysis, based on multivariable analysis, demonstrated a positive correlation between SIRI values and the risk of all-cause mortality. There was a general trend of increasing all-cause mortality risk with rising SIRI values, although the risk appeared to plateau when SIRI values approached 2.7 (Figure 3A and B).

Verified of Results in the Validation Cohort

In the validation cohort, the AUC values for SIRI at 3 and 6 months were 0.773 and 0.747, respectively, suggesting promising predictive capabilities (Figure 2C and D). Furthermore, although the AUC value of SIRI was higher than that of the NLR, MLR, and PLR at 3 and 6 months in the initial cohort, it did not reach statistical significance. In the validation cohort, the SIRI demonstrated significantly better predictive ability than MLR and PLR at 3 months, and significantly better predictive ability than NLR, MLR, and PLR at 6 months (Supplementary Figure 1). Our findings confirmed that high SIRI levels are independently associated with all-cause mortality at both 3- and 6-month endpoints (Table 3). The RCS analysis corroborated results akin to those of the initial cohort (Figure 3C and D).

Table 2 Comparison of Clinical and Laboratory Characteristics Between Low and High SIRI Groups in the Initial and Validation Cohort in Patients with Decompensated Liver Cirrhosis

Variables	Initial cohort						Validation cohort					
	3 months			6 months			3 months			6 months		
	SIRI < 2.227 (n=144)	SIRI > 2.227 (n=37)	P	SIRI < 0.961 (n=97)	SIRI > 0.961 (n=84)	P	SIRI < 2.227 (n=613)	SIRI > 2.227 (n=132)	P	SIRI < 0.961 (n=440)	SIRI > 0.961 (n=305)	P
Gender (n, %)			<0.001			0.016			0.309			0.009
Male	69 (47.9%)	30 (81.1%)		45 (46.4%)	54 (64.3%)		356 (58.1%)	83 (62.9%)		242 (55.0%)	197 (64.6%)	
Female	75 (52.1%)	7 (18.9%)		52 (53.6%)	30 (35.7%)		257 (41.9%)	49 (37.1%)		198 (45.0%)	108 (35.4%)	
Age (years)	65.0 (53.0–75.8)	61.5 ± 11.2	0.185	64.0 (52.0–75.0)	64.5 ± 12.5	0.551	61.0 (52.0–70.0)	61.1 ± 12.4	0.864	59.0 (52.0–69.0)	62.0 (52.0–71.0)	0.26
