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ORIGINAL RESEARCH

Systemic Inflammatory Response Index Is a More Promising Prognostic Index Than Systemic Immune Inflammation Index in Critically Ill Heart Failure Patients: A Retrospective Cohort Analysis of the MIMIC-IV Database

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Aim: The incidence of heart failure (HF) remains high throughout the world, posing a serious threat to human health, with inflammation being a pivotal factor in the entire pathophysiologic process. Systemic inflammatory response index (SIRI) and systemic immune inflammation index (SII) are novel indicators for poor prognosis of HF. This paper aimed to ascertain the connection between SIRI and mortality in critically ill HF patients and to compare the prognostic value with SII.

Methods: All data on HF patients were sourced from MIMIC-IV. Cox proportional hazards analysis, restricted cubic spline, and Kaplan-Meier survival analysis were utilized to determine the link between SIRI or SII and in-hospital mortality. Receiver operating characteristic curve, area under the curve (AUC), and Youden index were employed to compare the prognostic value of SIRI and SII. Subgroup analysis was conducted to confirm the predictive capability of SIRI on mortality. Propensity score matching was utilized to reveal the connection between SIRI and secondary outcomes.

Results: 754 patients were included and 45 patients (6.0%) died. There was a positive link between SIRI and in-hospital mortality in both unadjusted ($p < 0.001$) and adjusted models ($p < 0.001$ and $p = 0.001$, respectively), outperforming SII in all models ($p > 0.05$ in all models). SIRI had a higher AUC and Youden index than SII, indicating better prognostic power. In addition, hospital stay was shorter in the low SIRI group ($p = 0.034$).

Conclusion: SIRI predicts in-hospital mortality in critically ill HF patients, and the prognostic power is superior to SII.

Keywords: systemic inflammatory response index, systemic immune inflammation index, heart failure, mortality, MIMIC-IV

Introduction

Despite significant advancements in recent years, heart failure (HF) remains a major economic burden worldwide.[1] Epidemiological data from Western developed countries show that the estimated prevalence of HF ranges from 1% to 3%, similar to that in Asia.[1–3] The 1-year mortality rate varies considerably, ranging from 10.9% in developed countries to 34.1% in developing regions.[2,3] The above data are underestimated when considering missing records or unrecognized cases.[1] Notably, HF with preserved ejection fraction (HFpEF), which accounts for almost half of total HF cases, has more complex causes and is more difficult to diagnose than HF with reduced ejection fraction (HFrEF). Therefore, there is an urgent need for sensitive indicators for early diagnosis and assessment.[4,5] Despite differences in etiology and comorbidities, inflammation is a consistent feature across all forms of HF, suggesting an underlying shared pathophysiological basis.[1,2,5]

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Inflammation in HF involves both innate and adaptive immunity and manifests in both acute and chronic phases.[4,6] Once in the chronic phase, myocardial damage becomes irreversible, leading to remodeling and further exacerbating HF. Multiple non-cellular and cellular components are involved in this process. Among non-cellular effectors, several biomarkers (C-reactive protein, tumor necrosis factor-α, and interleukin-6) have been revealed to connect with prognosis.[4,6] In contrast, blood routine count tests are less expensive and more accessible. Several reports have noted that neutrophil-to-lymphocyte ratio (NLR), monocyte-to-lymphocyte ratio (MLR), and platelet-to-lymphocyte ratio (PLR) are predictive indicators of cardiovascular disease outcomes.[7–9] More recently, the systemic inflammatory response index (SIRI) and systemic immune inflammation index (SII) have been proposed as more sensitive predictors of cardiovascular events and all-cause mortality.[10–16]

SIRI incorporates monocyte, neutrophil, and lymphocyte counts. Following cardiac injury due to various etiologies, endothelial cells are activated, leading to the swift recruitment of neutrophils and monocytes in response to stress.[6,7,17] Subsequently, an adaptive immune response is initiated, which engages lymphocytes such as B and T cells.[6] Lymphopenia reflects immunosuppression and connects with greater disease severity and all-cause mortality.[7,18–20] Accordingly, SIRI reveals the balance between inflammation and immune regulation in cardiovascular diseases. Although studies have suggested a positive link between elevated SIRI and poor prognosis in acute or chronic inflammation-related conditions, there is a paucity of research indicating the prognostic or diagnostic value of SIRI in HF, irrespective of age or cause.

SII index incorporates platelet count (PLT), neutrophil count, and lymphocyte count (LC). Several articles have indicated a connection between SII levels and poor prognosis in the HF population. Notably, the relationship between SII and mortality is non-linear, indicating that either too low or too high is detrimental.[14,21] Increased PLT and activation are linked to elevated total and cardiovascular mortality.[22,23] Additionally, thrombocytopenia is proposed as a single risk factor for composite outcomes.[24–26] Therefore, further investigation is warranted to ascertain the stability of SII as a prognostic indicator in HF patients.

This paper compared the prognostic power of SIRI and SII in critically ill HF patients and provided a theoretical basis for a novel indicator for clinical use.

Methods

Data Source

All data in the study were sourced from the publicly available Medical Information Mart for Intensive Care database IV (MIMIC-IV) version 2.2, which contains medical information from approximately 73,181 ICU admissions at the Beth Israel Deaconess Medical Center (BIDMC; Boston, MA, USA) from 2008 to 2019. We have obtained the Collaborative Institutional Training Initiative license to access the database (ID: 13285556) and obtained approval from the institutional review boards of Massachusetts Institute of Technology and BIDMC. All procedures involving human participants conformed to the ethical standards of the institutional and national research committee, as well as the Helsinki Declaration in 1964 and its subsequent amendments or comparable ethical standards. In addition, the study complied with items 1 and 2 of Article 32 of the Measures for Ethical Review of Life Science and Medical Research Involving Human Subjects dated February 18, 2023, China, which states that ethical review may be exempted when human information data or biological samples are used to conduct life science and medical research involving human subjects under the following conditions: using legally obtained public data or data generated by observation without interfering with public acts to conduct research; and using anonymized information and data to conduct research. Therefore, ethical approval and informed consent were waived for this study.

Population and Exclusion Criteria

This study included patients first admitted to the ICU with a primary diagnosis of HF. HF was defined based on the International Classification of Diseases, ninth and tenth revisions (ICD-9 and ICD-10), coded separately as 428.0 and I50.0.

