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Systemic Inflammation Response Index as an Independent Predictor of In-Hospital Mortality in Critically Ill Cirrhotic Patients: A MIMIC-IV Study

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Abstract

Background: Liver cirrhosis (LC) remains a major global health challenge, characterized by recurrent inflammation, repair, and fibrosis. The systemic inflammatory response index (SIRI), a novel biomarker integrating neutrophil, monocyte, and lymphocyte counts, has shown prognostic potential in several conditions, but its role in critically ill cirrhotic patients has not been fully defined.

Aim: The aim of this study was to evaluate the prognostic value of SIRI and its association with in-hospital mortality among critically ill cirrhotic patients.

Methodology: This retrospective cohort study analyzed ICU-admitted cirrhotic patients (2008–2019) using the MIMIC-IV database. SIRI was calculated as neutrophils × monocytes/lymphocytes and stratified into high (≥4.35) and low (<4.35) groups. Demographic, clinical, and laboratory data were extracted. Statistical analyses included chi-square tests, multivariable logistic regression adjusted for confounders, ROC curve analysis, and Kaplan–Meier survival curves with log-rank testing.

Results: Among 2,344 patients (61.2% male; mean age 58.7±12.9 years), 668 (28.5%) died during hospitalization. Non-survivors were older, had more comorbidities, and had significantly higher SIRI values (6.8 vs. 4.2, $p<0.001$). Elevated SIRI independently predicted in-hospital mortality (OR 1.007, $p=0.027$) alongside age, albumin, SOFA score, and SpO_2. ROC analysis showed moderate discrimination (AUC=0.646, cutoff 4.35; sensitivity 69.3%, specificity 53.3%). Kaplan–Meier analysis confirmed worse survival in patients with high SIRI ($p<0.001$).

Conclusion: High SIRI (≥4.35) is significantly associated with increased in-hospital mortality in critically ill cirrhotic patients. As a readily available and cost-effective biomarker, SIRI may serve as a useful tool for early risk stratification and clinical decision-making in this high-risk population.

Introduction

Cirrhosis remains a global health burden, contributing to over 1.3 million deaths each year and is among the top 10 causes of mortality worldwide (1). In the U.S., it leads to more than 50,000 hospitalizations each year, which causes substantial healthcare costs due to frequent hospital visits and the need for advanced care (2). Despite advancements in management, the incidence of cirrhosis is bound to increase further, as the rate of Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD), Alcohol-Associated Liver Disease (ALD), and dual-etiology hepatic injuries is getting higher (3). Considering this trend, it is important to identify high-risk patients as early as possible to improve outcomes.

Systemic inflammation plays a key role in cirrhosis progression, particularly in decompensated or critically ill stages (4). Dysregulated immune activity, marked by neutrophilia, monocytosis, and lymphopenia, has been linked to worse outcomes including multiorgan failure, sepsis, and death (5). These immunological changes are assessed through the composite hematologic indices to provide

prognostic reflection. Indexes such as Neutrophil-to-Lymphocyte Ratio (NLR), Monocyte-to-Lymphocyte Ratio (MLR), and Platelet-to-Lymphocyte Ratio (PLR) have been proven to be of use across hepatic and cardiovascular diseases (6, 7). Recently, the Systemic Inflammatory Response Index (SIRI), calculated as (neutrophils × monocytes) / lymphocytes, has proven to have predictive value as an inflammation-based biomarker in malignancies, stroke, and rheumatologic diseases (8–10). Nevertheless, the clinical role of SIRI in critically ill cirrhotic patients has not been adequately explored.

This study intends to assess the prognostic potential of SIRI in critically ill cirrhosis patients using MIMIC-IV data, comparing it with traditional inflammatory markers and clinical scores. More specifically, to assess whether SIRI independently can predict in-hospital mortality and one-year survival, and its utility for risk stratification in acute care settings.

Methodology

Study Population: The current investigation utilized health-related data for critically ill cirrhotic patients admitted to the ICU (2008–2019) using the MIMIC-IV database (version 3.0) repository, a widely-used extensive database developed and overseen by the MIT Computational Physiology Laboratory (19). A researcher adhered to all access requirements and conducted the data extraction and it was independently cross checked by another team member. This study included critically ill cirrhotic patients based on the International Classification of Diseases, 9th and 10th Revision (ICD code: ICD-9th: 5712, 5715; ICD-10th: K7030, K7031, K7460, K7469). Specific exclusion criteria were applied as follows: (1) individuals under the age of 18 upon their initial admission; (2) non-confirmed diagnosis of liver cirrhosis; (3) non-ICU or other than 1st ICU admission; (3) unavailability of lab values needed to calculate SIRI; (4) patients with hematologic conditions like leukemia, lymphoma, and other diseases, or malignant tumors (to possibly cut down the potential bias generated by abnormal hematology indexes on the study's results). (5) ICU stay shorter than 24 hours

Data collection: The information extraction process utilized Bigquery on Google Cloud, with Structured Query Language (SQL) being the tool for extraction. The potential variables were grouped into six main categories: (1) demographic variables, including age, race, gender, and weight, (2) baseline variables like respiratory rate, heart rate, systolic, diastolic and mean blood pressure, temperature, SpO2, and BMI (3) comorbidities, encompassing chronic pulmonary disease, congestive heart failure, peripheral vascular disease, cerebrovascular disease, myocardial infarction, diabetes with & without complications, renal disease, and severe liver disease, (4) laboratory indicators, consisting of hemoglobin, platelets, blood urea nitrogen, creatinine, white blood cells, neutrophils, lymphocytes, monocytes, and albumin ,(5) biomarkers like NLR, MLR, PLR, SII, and SIRI; (5) outcome included was in-hospital mortality. Equations were applied to calculate various parameters, such as NLR, PLR, SII, and SIRI, as follows: NLR = count of neutrophils/count of lymphocytes; MLR = count of monocytes/count of lymphocytes; PLR = count of platelets/count of lymphocytes; SIRI = (count of neutrophils × count of monocytes)/count of lymphocytes; and SII = (count of neutrophils × count of platelets)/count of lymphocytes. All laboratory variables and disease severity scores were obtained from data generated during patient admission in

ICU. For determining the cut off value of SIRI, we used Youden's index that was calculated as Youden Index = Sensitivity + Specificity – 1.