Neut (10^9/L)	2.0 (1.5–2.8)	5.0 (4.0–7.1)	<0.001	1.7 (1.3–2.2)	3.7 (2.6–4.9)	<0.001	2.0 (1.4–2.9)	6.4 (4.7–7.8)	<0.001	1.6 (1.2–2.1)	4.2 (3.2–6.4)	<0.001
LYM (10^9/L)	0.8 (0.6–1.3)	0.8 ± 0.4	0.184	0.9 (0.6–1.6)	0.7 (0.5–1.0)	0.003	0.9 (0.6–1.3)	0.9 (0.6–1.3)	0.043	0.9 (0.6–1.3)	0.9 (0.6–1.4)	0.624
Mono (10^9/L)	0.3 (0.2–0.4)	0.6 ± 0.3	<0.001	0.3 (0.2–0.4)	0.4 (0.3–0.6)	<0.001	0.3 (0.2–0.4)	0.6 (0.4–0.8)	<0.001	0.2 (0.2–0.3)	0.4 (0.3–0.6)	<0.001
HGB (g/L)	102.4 ± 26.2	92.2 ± 28.5	0.041	103.8 ± 24.6	96.3 ± 29.0	0.061	100.0 (80.0–116.0)	92.2 ± 28.1	0.019	100.5 (81.0–116.0)	95.5 ± 28.1	0.24
PLT (10^9/L)	71.5 (51.0–107.0)	87.0 (50.5–141.5)	0.193	71.0 (49.5–114.5)	77.5 (52.0–125.3)	0.542	63.0 (44.0–92.0)	80.0 (54.0–126.8)	<0.001	57.0 (42.0–86.0)	76.0 (52.0–117.5)	<0.001
Alb (g/L)	32.9 ± 6.9	29.7 ± 4.7	0.002	33.3 ± 6.7	30.9 (26.2–34.7)	0.013	30.2 ± 6.0	27.6 ± 5.3	<0.001	31.0 ± 5.8	28.0 ± 5.7	<0.001
Tbil (umol/L)	18.5 (11.7–30.0)	27.7 (17.4–118.6)	<0.001	18.6 (11.6–29.2)	22.7 (13.2–57.3)	0.043	26.9 (17.9–43.6)	33.5 (18.2–63.3)	0.016	25.3 (17.3–39.2)	33.2 (20.2–62.9)	<0.001
ALT (U/L)	21.0 (15.3–36.0)	25.0 (16.0–41.0)	0.548	23.0 (17.0–37.0)	18.0 (14.0–34.0)	0.094	26.0 (18.0–48.5)	26.5 (18.0–41.8)	0.743	26.0 (18.0–48.0)	27.0 (17.5–49.5)	0.694
GGT (U/L)	44.0 (26.3–131.8)	37.0 (22.5–119.5)	0.627	44.0 (26.5–129.5)	41.0 (24.0–121.8)	0.872	49.0 (24.0–108.0)	41.5 (19.3–91.0)	0.164	50.0 (24.0–100.0)	44.0 (21.0–120.0)	0.782
Cr (umol/L)	81.8 (66.9–98.6)	86.8 (71.5–130.7)	0.177	81.2 (64.4–97.9)	87.0 (71.6–122.1)	0.049	66.2 (52.7–84.4)	65.4 (55.9–83.7)	0.489	63.8 (51.2–81.8)	69.0 (56.0–90.0)	0.003
PT (s)	13.0 (11.7–14.4)	14.2 (12.8–16.9)	0.002	13.1 (11.7–14.4)	13.8 (12.2–16.5)	0.005	14.8 (13.4–16.5)	15.5 (14.2–18.2)	0.001	14.7 (13.4–16.2)	15.3 (13.6–17.7)	0.001
SIRI	0.7 (0.4–1.1)	3.4 (2.7–5.1)	<0.001	0.5 (0.3–0.7)	2.0 (1.5–3.3)	<0.001	0.6 (0.3–1.1)	3.8 (2.9–5.1)	<0.001	0.4 (0.3–0.6)	2.0 (1.3–3.5)	<0.001
Mortality (n, %)	4 (2.7%)	12 (32.4%)	<0.001	2 (2.0%)	19 (22.6%)	<0.001	40 (6.5%)	32 (24.2%)	<0.001	26 (5.9%)	70 (22.9%)	<0.001