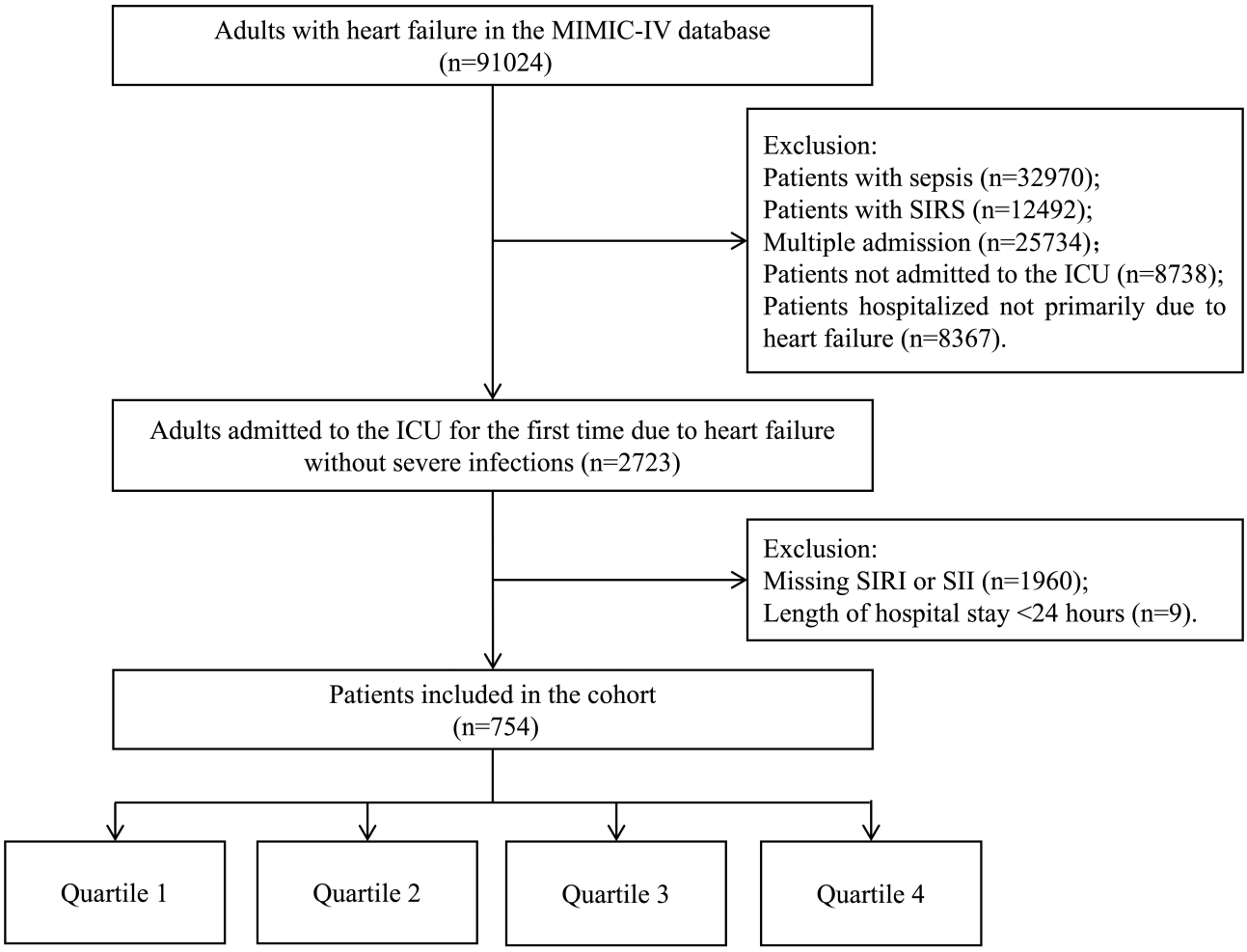

Figure 1 Flow chart of patient screening. SIRI, systemic inflammatory response index.
Abbreviations: MIMIC-IV, medical information mart for intensive care database IV; SII, systemic immune inflammation index; SIRS, systemic inflammatory response syndrome.

The exclusion criteria covered: (1) patients with sepsis or systemic inflammatory response syndrome (SIRS); (2) the primary diagnosis was not HF; (3) patients who were not admitted to the ICU; (4) hospital stay was less than 24 hours; (5) not the first time of ICU admission; (6) missing data on LC, monocyte count, or neutrophil count.

Ultimately, 754 hF patients were enrolled and categorized into four groups according to quartiles of log2-transformed SIRI or SII obtained within the first 24 hours of ICU admission. Figure 1 shows the details of inclusion and exclusion.

Data Collection

Relevant information from the MIMIC-IV database was acquired utilizing Structured Query Language (SQL) with PostgreSQL 16.2. The variables included: (1) patient demographics: age, gender, body mass index (BMI), race, and marital status; (2) vital signs: heart rate, systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), respiratory rate, and oxygen saturation (SaO_2); (3) laboratory indicators: LC, monocyte count, neutrophil count, white blood cell count, hematocrit, hemoglobin, PLT, serum creatinine, urea nitrogen, glucose, and lactate; (4) comorbidities: atrial fibrillation, ischemic heart disease, hypertension, valvular disease, ventricular thrombus, ventricular arrhythmia, acute kidney injury (AKI), chronic kidney disease (CKD), chronic obstructive pulmonary disease (COPD), respiratory failure, pulmonary embolism, cerebral infarction, diabetes, hyperlipidemia, goat, liver dysfunction, and iron-deficiency anemia; (5) operations and procedures: mechanical ventilation, renal replacement therapy (RRT) and cardiac assistance (veno-arterial extracorporeal membrane oxygenation and intra-aortic balloon pump); (6) severity

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assessment: sequential organ failure assessment (SOFA) score. Furthermore, vital signs, laboratory indices, and SOFA scores were collected within the first 24 hours of ICU admission. All comorbidities and operations were defined using ICD-9 and ICD-10 codes.

SIRI and SII indices were computed:

SIRI = (neutrophil count × monocyte count)/LC;

SII = (neutrophil count × PLT)/LC.

Where the proportion of missing values was below 20%, a random forest model-based multiple imputation (*missForest*) was employed to predict missing ones. For variables with over 20% missing data, they were converted to categorical variables according to the reference ranges specified in the database and subsequently included as dummy variables in the analysis. In the study, BMI exhibited over 20% missing data.

Outcome Investigation

The in-hospital mortality was the primary outcome. Secondary endpoints encompassed hospital stay, ICU stay, incidence of AKI, and use of RRT. AKI was defined based on Kidney Disease: Improving Global Outcomes guidelines.[27]

Statistical Analysis

Continuous variables in normal distribution were manifested as mean ± standard deviation and compared through *t*-test or ANOVA, otherwise as the median and interquartile range (IQR) and compared through the Mann–Whitney *U*-test or Kruskal–Wallis test. Shapiro–Wilk was employed to check the normal distribution of data. Categorical variables were manifested as frequencies and percentages (%) and compared utilizing the Pearson chi-square test or Fisher's exact test. SIRI and SII data had a non-normal distribution and were log-transformed as continuous variables and stratified by quartiles.