Statistical Analysis

Continuous variables were presented as median (interquartile ranges, IQRs) and compared using Student's t-test or Mann Whitney U test, as appropriate. Categorical variables were expressed as mean and SD, frequency and percentages, and cross tabulated within hospital mortality and chi square were applied to analyze their association. Univariate logistic regression was performed to individually evaluate variables from six main categories for their association with in-hospital mortality. Statistically significant variables from the univariate analysis were then included in a multivariate logistic regression model to assess their independent effects after adjusting for potential confounders. A significance level of two-sided p values < 0.05 was considered statistically significant. The predictive value of the inflammatory marker (SIRI) was assessed by calculating the area under the receiver operating characteristic curve (AUC-ROC). Additionally, stratified analyses were conducted to find out potential effect modification of the association between SIRI and ICU mortality by sex, race, myocardial infarction, peripheral vascular disease, cerebrovascular disease, and duration until death in ICU or hospital. Predictive value of SIRI for one-year survival was further determined by using Kaplan–Meier curves (KMC) (comparing mortality between groups with high vs. low SIRI levels). Statistical analyses were conducted using SPSS v26. The reporting of this study adheres to the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) guidelines for cohort studies.

NOTE:

In critically ill cirrhosis patients, SIRI measures systemic inflammation driven by imbalances in neutrophils, monocytes, and lymphocytes. Due to splenic sequestration, portal hypertension, and bone marrow suppression in cirrhosis, often leads to leukopenia, lymphopenia; thus, differential leukocyte counts are frequently abnormal in patients with decompensated cirrhosis. These factors can distort leukocyte-based indices and compress their distributions, potentially affecting discrimination and calibration. However, because SIRI is a ratio rather than an absolute measure, it primarily depicts the relative cellular imbalances rather than total counts, which helps maintain its predictive value even in the presence of baseline leukopenia. There is a consensus approach in existing literature not to modify / adjust leukocyte counts prior to computing SIRI as this could deviate from the standard formula and may make comparisons more complicated across the research. To avoid such complications, the set standard is to calculate SIRI using unadjusted differential counts and then adjust it against potential confounders, (e.g. total leukocyte levels), through post-hoc statistical methods like multivariate regression. We followed the same standard methodology for our study and calculated SIRI first without adjusting leukocyte count and then adjusted all possible confounding variables against SIRI through multivariate regression to reduce any potential bias.

Results

Patient Characteristics: Data of 2,344 adult patients with Liver Cirrhosis were retrieved from MIMIC-IV (Medical Information Mart for Intensive Care) database. Mortality occurred in 577 (24.61%) patients, with mean age of 61.2 ± 11.7. Patients were stratified into two groups: survivors and non-survivors, and their baseline characteristics are presented in Table 1. As Table 1 suggests that (mean) respiratory rate (mean), heart rate (mean) and body mass Index (BMI) were higher in non-survivors' group as compared to survivors (p = 0.00). In contrast, systolic, diastolic (mean) and Mean blood pressures were significantly elevated in survivors (p = 0.00). The most prevalent comorbid conditions in the study population were peripheral vascular disease (11.3%) and cerebrovascular disease (8.5%) with statistically significant differences between survivors and non-survivors (*p* = 0.01 and 0.03 respectively). A longer ICU length of stay was observed in non-survivors, with a median of 5 (2–10) days (p = 0.00). All predictive markers such as NLR, PLR, MLR, SII, and SIRI were displaying significantly higher values in non-survivor's group. In contrast, calcium, Hb, platelets and Albumin values were higher in survivors' group. Patients who died had significantly higher Systemic Inflammation Response Index (SIRI) values (6.8 [5.3–9.2]) compared to survivors (4.2 [3.1–6.2], *p* = 0.001)

Table 1
Baseline characteristics of study population

Baseline characteristics of study population			
Baseline Characteristics	**Survivors**	**Non-Survivors**	**P-value**
Number of patients (n = 2344)			
Age	58(50–65)	60(50–68)	0.06
Gender, n (%)			
Female	595 (33.7%)	205 (35.5%)	0.41
Male	1172 (66.3%)	372 (64.5%)	0.41
Baseline (median-IQR)			
Resp_rate(mean)	18.3(16–21)	20.5(17.6–24)	0.00
Heart_rate(mean)	87.5(77.9–99)	95.05(81.7–104.4)	0.00
SBP(mean)	110.3(102.5–122.4)	106.7(100.1–113.75)	0.00
DBP (mean)	61.4(55.35–68)	57.45(52.4–62.75)	0.00
MBP(mean)	75.2(69.8–82.6)	71.3(67.08–76.4)	0.00
Temperature (C)	36.8(36.6–37.1)	36.7(36.4–36.9)	0.00
Spo2	97.4(95.8–98.8)	96.5(94.9–98.4)	0.00
BMI	12.7(11–14.9)	13.7(11.5–16.3)	0.00
Comorbid Conditions (n,(%))			
Myocardial infarct	149 (8.4%)	65 (11.3%)	0.04
Congestive heart failure	348 (19.7%)	128 (22.2%)	0.20
Peripheral vascular disease	103 (5.8%)	52 (5.8%)	0.01
Cerebrovascular disease	123 (7.0%)	56 (9.7%)	0.03
Chronic pulmonary disease	398 (22.5%)	127 (22.0%)	0.80
Diabetes without-cc	436 (24.7%)	135 (23.4%)	0.54

Abbreviations: Resp_rate – respiratory rate; Heart_rate – heart rate; SBP – systolic blood pressure; DBP – diastolic blood pressure; MBP – mean blood pressure; SpO_2 – peripheral capillary oxygen saturation; BMI – body mass index; BUN – blood urea nitrogen; WBC – white blood cell count; abs_monocytes – absolute monocyte count; abs_lymphocytes – absolute lymphocyte count; abs_neutrophils – absolute neutrophil count; NLR – neutrophil-to-lymphocyte ratio; MLR – monocyte-to-lymphocyte ratio; PLR – platelet-to-lymphocyte ratio; SII – systemic immune-inflammation index; SIRI – systemic inflammation response index; APSIII – Acute Physiology Score III; SOFA – Sequential Organ Failure Assessment; LOS – length of stay.