Note: Data are presented as number, mean ± standard deviation, median (25th–75th percentiles), or frequency [percentage (%)].

Abbreviations: Neut, neutrophils; LYM, lymphocyte; Mono, monocytes; HGB, hemoglobin; PLT, platelet; Alb, albumin; Tbil, total bilirubin; ALT, alanine aminotransferase; GGT, γ–glutamyl transpeptidase; Cr, creatinine; PT, prothrombin time; SIRI, Systemic Inflammation Response Index.

Table 3 SIRI is Independently Associated with the All-Cause Mortality of Patients with Decompensated Liver Cirrhosis in the Initial Cohort and Validation Cohort

Variables	Initial cohort								Validation cohort			
	3 months (univariable analysis)		3 months (multivariable analysis)		6 months (univariable analysis)		6 months (multivariable analysis)		3 months (multivariable analysis)		6 months (multivariable analysis)	
	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P
Age (years)	1.039 (0.997–1.086)	0.081			1.038 (1.000–1.080)	0.052						
Gender		0.098				0.108						
Female	reference				Reference							
Male	2.690 (0.895–9.933)				2.262 (0.871–6.613)							
HGB (g/L)	0.995 (0.976–1.014)	0.572			0.993 (0.976–1.010)	0.434						
Alb (g/L)	0.941 (0.861–1.021)	0.160			0.931 (0.859–1.002)	0.066						
GGT (U/L)	1.001 (0.997–1.004)	0.604			1.001 (0.998–1.004)	0.404						
PLT (10^9/L)	1.007 (1.000–1.015)	0.048	1.010 (1.000–1.021)	0.043	1.005 (0.998–1.012)	0.165			1.007 (1.004–1.011)	<0.001		
Tbil (umol/L)	1.015 (1.008–1.025)	<0.001	1.008 (0.998–1.021)	0.159	1.013 (1.007–1.022)	<0.001	1.007 (0.998–1.017)	0.168	1.004 (1.001–1.008)	0.012	1.003 (1.000–1.006)	0.053
ALT (U/L)	1.007 (1.002–1.013)	0.004	1.001 (0.990–1.010)	0.871	1.006 (1.001–1.011)	0.012	1.003 (0.993–1.012)	0.566	1.000 (0.998–1.001)	0.651	0.999 (0.998–1.001)	0.257
Cr (umol/L)	1.009 (1.001–1.017)	0.022	1.008 (0.997–1.018)	0.138	1.008 (1.000–1.015)	0.033	1.005 (0.996–1.013)	0.220	1.012 (1.006–1.018)	<0.001	1.008 (1.003–1.014)	0.002
PT (s)	1.303 (1.144–1.502)	<0.001	1.167 (0.918–1.473)	0.192	1.309 (1.157–1.500)	<0.001	1.106 (0.922–1.331)	0.273	1.237 (1.139–1.346)	<0.001	1.162 (1.083–1.249)	<0.001
SIRI		<0.001		0.011		<0.001		0.009		<0.001		<0.001
Low	reference		reference		reference		reference		reference		reference	
High	17.625 (5.635–67.306)		6.414 (1.542–28.968)		13.885 (3.855–89.043)		8.615 (2.065–61.830)		2.970 (1.635–5.327)		3.540 (2.162–5.930)	

Note: Age, Gender, HGB, PLT, Alb, Tbil, ALT, GGT, Cr, PT, and SIRI were included in the univariate logistic regression analysis. Variables that did not have a significant effect on all-cause mortality in the univariate logistic regression analysis (P > 0.05) were not included in the multivariable logistic regression analysis.

Abbreviations: HGB, hemoglobin; GGT, γ–glutamyl transpeptidase; Alb, albumin; PLT, platelet; Tbil, total bilirubin; ALT, alanine aminotransferase; PT, prothrombin time; Cr, creatinine; SIRI, Systemic Inflammation Response Index; OR, odds ratio; CI, confidence interval.

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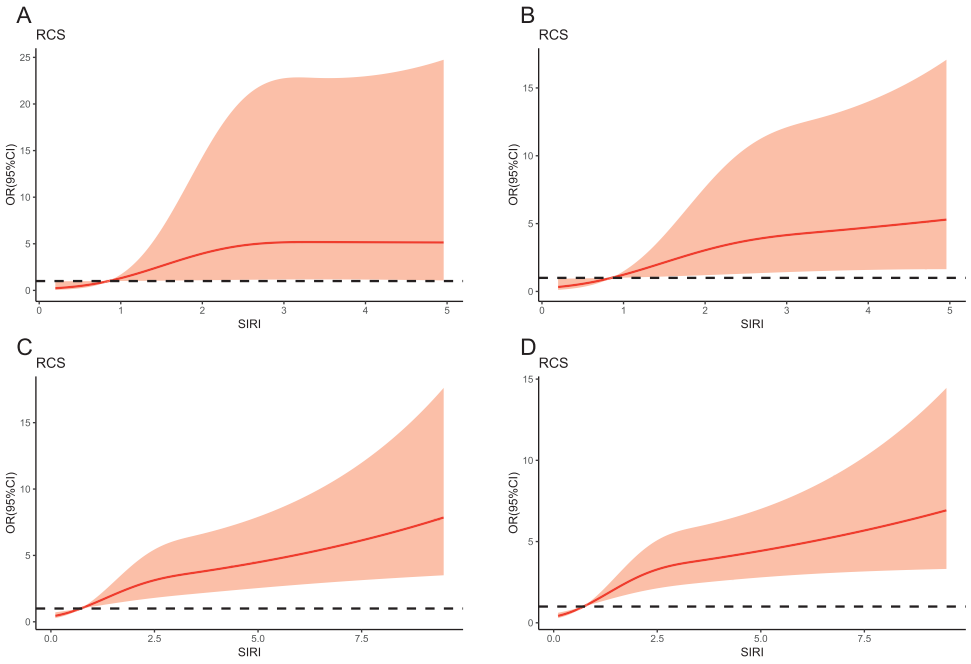