Cox proportional hazard models were adopted to calculate the hazard ratio (HR) and 95% confidence interval (CI) and adjusted for multiple variables. Model 1 was unadjusted; Model 2 was adjusted for age, gender, race, and marital status; Model 3 was adjusted for age, gender, race, marital status, atrial fibrillation, ischemic heart disease, valvular disease, ventricular arrhythmia, COPD, respiratory failure, pulmonary embolism, heart rate, SBP, DBP, white blood cell count, hematocrit, hemoglobin, and PLT. For the association between SIRI (log) and secondary outcomes, propensity score matching (PSM) was matched in agreement with Model 3. The restricted cubic spline (RCS) model was employed to reveal the potential non-linear relationships between SIRI or SII and the prognosis of HF patients. The Kaplan-Meier curve was plotted to reveal the in-hospital mortality of HF patients with different quartiles of SIRI (log) or SII (log), and the Log rank test calculated the *p*-value. Subgroup analyses were implemented to ascertain the consistency of the predictive value of SIRI for HF prognosis in different subgroups. To appraise the prognostic power of SIRI and SII, the receiver operating characteristic (ROC) curves were plotted, the area under the curve (AUC) was measured, sensitivity and specificity were determined, and Youden index was calculated individually. All statistical analyses were done using R software 4.3.3. $p < 0.05$ implied statistical significance.

Results

Population Characteristics

754 patients from the MIMIC-IV database were included. The median [IQR] age was 72 [63,80] years old, 59% were male, and 63% were white. The in-hospital mortality was 6.0% and the median [IQR] follow-up duration was 9 [6,14] days. The median [IQR] SIRI (log) index was 2.23 [1.52,3.12] [Q1: 0.05–1.52; Q2: 1.52–2.23; Q3: 2.23–3.12; Q4: 3.12–7.73]. The median [IQR] SII (log) index was 10.12 [9.29,11.00] [Q1: 2.84–9.29; Q2: 9.29–10.11; Q3: 10.11–11.00; Q4: 11.00–14.08].

Table 1 shows the comparison of basic features between survivors and non-survivors. In general, non-survivors tended to have shorter hospital stays, older age, higher SIRI and SII, a higher incidence of renal dysfunction and respiratory failure, more use of mechanical ventilation, RRT, and cardiac assistance.

Table 1 Baseline Characteristics of the study population according to the primary outcome

Characteristics	Overall, n = 754[1]	Survivors, n = 709[1]	Non-survivors, n = 45[1]	*p*-value[2]
Length of hospital stay, day	9 [6,14]	9 [6,14]	7 [3,15]	0.038*
Length of ICU stay, day	2.06 [1.24,3.35]	2.07 [1.25,3.33]	1.77 [0.92,3.70]	0.2
Marital status				0.078
Married	330 (44%)	316 (45%)	14 (31%)	
Other	424 (56%)	393 (55%)	31 (69%)	
Race				>0.9
Non-white	280 (37%)	263 (37%)	17 (38%)	
White	474 (63%)	446 (63%)	28 (62%)	
Gender				0.3
Female	309 (41%)	287 (40%)	22 (49%)	
Male	445 (59%)	422 (60%)	23 (51%)	
Age, years	72 [63,80]	72 [62,79]	82 [74,89]	<0.001***
BMI				0.2
Normal (18.5~23.9)	93 (12%)	90 (13%)	3 (6.7%)	
Obese (24.0~29.9)	160 (21%)	155 (22%)	5 (11%)	
Overweight (>30.0)	176 (23%)	162 (23%)	14 (31%)	
Underweight (≤18.5)	12 (1.6%)	11 (1.6%)	1 (2.2%)	
Missing	313 (42%)	291 (41%)	22 (49%)	
Vital Signs				
SaO2, %	98.00 [95.00,100.00]	98.00 [95.00,100.00]	97.84 [95.00,100.00]	0.2
Respiratory rate, times/min	18 [15,22]	17 [14,22]	22 [19,26]	<0.001***
Heart rate, beats/min	83 [74,95]	83 [74,95]	91 [75,102]	0.11
Systolic pressure, mmHg	117 [105,134]	118 [105,134]	113 [102,127]	0.3
Diastolic pressure, mmHg	66 [57,78]	66 [57,78]	62 [54,74]	0.14
MAP, mmHg	80 [70,92]	80 [70,92]	77 [69,87]	0.2
Laboratory indicators				
SIRI index	4 [2,8]	4 [2,7]	8 [5,18]	<0.001***
SIRI (log)	2.23 [1.52,3.12]	2.18 [1.50,3.02]	3.21 [2.60,4.23]	<0.001***
SII index	1,111 [626,2,041]	1,072 [619,1,943]	1,995 [1,201,2,822]	<0.001***
SII (log)	10.12 [9.29,11.00]	10.07 [9.28,10.93]	10.96 [10.23,11.46]	<0.001***
Lymphocyte count, 10^9/L	1.39 [0.95,2.02]	1.41 [0.98,2.05]	0.93 [0.67,1.45]	<0.001***
Monocyte count, 10^9/L	0.69 [0.45,0.98]	0.68 [0.44,0.96]	0.93 [0.61,1.16]	<0.001***
Neutrophil count, 10^9/L	8.3 [5.8,11.5]	8.3 [5.8,11.4]	9.3 [5.9,13.3]	0.13
White blood cell count, 10^9/L	9.6 [7.1,12.6]	9.5 [7.1,12.5]	10.5 [7.9,16.0]	0.051
Hematocrit, %	35 [29,39]	35 [29,40]	32 [24,36]	<0.001***
Hemoglobin, mg/dL	11.20 [9.30,12.78]	11.20 [9.30,12.80]	10.00 [7.70,11.30]	<0.001***
Platelet count, 10^9/L	196 [151,250]	197 [151,251]	174 [151,238]	0.3
Serum creatinine, mg/dL	1.00 [0.80,1.50]	1.00 [0.80,1.40]	1.50 [1.10,2.30]	<0.001***
Urea nitrogen, mg/dL	21 [16,32]	21 [16,30]	40 [21,49]	<0.001***
Glucose, mg/dL	130 [106,162]	130 [106,161]	125 [112,173]	0.5
Lactate, mmol/L	1.60 [1.20,2.10]	1.60 [1.20,2.07]	1.70 [1.30,2.70]	0.027*
Comorbidities				
Atrial fibrillation	394 (52%)	371 (52%)	23 (51%)	0.9
Ischemic heart disease	216 (29%)	199 (28%)	17 (38%)	0.2
Hypertension	93 (12%)	88 (12%)	5 (11%)	0.8
Valvular disease	312 (41%)	291 (41%)	21 (47%)	0.5
Ventricular thrombus	13 (1.7%)	13 (1.8%)	0 (0%)	>0.9
Ventricular arrhythmia	21 (2.8%)	20 (2.8%)	1 (2.2%)	>0.9
AKI	629 (83%)	590 (83%)	39 (87%)	0.5
CKD	218 (29%)	198 (28%)	20 (44%)	0.018*

(*Continued*)

Table 1 (Continued).