Baseline characteristics of study population			
Baseline Characteristics	**Survivors**	**Non-Survivors**	**P-value**
Diabetes with-cc	195 (11.0%)	51 (8.8%)	0.14
Renal disease	346 (19.6%)	132 (22.9%)	0.09
Laboratory Values (median - IQR)			
Hemoglobin (min)	8.7(7.3–10.2)	8.1(6.8–9.775)	0.00
Platelets (min)	83(53–135)	72(44.25–135.75)	0.00
BUN (max)	28(18–48)	42(25–68)	0.00
Creatinine (max)	1.3(0.85–2.1)	2.2(1.4–3.6)	0.00
Calcium (min)	7.8(7.3–8.3)	8.65 (7.3–8.5)	0.49
WBC (max)	12.4(8.2–17.55)	15.5(10.125–21.95)	0.00
Abs. monocytes (max)	.61 (0.37–1.05)	0.76 (0.48–1.05)	0.00
Abs. lymphocytes (max)	1.06 (0.67–1.70)	0.98 (0.54–1.51)	0.01
Abs. neutrophils (max)	8.06 (4.88–12.59)	10.98 (6.63–16.35)	0.00
Albumin (min)	2.8(2.4–3.3)	2.7(2.2–3.3)	0.00
Bio-markers (median- IQR)			
NLR	7.7(4.15–13.8)	11.15(6.32–20.42)	0.00
MLR	0.6(0.4–1)	0.8(0.5–1.4)	0.00
PLR	116.5(69.9–198.5)	125.4(71.22–230.38)	0.20
SII	903.1(448.3–1962.4)	1391.9(636.48–2723.08)	0.00
SIRI	4.6(2–10.1)	8.8(3.8–18.82)	0.00
APSIII	53(41–69)	80(63–99)	0.00
SOFA	8(5.5–11)	12(9–15)	0.00
Days to Death (median-IQR)			

Abbreviations: Resp_rate – respiratory rate; Heart_rate – heart rate; SBP – systolic blood pressure; DBP – diastolic blood pressure; MBP – mean blood pressure; SpO_2 – peripheral capillary oxygen saturation; BMI – body mass index; BUN – blood urea nitrogen; WBC – white blood cell count; abs_monocytes – absolute monocyte count; abs_lymphocytes – absolute lymphocyte count; abs_neutrophils – absolute neutrophil count; NLR – neutrophil-to-lymphocyte ratio; MLR – monocyte-to-lymphocyte ratio; PLR – platelet-to-lymphocyte ratio; SII – systemic immune-inflammation index; SIRI – systemic inflammation response index; APSIII – Acute Physiology Score III; SOFA – Sequential Organ Failure Assessment; LOS – length of stay.

Baseline characteristics of study population			
Baseline Characteristics	**Survivors**	**Non-Survivors**	**P-value**
Hospital_LOS	13(7–22)	8(4–15)	0.00
ICU_LOS	4(2–7)	5(2–10)	0.00

Abbreviations: Resp_rate – respiratory rate; Heart_rate – heart rate; SBP – systolic blood pressure; DBP – diastolic blood pressure; MBP – mean blood pressure; SpO_2 – peripheral capillary oxygen saturation; BMI – body mass index; BUN – blood urea nitrogen; WBC – white blood cell count; abs_monocytes – absolute monocyte count; abs_lymphocytes – absolute lymphocyte count; abs_neutrophils – absolute neutrophil count; NLR – neutrophil-to-lymphocyte ratio; MLR – monocyte-to-lymphocyte ratio; PLR – platelet-to-lymphocyte ratio; SII – systemic immune-inflammation index; SIRI – systemic inflammation response index; APSIII – Acute Physiology Score III; SOFA – Sequential Organ Failure Assessment; LOS – length of stay.

Predictive power of SIRI

We performed ROC curve analysis (Fig. 1) for the assessment of the prognostic value of SIRI for all-cause mortality in cirrhosis patients, which showed modest predictive ability of SIRI alone with an area under the curve (AUC) of 0.646. The optimal cut-off value of SIRI was 4.35, derived through Youden's Index. SIRI predicted modest risk of assessment for in-hospital mortality with sensitivity and specificity of 69.3% and 53.3%, respectively.

Area Under the ROC Curve					
Test Result Variable(s)	Area	Std. Error[a]	Asymptotic Sig.[b]	Asymptotic 95% Confidence Interval	
				Lower Bound	Upper Bound
siri	.646	.013	.000	.620	.672
The test result variable(s): siri has at least one tie between the positive actual state group and the negative actual state group. Statistics may be biased.					
a. Under the nonparametric assumption					
b. Null hypothesis: true area = 0.5					

Kaplan-Meier survival analysis by SIRI stratification: A total of 2,344 patients were included in the analysis and stratified in two groups: SIRI < 4.35 and SIRI ≥ 4.35. Kaplan-Meier analysis demonstrated significant differences between two groups. The survival probability (Fig. 2) was notably higher in the SIRI < 4.35 group across the follow-up period. Patients with SIRI ≥ 4.35 exhibited a sharp decline in survival probability early during follow-up, with the curve plateauing at a lower cumulative survival compared to the low SIRI group. The cumulative hazard plot (Fig. 3) further confirmed this pattern, showing a steeper and higher cumulative hazard in patients with SIRI ≥ 4.35. A significant difference in survival distribution between two groups was observed by a Mental-cox test with a Log-Rank p-value of

< 0.0001. These findings suggest that higher SIRI values are associated with worsened outcomes and increased mortality during the whole follow-up period.

Means and Medians for Survival Time								
SIRI Group (High vs Low)	Mean[a]				Median			
	Estimate	Std. Error	95% Confidence Interval		Estimate	Std. Error	95% Confidence Interval	
			Lower Bound	Upper Bound			Lower Bound	Upper Bound
.00	1474.948	88.200	1302.076	1647.820	83.000	15.284	53.044	112.956
1.00	625.701	51.774	524.224	727.178	23.000	1.679	19.709	26.291
Overall	1010.844	50.412	912.036	1109.653	33.000	2.882	27.352	38.648
a. Estimation is limited to the largest survival time if it is censored.								