Figure 3 Association between SIRI and the prognosis of patients with decompensated liver cirrhosis. (**A**) 3 months of initial cohort; (**B**) 6 months of initial cohort; (**C**) 3 months of validation cohort; (**D**) 6 months of validation cohort.

Discussion

This study evaluated the relationship between the SIRI and short-term prognosis in patients with DLC. Our findings indicate that SIRI levels were significantly elevated in deceased patients compared to survivors across both cohorts. A higher SIRI is independently associated with adverse short-term outcomes in DLC, suggesting that SIRI could serve as a potential new prognostic predictor for patients with DLC. Furthermore, we observed a positive correlation between SIRI values and the risk of all-cause mortality across two cohorts. As SIRI values increased, there was an overall trend of rising risk for all-cause mortality.

Inflammation plays a crucial role in the prognosis of DLC; It not only speeds up the progression of cirrhosis but also significantly increases the risk of complications.[22] Inflammatory cells trigger a series of complications, including infections and organ failure, by releasing inflammatory factors; these complications exacerbate the condition, leading to a poorer prognosis.[23,24] Neutrophils trigger a systemic inflammatory response by producing a large number of pro-inflammatory factors, such as tumor necrosis factor-alpha (TNF-α), interleukin-1 (IL-1), and interleukin-6 (IL-6).[25] Transforming growth factor-β1 (TGF-β1), released by neutrophils, activates hepatic stellate cells, leading to the secretion of fibrogenic factors, which accelerates the process of liver fibrosis.[26] Moreover, impaired chemotaxis, phagocytosis, and bactericidal capacity of neutrophils increase the risk of infection, organ failure, and death.[27,28] Numerous studies indicate that monocytes can accelerate the progression of cirrhosis, leading to poor patient outcomes.[29–31] Xu et al observed a significant increase in the number of CD169+ monocytes in the blood and liver of patients with cirrhosis, leading to elevated levels of pro-inflammatory factors (including IL-6, IL-1β, TNF-α, and IL-10); Additionally, CD169+ monocytes prolong the lifespan of neutrophils, further exacerbating the inflammatory response.[30] Wu et al reported that the HBV enhances the expression of Triggering Receptor Expressed on Myeloid cells-1 on monocytes, leading to elevated levels of inflammatory cytokines such as TNF-α, IL-1β, and IL-6; This process contributes to liver damage, inflammation, and fibrosis in patients with liver cirrhosis.[31] The reduction in lymphocyte count and function is associated with the occurrence of DLC complications and is linked to adverse outcomes in patients. In patients with alcoholic cirrhosis, the absolute numbers of circulating mucosal-associated invariant T cells, NKT cells, and NK cells are lower than those in healthy individuals; This reduction is associated with the occurrence of complications, leading to poorer outcomes.[32] HBV impairs

lymphocyte function by interfering with their activation and differentiation processes, increasing the risk of infection and adversely affecting patient prognosis.[33] In hepatitis C virus (HCV), the reduction of T and B cells, along with a decrease in NK cell activity, is associated with adverse outcomes in DLC.[34] Therefore, the combined profile of neutrophils, monocytes and lymphocytes primarily reflects the inflammatory state in patients with DLC, potentially predicting their prognosis.