Characteristics	Overall, n = 754[1]	Survivors, n = 709[1]	Non-survivors, n = 45[1]	*p*-value[2]
COPD	153 (20%)	143 (20%)	10 (22%)	0.7
Respiratory failure	168 (22%)	145 (20%)	23 (51%)	<0.001***
Pulmonary embolism	24 (3.2%)	22 (3.1%)	2 (4.4%)	0.6
Cerebral infarction	36 (4.8%)	31 (4.4%)	5 (11%)	0.057
Diabetes	287 (38%)	271 (38%)	16 (36%)	0.7
Hyperlipidemia	437 (58%)	416 (59%)	21 (47%)	0.11
Goat	62 (8.2%)	57 (8.0%)	5 (11%)	0.4
Iron-deficiency anemia	38 (5.0%)	37 (5.2%)	1 (2.2%)	0.7
Operations and procedures				
Mechanical ventilation	200 (27%)	180 (25%)	20 (44%)	0.005**
RRT	44 (5.8%)	37 (5.2%)	7 (16%)	0.012*
Cardiac assistance	35 (4.6%)	27 (3.8%)	8 (18%)	<0.001***
Scoring system				
SOFA	3 [2,5]	3 [1,5]	5 [3,7]	<0.001***

Notes: [1] Continuous variables were described as median and interquartile range (IQR) (median [IQR]), categorical variables were described as frequencies and percentages (n (%)). [2] *p <0.05; **p <0.01; ***p <0.001.

Abbreviations: BMI, body mass index; MAP, mean arterial pressure; AKI, acute kidney injury; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; RRT, renal replacement therapy; SOFA, sequential organ failure assessment.

Baseline characteristics were also analyzed by groups of SIRI (log) and SII (log) quartiles. According to Table 2, the highest quartile of SIRI (log) (Q4 group) had remarkably higher mortality than others. Patients with high SIRI tended to be older and exhibit more unstable vital signs: lower SaO_2, rapid respiratory rate, and heart rate, higher levels of renal and metabolic indicators (glucose and lactate), a higher incidence of respiratory failure, and a greater need for cardiac support, but less use of mechanical ventilation. In addition, SIRI did not affect the incidence of AKI or the need for RRT. SII was similar to SIRI in most aspects mentioned above, except that SII had little impact on the use of ventilation (Table 3).

Table 2 Baseline Characteristics of the study population according to the quartiles of SIRI (log)

Characteristics	Overall, n = 754[1]	Q1[a], n = 187[1]	Q2[a], n = 189[1]	Q3[a], n = 189[1]	Q4[a], n = 189[1]	*p*-value[2]
In-hospital mortality	45 (6.0%)	5 (2.7%)	5 (2.6%)	9 (4.8%)	26 (14%)	<0.001***
Length of hospital stay, day	9 [6,14]	9 [6,13]	9 [6,13]	10 [7,15]	10 [6,14]	0.2
Length of ICU stay, day	2.06 [1.24,3.35]	1.96 [1.17,3.09]	2.06 [1.24,3.53]	2.21 [1.24,3.33]	2.09 [1.32,3.51]	0.3
Marital status						0.5
Married	330 (44%)	84 (45%)	89 (47%)	82 (43%)	75 (40%)	
Other	424 (56%)	103 (55%)	100 (53%)	107 (57%)	114 (60%)	
Race						0.5
Non-white	280 (37%)	71 (38%)	75 (40%)	62 (33%)	72 (38%)	
White	474 (63%)	116 (62%)	114 (60%)	127 (67%)	117 (62%)	
Gender						0.7
Female	309 (41%)	83 (44%)	75 (40%)	77 (41%)	74 (39%)	
Male	445 (59%)	104 (56%)	114 (60%)	112 (59%)	115 (61%)	
Age, years	72 [63,80]	71 [63,77]	70 [61,78]	71 [60,82]	75 [65,83]	0.003**
BMI						0.483
Normal (18.5~23.9)	93 (12%)	27 (14%)	23 (12%)	24 (13%)	19 (10%)	
Obese (24.0~29.9)	160 (21%)	39 (21%)	44 (23%)	40 (21%)	37 (20%)	
Overweight (≥30.0)	176 (23%)	52 (28%)	42 (22%)	46 (24%)	36 (19%)	
Underweight (<18.5)	12 (1.6%)	4 (2.1%)	3 (1.6%)	2 (1.1%)	3 (1.6%)	
Missing	313 (42%)	65 (35%)	77 (41%)	77 (41%)	94 (50%)	

(*Continued*)

Table 2 (Continued).