· **Association with clinical outcomes**: Both univariate and multivariate regression analysis of 2,344 individuals exhibited several associations of comorbid conditions and inflammatory markers with the primary outcome. According to multivariate regression analysis, Cerebrovascular disease displayed a significant association with increased risk (OR 2.16; 95% CI: 1.38–3.38; p = 0.000). Longer hospital stays were associated with a statistically significant risk reduction (OR 0.95; 95% CI: 0.93–0.96; p < 0.000). In contrast, longer ICU LOS was associated with increased risk (OR 1.06; 95% CI: 1.04–1.09; p < 0.000). Among inflammatory markers, MLR (OR 1.31; 95% CI: 1.04–1.65; p < 0.02) and SIRI (OR 0.99; 95% CI: 0.97–1.00; p < 0.05) were significantly associated with increased risk of all-cause mortality. In terms of the scoring system, higher SOFA scores were strongly predictive of adverse outcomes, as displayed by (OR 1.12; 95% CI: 1.07–1.18; p < 0.000). All findings are summarized in Table 2. Additionally, Fig. 4 shows significant findings according to multivariate regression analysis.

Table 2
Association with clinical outcomes as analyzed through both Univariate and Multivariate Regression Analysis

Association With Outcomes: Univariate and Multivariate Analysis				
Predictor Variables	**Multivariate OR (95% C.I)**	**P value**	**Univariate OR (95% C.I)**	**P value**
Age	1.003 (0.80–1.25)	0.63	1.007 (1.00-1.015)	0.06
Gender	0.866 (0.658–1.141)	0.31	1.085 (.891-1.321)	0.41
Comorbid Conditions				
Myocardial infarct	1.19 (0.762–1.857)	0.44	1.379 (1.01–1.876)	0.04
Peripheral vascular disease	1.546 (0.959–2.494)	0.07	1.6 (1.6-2.265)	0.01
Cerebrovascular disease	2.162 (1.381–3.384)	0.00	1.437 (1.03-2)	0.03
Baselines				
SpO2 (mean)	0.897 (0.843–0.954)	0.00	0.88 (0.84–0.919)	0.00
Resp. rate (mean)	1.043 (1.01–1.077)	0.01	1.12 (1.1-1.145)	0.00
Heart rate (mean)	1.016 (1.006–1.025)	0.00	1.024 (1.02–1.03)	0.00
SBP (mean)	0.988 (0.972–1.004)	0.14	0.97 (0.96–0.977)	0.00
DBP (mean)	0.964 (0.927–1.003)	0.07	0.953 (0.94–0.963)	0.00
MBP (mean)	1.033 (0.985–1.083)	0.18	0.955 (0.95–0.965)	0.00
Temperature (mean)	0.526 (0.403–0.686)	0.00	1.08 (1.046–1.116)	0.00
Lab values				
Hemoglobin (min)	0.939 (0.882–0.999)	0.05	0.915 (0.88–0.956)	0.00
Platelets (min)	1.001 (0.999–1.003)	0.37	0.998 (.997-.999)	0.00
BUN (max)	1.004 (0.998–1.009)	0.19	1.014 (1.01–1.017)	0.00
Creatinine (max)	0.943 (0.862–1.031)	0.20	1.209 (1.16–1.267)	0.00
WBC (max)	1.017 (1-1.034)	0.05	1.041 (1.03–1.052)	0.00

Abbreviations: SpO_2 – peripheral capillary oxygen saturation; Resp. rate – respiratory rate; Heart rate – heart rate; SBP – systolic blood pressure; DBP – diastolic blood pressure; MBP – mean blood pressure; Temperature – body temperature; Hemoglobin – hemoglobin; Platelets – platelet count; BUN – blood urea nitrogen; Creatinine – serum creatinine; WBC – white blood cell count; Albumin – serum albumin; NLR – neutrophil-to-lymphocyte ratio; MLR – monocyte-to-lymphocyte ratio; SII – systemic immune-inflammation index; SIRI – systemic inflammation response index; APSIII – Acute Physiology Score III; SOFA – Sequential Organ Failure Assessment.

Association With Outcomes: Univariate and Multivariate Analysis				
Predictor Variables	**Multivariate OR (95% C.I)**	**P value**	**Univariate OR (95% C.I)**	**P value**
Albumin (min)	0.958 (0.782–1.173)	0.68	0.64 (0.55–0.749)	0.00
Biomarkers				
NLR	1.006 (0.991–1.022)	0.45	1.019 (1.01–1.025)	0.00
MLR	1.31 (1.039–1.653)	0.02	1.334 (1.21–1.475)	0.00
SII	1 (1–1)	0.83	1.00 (1.00–1.00)	0.00
SIRI	0.987 (0.974-1)	0.05	1.016 (1.01–1.022)	0.00
APSIII	1.023 (1.014–1.032)	0.00	1.05 (1.04–1.055)	0.00
SOFA	1.124 (1.068–1.184)	0.00	1.275 (1.24–1.309)	0.00
Days to Death				
Hospital length of stay	0.945 (0.932–0.959)	0.00	0.984 (.976-.991)	0.00
ICU length of stay	1.064 (1.036–1.094)	0.00	1.048 (1.03–1.064)	0.00

Abbreviations: SpO_2 – peripheral capillary oxygen saturation; Resp. rate – respiratory rate; Heart rate – heart rate; SBP – systolic blood pressure; DBP – diastolic blood pressure; MBP – mean blood pressure; Temperature – body temperature; Hemoglobin – hemoglobin; Platelets – platelet count; BUN – blood urea nitrogen; Creatinine – serum creatinine; WBC – white blood cell count; Albumin – serum albumin; NLR – neutrophil-to-lymphocyte ratio; MLR – monocyte-to-lymphocyte ratio; SII – systemic immune-inflammation index; SIRI – systemic inflammation response index; APSIII – Acute Physiology Score III; SOFA – Sequential Organ Failure Assessment.