Previous studies have found that the SIRI is independently associated with the prognosis of various diseases. A retrospective study by Wang et al showed that the SIRI is independently associated with both 5-year and 10-year survival rates in breast cancer patients.[14] Jiang et al reported that SIRI serves as an independent prognostic factor for patients with advanced EGFR-mutant lung adenocarcinoma.[18] Zhang et al observed SIRI as a promising inflammatory marker for predicting the prognosis of stroke.[12] Similarly, SIRI is independently associated with the short-term prognosis of patients with DLC in our study. Interestingly, there was a difference in the optimal cutoff values between 3 months (2.23) and 6 months (0.96) in the initial cohort. The number of deaths within 6 months was higher by five patients compared to the number of deaths within 3 months. These five patients had SIRI values of 0.736, 0.980, 1.320, 1.499, and 9.391, with 4 patients having SIRI values exceeding 0.96. Therefore, by lowering the cutoff points from 2.23 to 0.96, it was statistically ensured that the high SIRI group (> 0.96) included more deceased patients, leading to the highest AUC value and supporting the concept that patients in the high SIRI group have an increased risk of mortality. As a predictive indicator, SIRI may offer the following advantages: (1) Non-invasive: SIRI is a non-invasive indicator that assesses a patients systemic inflammatory status by analyzing neutrophil, monocyte, and lymphocyte counts in peripheral blood. (2) Cost-effective: SIRI is cost-effective to measure since it is based on standard blood tests, making it highly feasible for clinical application.

This study has certain limitations. First, this study is retrospective and may be subject to selection bias and unidentified biases, necessitating further prospective research. Second, the potential mechanisms and clinical applications of SIRI in patients with DLC have not been extensively studied. While this study found higher levels of SIRI in patients with poorer prognosis of DLC, the underlying mechanisms of SIRI in DLC patients require further investigation. Third, there is an imbalance in sample sizes between the death group and the survivor group, which may lower the predictive accuracy of the minority class and weaken the power of statistical tests, thereby increasing bias in the analysis. Fourth, it is important to consider that decompensated cirrhosis patients may exhibit differing inflammatory statuses depending on the underlying etiology. Therefore, additional research is necessary to explore the influence of inflammatory status on the prognosis of patients with varying etiologies. Fifth, the amount of missing data (cases with incomplete data and with lost to follow-up) was relatively low in this study. We chose to directly deleted these cases; however, it is important to note that this approach may introduce selection bias.

Conclusion

Our research has established the SIRI as a clinically relevant biomarker for predicting short-term all-cause mortality in patients with DLC. The findings underscore the significance of systemic inflammation in the prognosis of liver cirrhosis, suggesting SIRI as a simple yet effective tool for risk stratification and clinical decision-making in this patient population. The independent association of SIRI with the risk of death in DLC highlights its potential utility in clinical practice. Identifying high-risk patients allows clinicians to prioritize resources and tailor treatment strategies more effectively, potentially improving patient outcomes.

Ethics Approval and Consent to Participate

The study was conducted in accordance with the Declaration of Helsinki. Ethical approval was granted by the ethics committee of the Second Affiliated Hospital of Wannan Medical College (WYEFYLS2023100) and the Scientific Research and New Technology Institutional Review Board of Yijishan Hospital of Wannan Medical College (2023037), informed consent was waived in accordance with national legislation and institutional guidelines and the anonymized processing of patient data.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