Characteristics	Overall, n = 754[1]	Q1[a], n = 187[1]	Q2[a], n = 189[1]	Q3[a], n = 189[1]	Q4[a], n = 189[1]	p-value[2]
Vital Signs						
SaO2, %	98.00 [95.00,100.00]	100.00 [97.00,100.00]	98.00 [96.00,100.00]	98.00 [95.00,100.00]	97.00 [95.00,99.00]	<0.001***
Respiratory rate, times/min	18 [15,22]	16 [14,19]	16 [14,21]	18 [15,23]	21 [16,25]	<0.001***
Heart rate, beats/min	83 [74,95]	80 [73,89]	83 [74,93]	85 [75,100]	88 [75,100]	0.001**
Systolic pressure, mmHg	117 [105,134]	114 [104,127]	118 [105,136]	117 [107,134]	121 [104,141]	0.038*
Diastolic pressure, mmHg	66 [57,78]	64 [55,75]	65 [56,77]	67 [57,78]	69 [58,79]	0.043*
MAP, mmHg	80 [70,92]	77 [69,86]	79 [69,92]	81 [72,91]	83 [72,96]	0.005**
Laboratory indicators						
SIRI index	4 [2,8]	1 [1,2]	3 [2,3]	5 [4,6]	12 [10,19]	<0.001***
SIRI (log)	2.23 [1.52,3.12]	1.05 [0.73,1.33]	1.84 [1.68,2.02]	2.63 [2.41,2.86]	3.75 [3.41,4.34]	<0.001***
Lymphocyte count, 10^9/L	1.39 [0.95,2.02]	1.73 [1.28,2.62]	1.58 [1.13,2.34]	1.37 [0.95,1.89]	0.97 [0.67,1.33]	<0.001***
Monocyte count, 10^9/L	0.69 [0.45,0.98]	0.37 [0.20,0.55]	0.59 [0.43,0.76]	0.81 [0.63,0.99]	1.09 [0.84,1.40]	<0.001***
Neutrophil count, 10^9/L	8.3 [5.8,11.5]	5.4 [3.4,7.7]	7.5 [5.3,9.8]	8.9 [6.9,12.3]	11.5 [9.1,15.8]	<0.001***
White blood cell count, 10^9/L	9.6 [7.1,12.6]	7.4 [5.7,9.6]	8.7 [6.9,11.3]	10.0 [8.0,12.5]	12.6 [9.9,16.8]	<0.001***
Hematocrit, %	35 [29,39]	34 [28,38]	34 [29,40]	35 [30,41]	35 [29,38]	0.029*
Hemoglobin, mg/dL	11.20 [9.30,12.78]	10.70 [9.20,12.50]	11.30 [9.20,12.90]	11.50 [9.50,13.40]	11.00 [9.00,12.40]	0.077
Platelet count, 10^9/L	196 [151,250]	173 [133,221]	191 [157,231]	199 [167,252]	217 [163,281]	<0.001***
Serum creatinine, mg/dL	1.00 [0.80,1.50]	1.00 [0.80,1.30]	1.00 [0.80,1.40]	1.00 [0.80,1.50]	1.20 [0.80,1.60]	0.004**
Urea nitrogen, mg/dL	21 [16,32]	19 [14,28]	21 [16,30]	21 [16,31]	25 [18,39]	<0.001***
Glucose, mg/dL	130 [106,162]	127 [102,159]	122 [101,158]	130 [106,163]	141 [115,173]	<0.001***
Lactate, mmol/L	1.60 [1.20,2.10]	1.50 [1.20,2.00]	1.50 [1.20,1.90]	1.56 [1.20,2.00]	1.83 [1.38,2.50]	<0.001***
Comorbidities						
Atrial fibrillation	394 (52%)	97 (52%)	90 (48%)	110 (58%)	97 (51%)	0.2
Ischemic heart disease	216 (29%)	43 (23%)	49 (26%)	57 (30%)	67 (35%)	0.044*
Hypertension	93 (12%)	21 (11%)	26 (14%)	21 (11%)	25 (13%)	0.8
Valvular disease	312 (41%)	86 (46%)	79 (42%)	80 (42%)	67 (35%)	0.2
Ventricular thrombus	13 (1.7%)	3 (1.6%)	4 (2.1%)	1 (0.5%)	5 (2.6%)	0.4
Ventricular arrhythmia	21 (2.8%)	5 (2.7%)	5 (2.6%)	6 (3.2%)	5 (2.6%)	>0.9
AKI	629 (83%)	149 (80%)	163 (86%)	160 (85%)	157 (83%)	0.4
CKD	218 (29%)	47 (25%)	52 (28%)	58 (31%)	61 (32%)	0.4
COPD	153 (20%)	28 (15%)	39 (21%)	37 (20%)	49 (26%)	0.07
Respiratory failure	168 (22%)	21 (11%)	34 (18%)	45 (24%)	68 (36%)	<0.001***
Pulmonary embolism	24 (3.2%)	6 (3.2%)	5 (2.6%)	4 (2.1%)	9 (4.8%)	0.5
Cerebral infarction	36 (4.8%)	9 (4.8%)	5 (2.6%)	11 (5.8%)	11 (5.8%)	0.4
Diabetes	287 (38%)	74 (40%)	73 (39%)	72 (38%)	68 (36%)	>0.9
Hyperlipidemia	437 (58%)	112 (60%)	116 (61%)	106 (56%)	103 (54%)	0.5
Goat	62 (8.2%)	12 (6.4%)	18 (9.5%)	17 (9.0%)	15 (7.9%)	0.7
Iron-deficiency anemia	38 (5.0%)	6 (3.2%)	6 (3.2%)	13 (6.9%)	13 (6.9%)	0.15
Operations and procedures						
Mechanical ventilation	200 (27%)	61 (33%)	59 (31%)	37 (20%)	43 (23%)	0.008**
RRT	44 (5.8%)	8 (4.3%)	14 (7.4%)	9 (4.8%)	13 (6.9%)	0.5
Cardiac assistance	35 (4.6%)	2 (1.1%)	9 (4.8%)	8 (4.2%)	16 (8.5%)	0.008**
Scoring system						
SOFA	3 [2,5]	4 [2,6]	3 [1,5]	3 [1,5]	2 [1,5]	0.003**

Notes: [1] Continuous variables were described as median and interquartile range (IQR) (median [IQR]), categorical variables were described as frequencies and percentages (n (%)). [2] *p <0.05; **p <0.01; ***p <0.001. [a] SIRI (log) quartiles: Q1: 0.05-1.52; Q2: 1.52-2.23; Q3: 2.23-3.12; Q4: 3.12-7.73.

Abbreviations: BMI, body mass index; MAP, mean arterial pressure; AKI, acute kidney injury; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; RRT, renal replacement therapy; SOFA, sequential organ failure assessment.

Association of SIRI and SII with in-Hospital Mortality

The analysis presented in Table 4 indicated that when SIRI was viewed as a continuous variable, Cox analysis exhibited a considerable positive correlation between SIRI and in-hospital mortality in both unadjusted model (Model 1, HR [95% CI]: 1.669 [1.364, 2.042], $p < 0.001$) and adjusted models (Model 2, HR [95% CI]: 1.516 [1.225, 1.877], $p < 0.001$;

Table 3 Baseline Characteristics of the study population according to the quartiles of SII (log)