Discussion

In this study, we retrospectively analyzed 2,344 elderly patients with cirrhosis admitted to the ICU, using the MIMIC-IV database. The overall in-hospital mortality was 24.6%, and non-survivors exhibited significantly higher respiratory, and heart rates, BMI, and inflammatory markers such as NLR, MLR, and SIRI. SIRI, as measured at ICU admission, was significantly higher in non-survivors. Univariate analysis showed a strong association between SIRI, and mortality in this cohort (OR 1.016, $p < 0.001$). However, in multivariate analysis, this association weakened to borderline significance (OR 0.987, 95% CI: 0.974-1.000, $p = 0.05$), indicating that SIRI may not be a strong independent predictor when adjusted for confounders such as SOFA score, and ICU length of stay.

For instance, Cheng et al. (11) reported that SIRI was an independent predictor of 3-month, and 6-month mortality in decompensated cirrhosis. In Cheng et al.'s study, patients with higher SIRI had significantly worse short-term survival, in line with our Kaplan-Meier curve showing poorer in-hospital survival for patients with SIRI ≥ 4.35. However, when adjusted for the confounding factors, SIRI alone showed a weak

association. This discrepancy could be attributed to variation in patient demographics. Cheng et al. included 936 patients from a tertiary care hospital, and we included acutely ill patients from ICU at higher mortality risks. While SIRI appears to be associated with outcomes, its utility as an independent predictor in the ICU setting seems limited. The prognostic performance of SIRI should be interpreted in context of other inflammation-based markers, and established scoring systems. NLR is the most widely studies of these indices. Elevated NLR has consistently been linked to worse outcomes in chronic liver disease, and cirrhosis (12). A recent meta-analysis (13) of 30 studies found that with each unit increase in NLR, there was a higher risk of death in end-stage liver disease (multivariate HR – 1.07). In patients with stable or compensated cirrhosis, NLR predicted mortality independent of conventional scoring systems such as MELD, and Child-Pugh (14, 15). It was found in a prospective cohort study (PRO-LIVER) that an NLR above 2.4 was associated with a 1.6 fold increase in hazard of mortality even after adjusting for age, and disease severity (12).

SIRI is conceptually an extension of NLR, incorporating monocyte counts into the index (neutrophils × monocytes/lymphocytes) (11). This theoretically provides a more comprehensive measure of immune-inflammatory status than NLR alone (16) among sepsis patients admitted in ICU. In a study including decompensated cirrhosis, SIRI's AUC for short-term mortality was higher than of NLR, MLR, or PLR (1). Our study did not directly compare these indices, but the literature indicates SIRI may outperform simpler ratios in some contexts. The PLR alone has shown inconsistent value in cirrhosis; one study found that PLR did not correlate with disease severity and could not predict 30-day mortality better than MELD or Child Pugh scoring systems (17). This may be because thrombocytopenia in cirrhosis is multifactorial, and not a specific marker of systemic inflammatory burden, The MLR has also been explored. In patients with advanced cirrhosis, and sepsis, a low MLR was a strong predictor of mortality. Hsu et al. reported that, in cirrhotic patients with septic shock, the MLR was an independent predictor of 60-day mortality (adjusted HR 1.54), and had an excellent discriminative ability (AUC 0.87) outperforming traditional scores like Child-Pugh, and MELD (18). These findings indicate that an imbalance between monocyte, and lymphocytes; a key component of SIRI, is prognostically important, especially during acute inflammation.

Our study, and prior literature supports the notion that inflammation-based cell indices such as NLR, MLR, and composite measure like SIRI carry prognostic significance in cirrhotic patients. SIRI's inclusion of neutrophils, monocytes, an lymphocytes in one metric theoretically capture the complex immune dysregulation of advanced liver disease compared to any single ratio (16). It is also important to emphasize that inflammation markers are not a substitute for comprehensive clinical scoring systems in critically ill patients. In our multivariate model, standard ICU severity assessments such as SOFA, and APS III, likely accounted for much of the mortality risk, leaving little additional prognostic value for SIRI. This is consistent with the understanding that mortality in ICU patients with cirrhosis is often driven by acute organ failure, and the presence of acute-on-chronic liver failure, and these factors are captured by scoring systems like SOFA, or the liver-specific scores such as MELD, and Child-Pugh (19). In our cohort, SIRI may correlate with these scores (for-example, higher SIRI was associated with higher SOFA in sepsis patients (16), but once the score is known, SIRI adds limited new information. Some recent

studies suggest that SIRI might complement or even enhance traditional scores in certain scenarios. A large MIMIC-based study (20) among sepsis patients found that SIRI was an independent predictor of 28-day, and 1-year mortality, and notably the AUC for 28-day mortality using SIRI (0.726) was higher than using SOFA (0.529) or SAPS II (0.644) alone. Similarly, an ICU study observed that adding SIRI improved the prognostic models for mortality as compared to models with conventional indices (16).

While comprehensive scores remain the gold standard, an inflammatory index like SIRI can provide prognostic insight, especially when full severity scoring is not yet available or when trying to refine risk stratification. In practice, SIRI can be calculated immediately from a complete blood count, whereas scores like APS III require multiple laboratory and physiologic inputs. Therefore, SIRI might have clinical utility as an early warning index, for example, on admission, or even pre-ICU triage, to flag high-risk cirrhotic patients pending more thorough evaluation. From a clinical perspective, the appeal of SIRI lies in its simplicity, and cost-effectiveness. In our cohort, the high SIRI group (≥ 4.35) had a markedly lower in-hospital survival probability ($p < 0.0001$), indicating that such patients require intensified monitoring or early interventions. However, the limitations of SIRI must be recognized. Its prognostic accuracy in our study was only modest, with an AUC of 0.646 for mortality prediction. This level of discrimination is considered poor in predictive model by comparison, many clinical scores achieve AUC's in the 0.75 to 0.85 range in ICU (19).

The sensitivity of 69.3% at the chosen cutoff means about one-third of the patents who died would not have been by SIRI alone, and low specificity (53.3%) means many patients with elevated SIRI survived (false positive). Thus, relying on SIRI in isolation could be misleading. A high SIRI might similarly be used to prompt early evaluation for liver transplant or ICU admission for at-risk patients. But before reaching that point more evidence is needed. The study had several limitations. This was a retrospective observational study of single database with its inherent biases. The findings may not be generalizable beyond elderly ICU patients as SIRI's prognostic value could differ in younger or less critically ill-patients. We focused only on in-hospital mortality, without assessing long-term or cause-specific outcomes. We also didn't compare SIRI against liver specific scores like MELD which may better capture hepatic dysfunction. Future research should explore SIRI trends, its integration with liver-specific models, and its utility in guiding clinical interventions in diverse cirrhotic populations.