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References

1. Wilson R, Williams DM. Cirrhosis. *Med Clin North Am*. 2022;106:437–446. doi:10.1016/j.mcna.2021.12.001
2. Ge PS, Runyon BA. Treatment of Patients with Cirrhosis. *N Engl J Med*. 2016;375:767–777. doi:10.1056/NEJMra1504367
3. Xu XY, Ding HG, Li WG, et al. Chinese guidelines on the management of liver cirrhosis (abbreviated version). *World J Gastroenterol*. 2020;26:7088–7103. doi:10.3748/wjg.v26.i45.7088
4. Gines P, Krag A, Abraldes JG, Sola E, Fabrellas N, Kamath PS. Liver cirrhosis. *Lancet*. 2021;398:1359–1376. doi:10.1016/S0140-6736(21)01374-X
5. Kasper P, Goeser T. Management of decompensated liver cirrhosis in the surgical intensive care unit. *Hepatobiliary Surg Nutr*. 2023;12:95–98. doi:10.21037/hbsn-22-553
6. D'Amico G, Morabito A, M D, et al. Clinical states of cirrhosis and competing risks. *J Hepatol*. 2018;68:563–576. doi:10.1016/j.jhep.2017.10.020
7. Moga TV, Foncea C, Bende R, et al. Impact of COVID-19 on Patients with Decompensated Liver Cirrhosis. *Diagnostics*. 2023;13. doi:10.3390/diagnostics13040600
8. Xie Y, He C, Wang W. A potential novel inflammation biomarker for predicting the prognosis of decompensated liver cirrhosis. *Ann Med*. 2022;54:3201–3210. doi:10.1080/07853890.2022.2142277
9. Tonon M, Piano S. Cirrhosis and Portal Hypertension: how Do We Deal with Ascites and Its Consequences. *Med Clin North Am*. 2023;107:505–516. doi:10.1016/j.mcna.2022.12.004
10. Engelmann C, Claria J, Szabo G, Bosch J, Bernardi M. Pathophysiology of decompensated cirrhosis: portal hypertension, circulatory dysfunction, inflammation, metabolism and mitochondrial dysfunction. *J Hepatol*. 2021;75(1):S49–S66. doi:10.1016/j.jhep.2021.01.002
11. Albillos A, Martin-Mateos R, Van der Merwe S, Wiest R, Jalan R, Alvarez-Mon M. Cirrhosis-associated immune dysfunction. *Nat Rev Gastroenterol Hepatol*. 2022;19:112–134. doi:10.1038/s41575-021-00520-7
12. Zhang Y, Xing Z, Zhou K, Jiang S. The Predictive Role of Systemic Inflammation Response Index (SIRI) in the Prognosis of Stroke Patients. *Clin Interv Aging*. 2021;16:1997–2007. doi:10.2147/CIA.S339221
13. Dziedzic EA, Gasior JS, Tuzimek A, et al. Investigation of the Associations of Novel Inflammatory Biomarkers-Systemic Inflammatory Index (SII) and Systemic Inflammatory Response Index (SIRI)-With the Severity of Coronary Artery Disease and Acute Coronary Syndrome Occurrence. *Int J Mol Sci*. 2022;23. doi:10.3390/ijms23179553
14. Wang L, Zhou Y, Xia S, et al. Prognostic value of the systemic inflammation response index (SIRI) before and after surgery in operable breast cancer patients. *Cancer Biomark*. 2020;28:537–547. doi:10.3233/CBM-201682
15. Sun L, Hu W, Liu M, et al. High Systemic Inflammation Response Index (SIRI) Indicates Poor Outcome in Gallbladder Cancer Patients with Surgical Resection: a Single Institution Experience in China. *Cancer Res Treat*. 2020;52:1199–1210. doi:10.4143/crt.2020.303
16. Xu Y, He H, Zang Y, et al. Systemic inflammation response index (SIRI) as a novel biomarker in patients with rheumatoid arthritis: a multi-center retrospective study. *Clin Rheumatol*. 2022;41:1989–2000. doi:10.1007/s10067-022-06122-1
17. Gao W, Zhang F, Ma T, Hao J. High Preoperative Fibrinogen and Systemic Inflammation Response Index (F-SIRI) Predict Unfavorable Survival of Resectable Gastric Cancer Patients. *J Gastric Cancer*. 2020;20:202–211. doi:10.5230/jgc.2020.20.e18
18. Jiang S, Wang S, Wang Q, et al. Systemic Inflammation Response Index (SIRI) Independently Predicts Survival in Advanced Lung Adenocarcinoma Patients Treated with First-Generation EGFR-TKIs. *Cancer Manag Res*. 2021;13:1315–1322. doi:10.2147/CMAR.S287897
19. Qi Q, Zhuang L, Shen Y, et al. A novel systemic inflammation response index (SIRI) for predicting the survival of patients with pancreatic cancer after chemotherapy. *Cancer*. 2016;122:2158–2167. doi:10.1002/cncr.30057
20. Xie Y, He C, Wang W. Prognostic nutritional index: a potential biomarker for predicting the prognosis of decompensated liver cirrhosis. *Front Nutr*. 2022;9:1092059. doi:10.3389/fnut.2022.1092059
21. DeLong ER, DeLong DM, Clarke-Pearson DL. Comparing the areas under two or more correlated receiver operating characteristic curves: a nonparametric approach. *Biometrics*. 1988;44:837–845.
22. Casulleras M, Zhang IW, Lopez-Vicario C, Leukocytes CJ. Systemic Inflammation and Immunopathology in Acute-on-Chronic Liver Failure. *Cells*. 2020;9. doi:10.3390/cells9122632
23. Engelmann C, Zhang IW, Claria J. Mechanisms of immunity in acutely decompensated cirrhosis and acute-on-chronic liver failure. *Liver Int*. 2023. doi:10.1111/liv.15644
24. Trebicka J, Fernandez J, Papp M, et al. The PREDICT study uncovers three clinical courses of acutely decompensated cirrhosis that have distinct pathophysiology. *J Hepatol*. 2020;73:842–854. doi:10.1016/j.jhep.2020.06.013
25. Ferstl P, Trebicka J. Acute Decompensation and Acute-on-Chronic Liver Failure. *Clin Liver Dis*. 2021;25:419–430. doi:10.1016/j.cld.2021.01.009
26. Koyama Y, Brenner DA. Liver inflammation and fibrosis. *J Clin Invest*. 2017;127:55–64. doi:10.1172/JCI88881