Characteristics	Overall, n = 754[1]	Q1[a], n = 189[1]	Q2[a], n = 188[1]	Q3[a], n = 188[1]	Q4[a], n = 189[1]	*p*-value[2]
In-hospital mortality	45 (6.0%)	6 (3.2%)	4 (2.1%)	13 (6.9%)	22 (12%)	<0.001***
Length of hospital stay, day	9 [6,14]	9 [6,13]	9 [6,14]	9 [6,13]	10 [6,16]	0.2
Length of ICU stay, day	2.06 [1.24,3.35]	1.99 [1.17,3.20]	2.08 [1.23,3.36]	2.21 [1.29,3.43]	2.00 [1.32,3.49]	0.6
Marital status						0.047*
Married	330 (44%)	80 (42%)	98 (52%)	72 (38%)	80 (42%)	
Other	424 (56%)	109 (58%)	90 (48%)	116 (62%)	109 (58%)	
Race						0.2
Non-white	280 (37%)	78 (41%)	59 (31%)	74 (39%)	69 (37%)	
White	474 (63%)	111 (59%)	129 (69%)	114 (61%)	120 (63%)	
Gender						0.8
Female	309 (41%)	74 (39%)	78 (41%)	74 (39%)	83 (44%)	
Male	445 (59%)	115 (61%)	110 (59%)	114 (61%)	106 (56%)	
Age, years	72 [63,80]	70 [62,77]	72 [62,78]	73 [65,83]	74 [64,81]	0.019*
BMI						0.882
Normal (18.5~23.9)	93 (12%)	26 (14%)	20 (11%)	23 (12%)	24 (13%)	
Obese (24.0~29.9)	160 (21%)	42 (22%)	45 (24%)	40 (21%)	33 (17%)	
Overweight (≥30.0)	176 (23%)	46 (24%)	43 (23%)	47 (25%)	40 (21%)	
Underweight (<18.5)	12 (1.6%)	2 (1.1%)	3 (1.6%)	2 (1.1%)	5 (2.6%)	
Missing	313 (42%)	73 (39%)	77 (41%)	76 (40%)	87 (46%)	
Vital Signs						
SaO2, %	98.00 [95.00,100.00]	99.00 [96.00,100.00]	98.00 [95.00,100.00]	98.00 [95.00,100.00]	97.00 [95.00,100.00]	0.001**
Respiratory rate, times/min	18 [15,22]	16 [14,20]	17 [14,21]	18 [15,22]	20 [16,25]	<0.001***
Heart rate, beats/min	83 [74,95]	82 [75,93]	80 [73,88]	81 [72,95]	91 [80,104]	<0.001***
Systolic pressure, mmHg	117 [105,134]	116 [102,128]	116 [106,130]	120 [107,137]	120 [104,140]	0.015*
Diastolic pressure, mmHg	66 [57,78]	66 [57,76]	63 [54,75]	64 [56,76]	71 [61,82]	<0.001***
MAP, mmHg	80 [70,92]	78 [69,87]	77 [69,89]	80 [70,92]	85 [75,96]	<0.001***
Laboratory indicators						
SII index	1,111 [626,2,041]	398 [283,524]	844 [740,961]	1,485 [1,259,1,741]	3,164 [2,508,4,533]	<0.001***
SII (log)	10.12 [9.29,11.00]	8.64 [8.15,9.04]	9.72 [9.53,9.91]	10.54 [10.30,10.77]	11.63 [11.29,12.15]	<0.001***
Lymphocyte count, 10^9/L	1.39 [0.95,2.02]	2.03 [1.34,3.15]	1.64 [1.30,2.38]	1.20 [0.89,1.64]	0.88 [0.55,1.25]	<0.001***
Monocyte count, 10^9/L	0.69 [0.45,0.98]	0.59 [0.38,0.84]	0.67 [0.44,0.90]	0.75 [0.49,0.99]	0.83 [0.52,1.18]	<0.001***
Neutrophil count, 10^9/L	8.3 [5.8,11.5]	5.2 [3.4,7.6]	7.8 [6.0,10.2]	8.9 [6.8,11.3]	11.6 [9.0,15.6]	<0.001***
White blood cell count, 10^9/L	9.6 [7.1,12.6]	7.7 [5.9,10.8]	9.0 [7.1,11.8]	9.6 [7.7,11.8]	12.1 [9.3,16.0]	<0.001***
Hematocrit, %	35 [29,39]	33 [28,39]	36 [30,40]	35 [30,40]	35 [28,38]	0.015*
Hemoglobin, mg/dL	11.20 [9.30,12.78]	10.50 [9.00,12.60]	11.55 [9.60,12.93]	11.15 [9.50,13.00]	11.00 [8.70,12.50]	0.017*
Platelet count, 10^9/L	196 [151,250]	151 [108,191]	189 [151,222]	203 [169,252]	254 [199,315]	<0.001***
Serum creatinine, mg/dL	1.00 [0.80,1.50]	0.90 [0.80,1.20]	1.00 [0.80,1.40]	1.10 [0.90,1.50]	1.10 [0.80,1.60]	<0.001***
Urea nitrogen, mg/dL	21 [16,32]	19 [16,26]	20 [15,28]	24 [17,34]	24 [17,38]	<0.001***
Glucose, mg/dL	130 [106,162]	125 [99,156]	120 [105,152]	130 [105,167]	143 [118,189]	<0.001***
Lactate, mmol/L	1.60 [1.20,2.10]	1.60 [1.20,2.07]	1.47 [1.10,1.91]	1.52 [1.20,2.10]	1.70 [1.30,2.26]	0.003**
Comorbidities						
Atrial fibrillation	394 (52%)	96 (51%)	103 (55%)	103 (55%)	92 (49%)	0.6
Ischemic heart disease	216 (29%)	41 (22%)	54 (29%)	53 (28%)	68 (36%)	0.024*
Hypertension	93 (12%)	29 (15%)	20 (11%)	19 (10%)	25 (13%)	0.4
Valvular disease	312 (41%)	84 (44%)	84 (45%)	78 (41%)	66 (35%)	0.2
Ventricular thrombus	13 (1.7%)	2 (1.1%)	3 (1.6%)	4 (2.1%)	4 (2.1%)	0.8
Ventricular arrhythmia	21 (2.8%)	4 (2.1%)	7 (3.7%)	5 (2.7%)	5 (2.6%)	0.8
AKI	629 (83%)	150 (79%)	162 (86%)	164 (87%)	153 (81%)	0.11
CKD	218 (29%)	38 (20%)	59 (31%)	64 (34%)	57 (30%)	0.017*
COPD	153 (20%)	31 (16%)	37 (20%)	38 (20%)	47 (25%)	0.2
Respiratory failure	168 (22%)	28 (15%)	26 (14%)	42 (22%)	72 (38%)	<0.001***
Pulmonary embolism	24 (3.2%)	6 (3.2%)	5 (2.7%)	4 (2.1%)	9 (4.8%)	0.5
Cerebral infarction	36 (4.8%)	12 (6.3%)	7 (3.7%)	7 (3.7%)	10 (5.3%)	0.6
Diabetes	287 (38%)	65 (34%)	77 (41%)	83 (44%)	62 (33%)	0.075

(*Continued*)

Table 3 (Continued).

Characteristics	Overall, n = 754[1]	Q1[a], n = 189[1]	Q2[a], n = 188[1]	Q3[a], n = 188[1]	Q4[a], n = 189[1]	*p*-value[2]
Hyperlipidemia	437 (58%)	109 (58%)	122 (65%)	111 (59%)	95 (50%)	0.038*
Goat	62 (8.2%)	17 (9.0%)	18 (9.6%)	15 (8.0%)	12 (6.3%)	0.7
Iron-deficiency anemia	38 (5.0%)	5 (2.6%)	6 (3.2%)	9 (4.8%)	18 (9.5%)	0.009**
Operations and procedures						
Mechanical ventilation	200 (27%)	57 (30%)	51 (27%)	44 (23%)	48 (25%)	0.5
RRT	44 (5.8%)	8 (4.2%)	9 (4.8%)	9 (4.8%)	18 (9.5%)	0.1
Cardiac assistance	35 (4.6%)	5 (2.6%)	5 (2.7%)	9 (4.8%)	16 (8.5%)	0.022*
Scoring system						
SOFA	3 [2,5]	4 [2,6]	3 [2,6]	3 [1,5]	2 [1,4]	<0.001***

Notes: [1] Continuous variables were described as median and interquartile range (IQR) (median [IQR]), categorical variables were described as frequencies and percentages (n (%)). [2] *p <0.05; **p <0.01; ***p <0.001. [a] SII (log) quartiles: Q1: 2.84-9.29; Q2: 9.29-10.11; Q3: 10.11-11.00; Q4: 11.00-14.08.
Abbreviations: BMI, body mass index; MAP, mean arterial pressure; AKI, acute kidney injury; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; RRT, renal replacement therapy; SOFA, sequential organ failure assessment.