In conclusion, our study suggests that SIRI is associated with mortality in cirrhotic patients, but has limited independent predictive value when accounting for established severity of illness scores. SIRI's prognostic ability is biologically plausible given the central role of systemic inflammation in cirrhosis outcomes, and it mirrors findings from other inflammation-based markers like NLR, and MLR. However, the clinical utility of SIRI as an independent prognostic tool appears limited by its modest accuracy. SIRI may be most useful as an adjunct. Further research is needed to validate SIRI in prospective studies, to determine how it can be combined with existing prognostic models, and to explore whether interventions guided by SIRI levels can improve patient outcomes.

Conclusion

Systemic Inflammatory Response Index (SIRI) emerged as a modest and statistically significant tool for mortality risk stratification among the liver cirrhosis patients. SIRI ≥ 4.35 was associated with higher ICU mortality and lower long-term survival. The findings also supported SIRI, Sequential Organ Failure Assessment (SOFA) score, and ICU stay as independent predictors of mortality. Furthermore, Laboratory findings such as low albumin, high creatinine, and elevated WBC were correlated with adverse outcomes.

Declarations

Author Contribution

Author ContributionsA.N.M. conceived and designed the study, performed statistical analysis, interpreted the results, and drafted the manuscript. U.S. contributed to study design and critical revision of the manuscript. M.S. assisted with data collection and extracted data. R.N. assisted with manuscript writing. F.H. participated in the interpretation of findings.A.H. assisted with result writing. S.A. contributed to graphical illustration. S.N.Q. assisted with manuscript writing. A.H. (Anfal Hamza) contributed to manuscript review. All authors reviewed and approved the final manuscript and agree to be accountable for all aspects of the work.

Data Availability

The data analyzed in this study are publicly available from the Medical Information Mart for Intensive Care IV (MIMIC-IV, version 3.0) database. Access to the database is available through PhysioNet (https://physionet.org/) after completion of the required training in human subjects research and acceptance of the Data Use Agreement. The authors did not generate any new datasets. The SQL code and statistical analysis methods used in this study are available from the corresponding author upon reasonable request.

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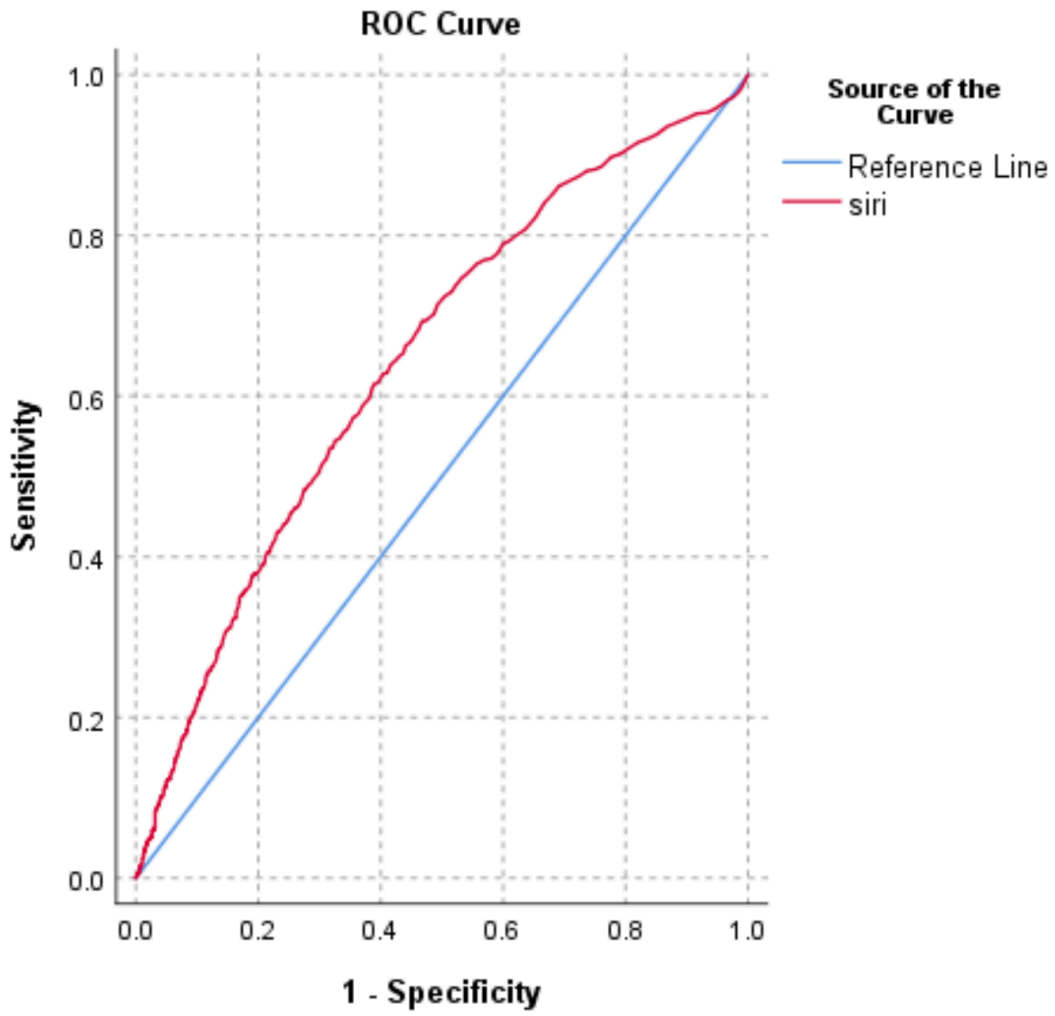
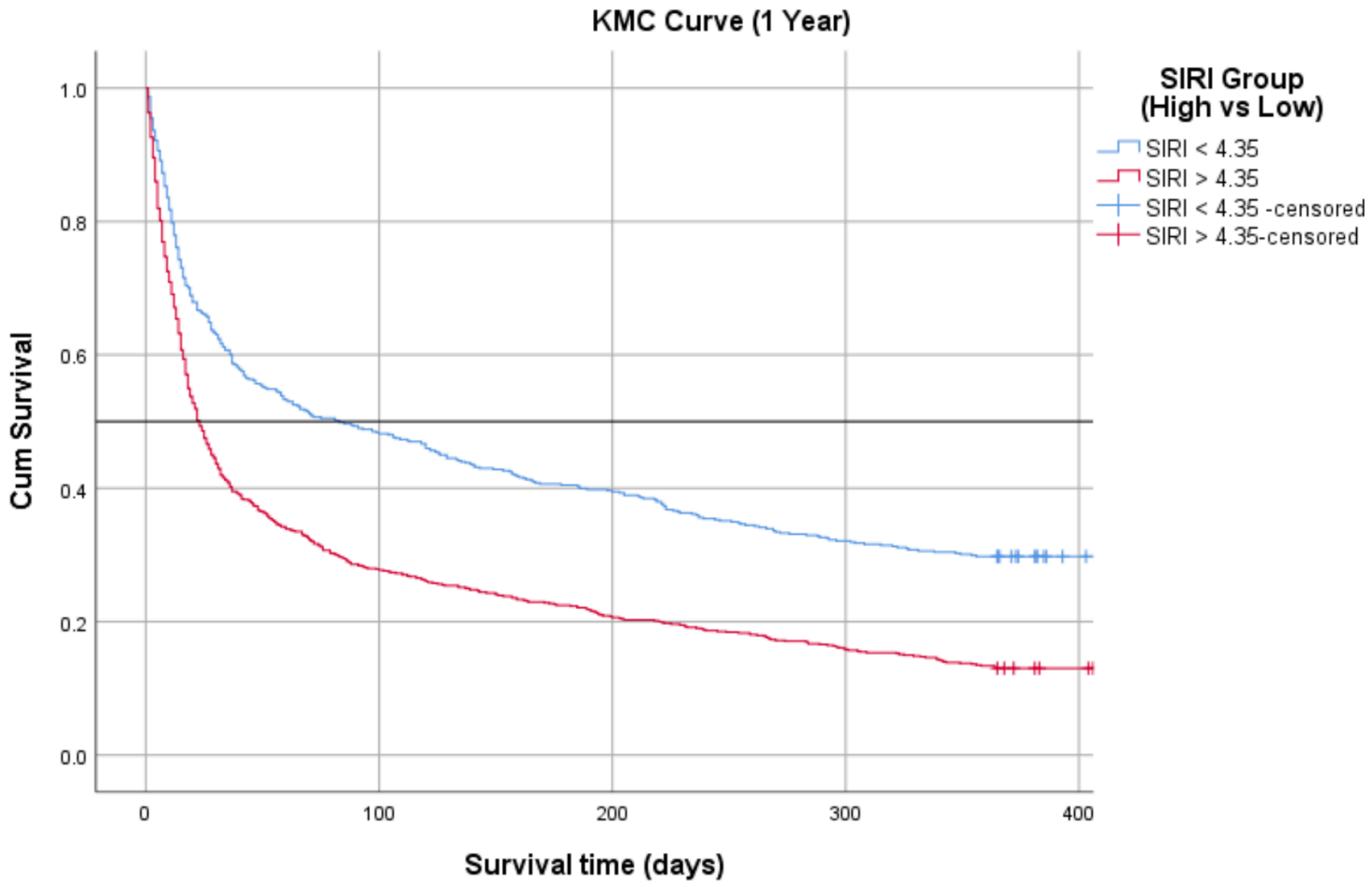
Figures