27. Balazs I, Stadlbauer V. Circulating neutrophil anti-pathogen dysfunction in cirrhosis. *JHEP Rep*. 2023;5:100871. doi:10.1016/j.jhepr.2023.100871
28. Weichselbaum L, Azouz A, Smolen KK, et al. Epigenetic basis for monocyte dysfunction in patients with severe alcoholic hepatitis. *J Hepatol*. 2020;73:303–314. doi:10.1016/j.jhep.2020.02.017
29. Riva A, Mehta G. Regulation of Monocyte-Macrophage Responses in Cirrhosis-Role of Innate Immune Programming and Checkpoint Receptors. *Front Immunol*. 2019;10:167. doi:10.3389/fimmu.2019.00167
30. Xu L, Huang C, Zheng X, et al. Elevated CD169 expressing monocyte/macrophage promotes systemic inflammation and disease progression in cirrhosis. *Clin Exp Med*. 2024;24:45. doi:10.1007/s10238-024-01305-3
31. Wu X, Cai B, Lu W, et al. HBV upregulated triggering receptor expressed on myeloid cells-1 (TREM-1) expression on monocytes participated in disease progression through NF-Kb pathway. *Clin Immunol*. 2021;223:108650. doi:10.1016/j.clim.2020.108650
32. Park KJ, Jin HM, Cho YN, et al. Altered Frequency, Activation, and Clinical Relevance of Circulating Innate and Innate-Like Lymphocytes in Patients With Alcoholic Liver Cirrhosis. *Immune Netw*. 2023:23:e22. doi:10.4110/in.2023.23.e22
33. Murata Y, Kawashima K, Sheikh K, Tanaka Y, Isogawa M. Intrahepatic Cross-Presentation and Hepatocellular Antigen Presentation Play Distinct Roles in the Induction of Hepatitis B Virus-Specific CD8(+) T Cell Responses. *J Virol*. 2018;92. doi:10.1128/JVI.00920-18
34. Martinez-Esparza M, Tristan-Manzano M, Ruiz-Alcaraz AJ, Garcia-Penarrubia P. Inflammatory status in human hepatic cirrhosis. *World J Gastroenterol*. 2015;21:11522–11541. doi:10.3748/wjg.v21.i41.11522