Table 4 Cox proportional hazards analysis for SIRI, SII and mortality of HF

Primary outcome	Model 1		Model 2		Model 3	
	HR [95%CI][1]	*p*-value	HR [95%CI][1]	*p*-value	HR [95%CI][1]	*p*-value
SIRI (log)						
In-hospital mortality continuous variable per 1 unit	1.669 [1.364, 2.042]	<0.001	1.516 [1.225, 1.877]	<0.001	1.509 [1.173, 1.941]	0.001
Quartiles[a]						
Q1 (n=187)	—	—	—	—	—	—
Q2 (n=189)	0.921 [0.266, 3.184]	0.9	1.004 [0.290, 3.478]	>0.9	0.819 [0.223, 3.011]	0.8
Q3 (n=189)	1.426 [0.476, 4.268]	0.5	1.143 [0.377, 3.470]	0.8	1.173 [0.360, 3.818]	0.8
Q4 (n=189)	4.562 [1.749, 11.899]	0.002	3.445 [1.301, 9.123]	0.013	3.402 [1.151, 10.055]	0.027
P for trend		0.001		0.017		0.025
SII (log)						
In-hospital mortality continuous variable per 1 unit	1.212 [0.989, 1.487]	0.064	1.128 [0.918, 1.387]	0.3	1.225 [0.980, 1.532]	0.074
Quartiles[b]						
Q1 (n=189)	—	—	—	—	—	—
Q2 (n=188)	0.643 [0.181, 2.279]	0.5	0.590 [0.166, 2.099]	0.4	0.972 [0.243, 3.883]	>0.9
Q3 (n=188)	2.581 [0.976, 6.827]	0.056	1.818 [0.678, 4.872]	0.2	4.110 [1.277, 13.228]	0.018
Q4 (n=189)	3.147 [1.273, 7.778]	0.013	2.532 [1.014, 6.323]	0.47	4.654 [1.439, 15.054]	0.01
P for trend		0.001		0.01		0.002

Notes: [1] HR, hazard ratio; CI, confidence interval. [a] SIRI (log) quartiles: Q1: 0.05-1.52; Q2: 1.52-2.23; Q3: 2.23-3.12; Q4: 3.12-7.73. [b] SII (log) quartiles: Q1: 2.84-9.29; Q2: 9.29-10.11; Q3: 10.11-11.00; Q4: 11.00-14.08. Model 1: unadjusted; Model 2: adjusted for age, gender, race and marital status; Model 3: adjusted for age, gender, race, marital status, atrial fibrillation, ischemic heart disease, valvular disease, ventricular arrhythmia, COPD, respiratory failure, pulmonary embolism, heart rate, SBP, DBP, white blood cell count, hematocrit, hemoglobin and platelet count.

Model 3, HR [95% CI]: 1.509 [1.173, 1.941], $p = 0.001$). When SIRI was deemed a categorical variable, the Q4 quartile of SIRI (log) presented a strong association with mortality in all models (Q4 vs Q1: Model 1, HR [95% CI]: 4.562 [1.749, 11.899], $p = 0.002$; Model 2, HR [95% CI]: 3.445 [1.301, 9.123], $p = 0.013$; Model 3, HR [95% CI]: 3.402

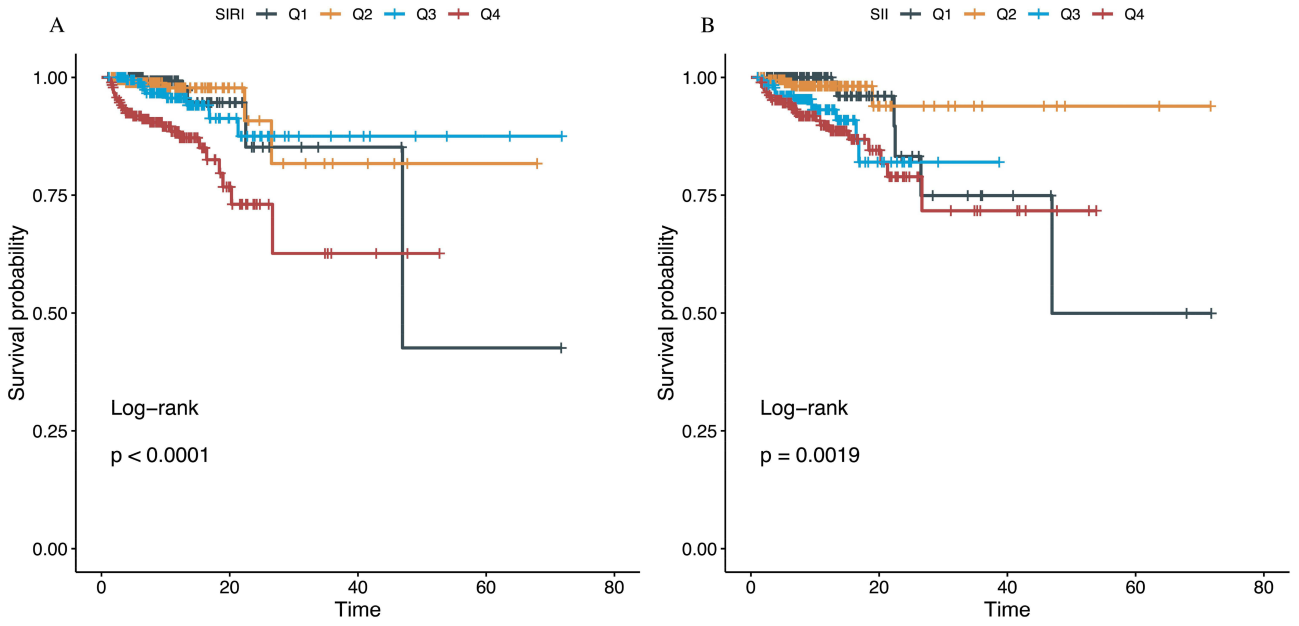

Figure 2 Kaplan-Meier survival analysis curves for the in-hospital mortality. (**A**) association between the quartiles of SIRI and mortality: SIRI (log) quartiles: Q1: 0.05–1.52, Q2: 1.52–2.23, Q3: 2.23–3.12, Q4: 3.12–7.73; (**B**) association between the quartiles of SII and mortality: SII (log) quartiles: Q1: 2.84–9.29, Q2: 9.29–10.11, Q3: 10.11–11.00, Q4: 11.00–14.08.