Area Under the ROC Curve					
Test Result Variable(s)	Area	Std. Error[a]	Asymptotic Sig.[b]	Asymptotic 95% Confidence Interval	
				Lower Bound	Upper Bound
siri	.646	.013	.000	.620	.672
The test result variable(s): siri has at least one tie between the positive actual state group and the negative actual state group. Statistics may be biased.					
a. Under the nonparametric assumption					
b. Null hypothesis: true area = 0.5					

Figure 1

ROC curve for predictive value of SIRI



Means and Medians for Survival Time								
SIRI Group (High vs Low)	Mean[a]				Median			
	Estimate	Std. Error	95% Confidence Interval		Estimate	Std. Error	95% Confidence Interval	
			Lower Bound	Upper Bound			Lower Bound	Upper Bound
.00	1474.948	88.200	1302.076	1647.820	83.000	15.284	53.044	112.956
1.00	625.701	51.774	524.224	727.178	23.000	1.679	19.709	26.291
Overall	1010.844	50.412	912.036	1109.653	33.000	2.882	27.352	38.648
a. Estimation is limited to the largest survival time if it is censored.								

Figure 2

Kaplan-Meier Survival probability curve between two groups

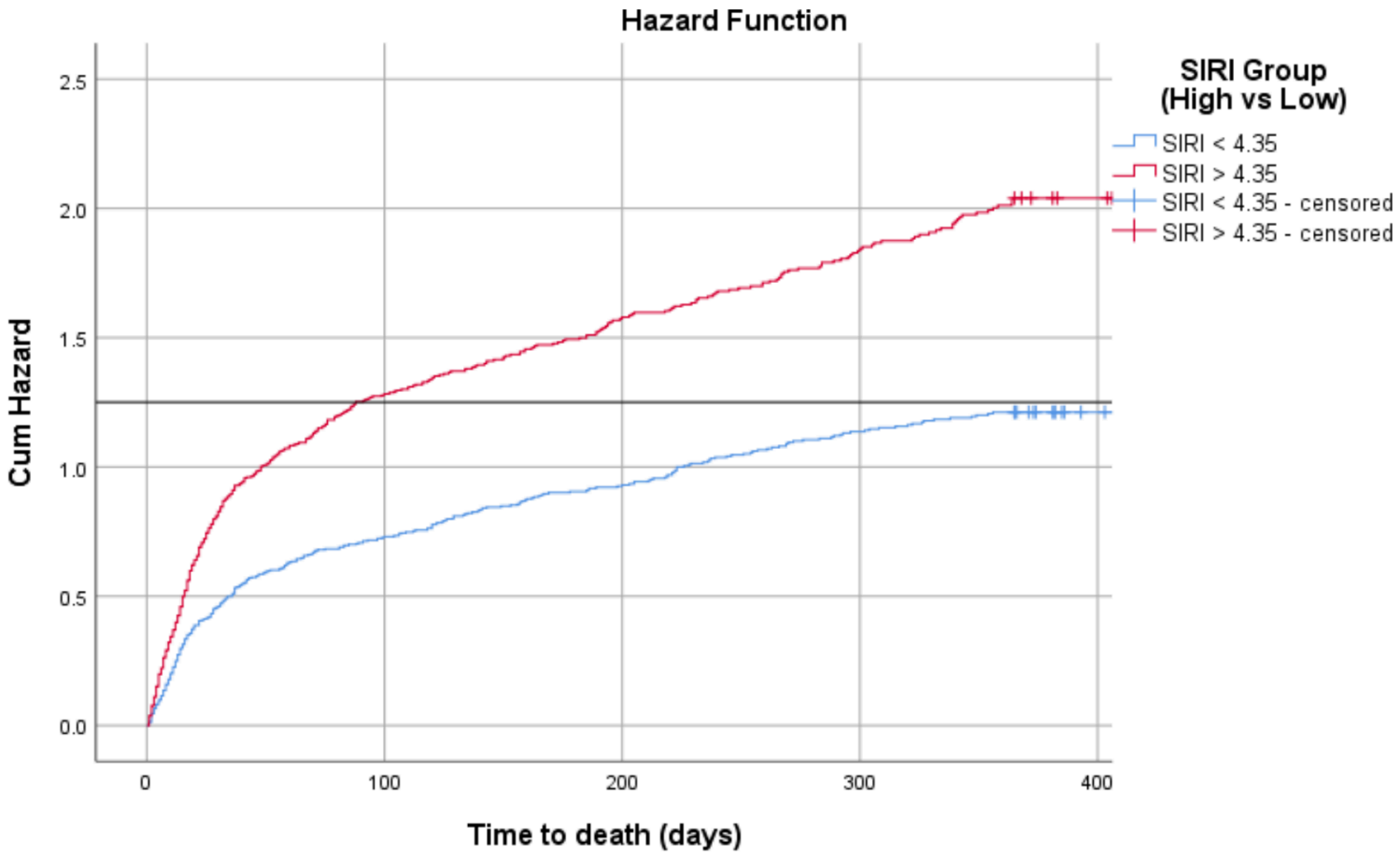


Figure 3

Cumulative Hazard plot between two groups

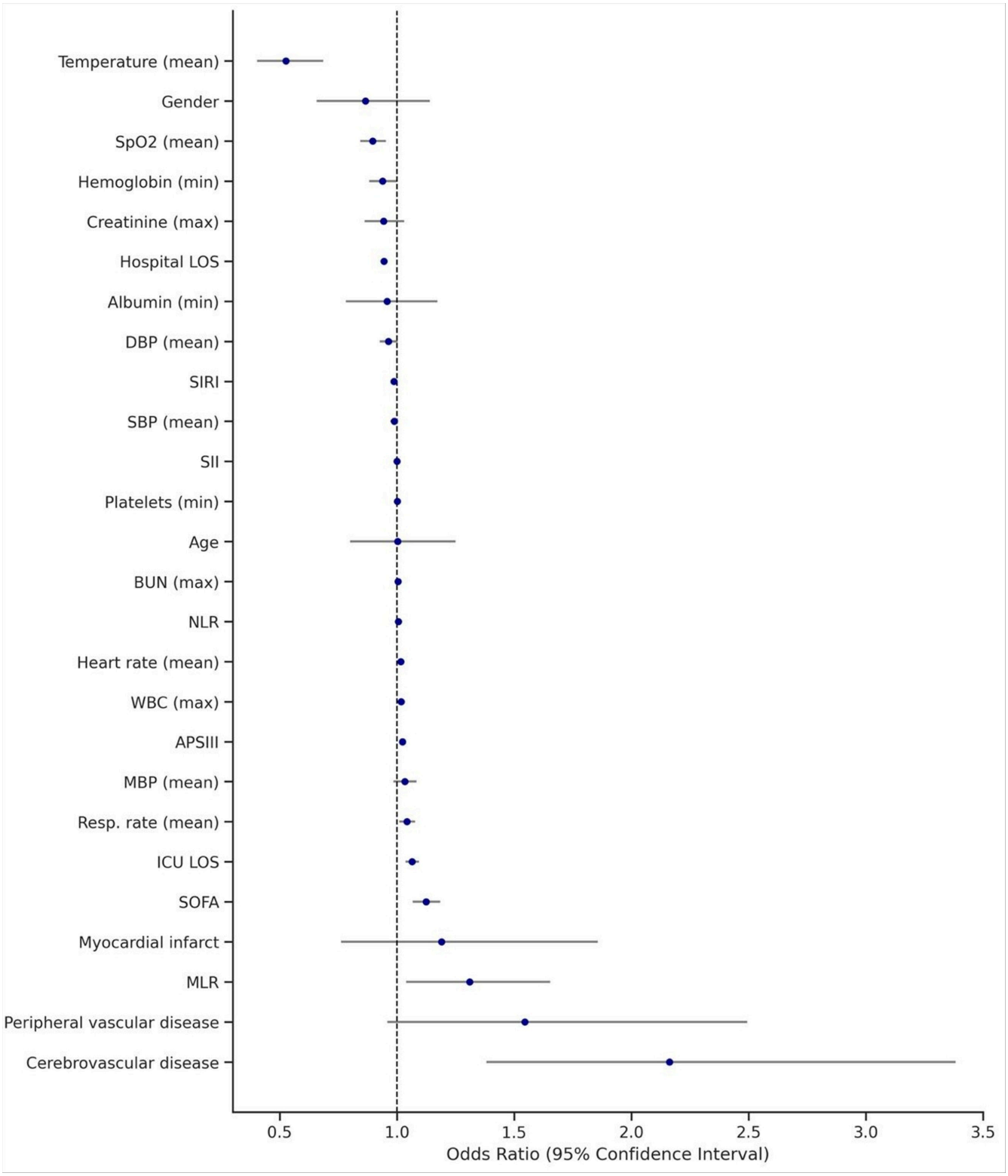


Figure 4

Multivariate Predictors of In-hospital Mortality