[1.151, 10.055], $p = 0.027$). In addition, all models demonstrated a trend of $p < 0.05$ (Model 1, $p = 0.001$; Model 2: $p = 0.017$; Model 3: $p = 0.025$). In contrast, SII when deemed a continuous variable showed little correlation with in-hospital mortality in all models (Model 1, HR [95% CI]: 1.212 [0.989, 1.487], $p = 0.064$; Model 2, HR [95% CI]: 1.128 [0.918, 1.387], $p = 0.3$; Model 3, HR [95% CI]: 1.225 [0.980, 1.532], $p = 0.074$), and Q4 quartile indicated a positive association with the primary outcome in Model 1 and Model 3, but not in Model 2 (Q4 vs Q1: Model 1, HR [95% CI]: 3.147 [1.273, 7.778], $p = 0.013$; Model 2, HR [95% CI]: 2.532 [1.104, 6.323], $p = 0.47$; Model 3, HR [95% CI]: 4.654 [1.439, 15.054], $p = 0.01$). All models demonstrated a trend of $p < 0.05$ (Model 1, $p = 0.001$; Model 2: $p = 0.01$; Model 3: $p = 0.002$).

Kaplan-Meier curve noted great differences in in-hospital mortality among groups with different SIRI levels, with patients in the highest quartile of SIRI (log) tending to have a higher risk of non-survival ($p < 0.0001$; Figure 2A). SII showed a similar trend to SIRI ($p = 0.0019$; Figure 2B).

Dose-Response Relationship Between SIRI (Log) or SII (Log) and in-Hospital Mortality

The RCS regression model unveiled a nearly linear correlation between SIRI and in-hospital mortality. The p for non-linearity was 0.074 in unadjusted Model 1, 0.090 in adjusted Model 2, and 0.114 in Model 3. When SIRI (log) value > 0.98, the HR for in-hospital mortality was > 1.0 in Model 1, and the value was 2.23 in both Model 2 and Model 3 (Figure 3A–C). However, SII showed a relatively mild non-linear relationship with in-hospital mortality in Models 1 and 2, and an S shape in Model 3. All models demonstrated a trend of $p < 0.05$ for non-linearity (Model 1, $p < 0.001$; Model 2: $p < 0.001$; Model 3: $p = 0.010$) (Figure 3D–F).

Comparison of Prognostic Values of SIRI and SII for in-Hospital Mortality

The ROC analysis uncovered that the prognostic power of SIRI for in-hospital mortality was greater than that of SII, but without statistical significance (AUC of SIRI (log): 0.713, AUC of SII (log): 0.658, $p = 0.051$) (Figure 4A). In addition, the sensitivity and specificity of SIRI (log) were 0.711 and 0.694, which for SII (log) were 0.733 and 0.601. The Youden indices of SIRI (log) and SII (log) were 0.405 and 0.334, respectively (Figure 4B).

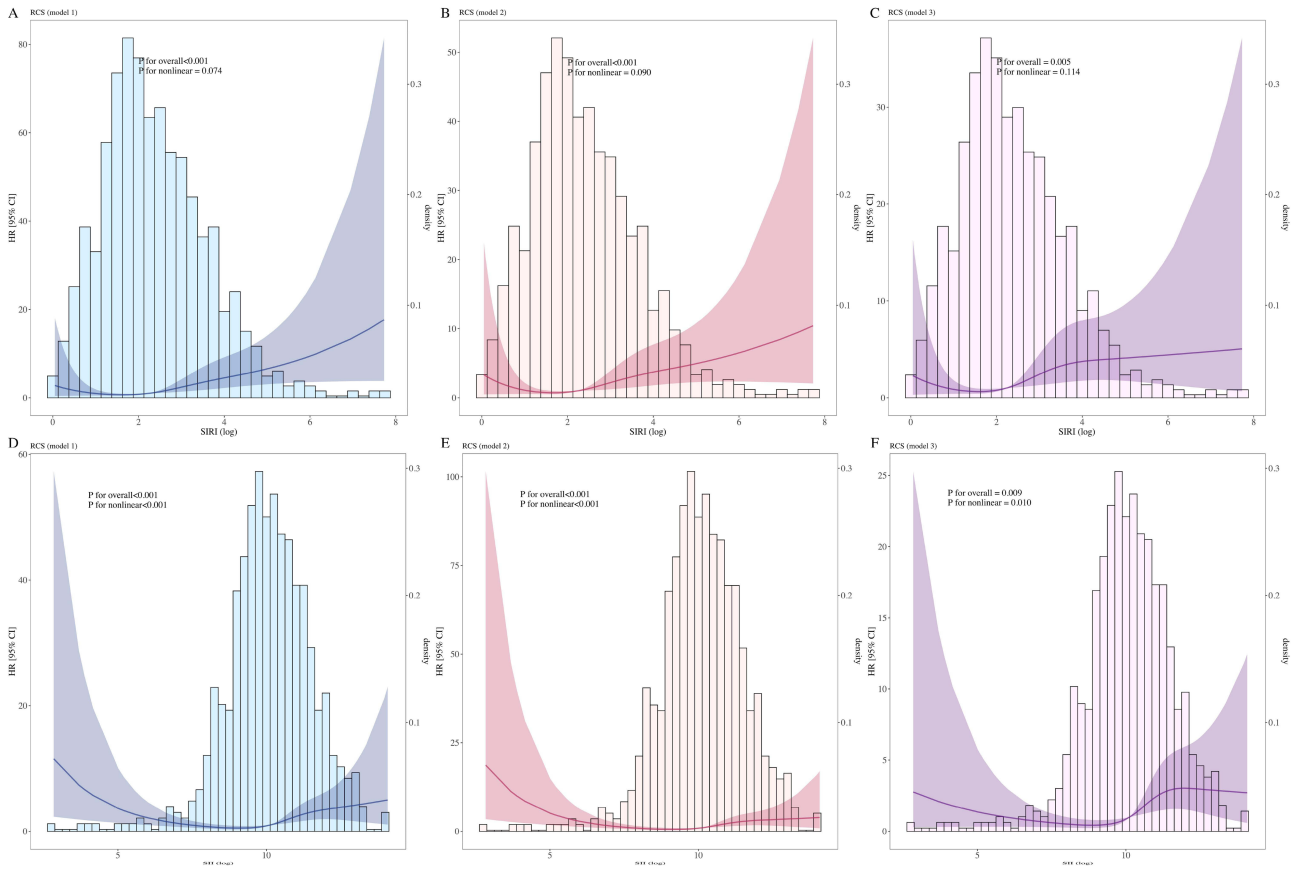

Figure 3 Restricted cubic spline (RCS) curves for SIRI and SII index hazard ratios and 95% confidence intervals (CI). (**A-C**) SIRI index hazard ratios and 95% CI in unadjusted and adjusted models; (**D-F**) SII index hazard ratios and 95% CI in unadjusted and adjusted models. Model 1: unadjusted; model 2: adjusted for age, gender, race and marital status; model 3: adjusted for age, gender, race, marital status, atrial fibrillation, ischemic heart disease, valvular disease, ventricular arrhythmia, COPD, respiratory failure, pulmonary embolism, heart rate, SBP, DBP, white blood cell count, hematocrit, hemoglobin and platelet count.

Association of SIRI with Secondary Endpoints

Secondary endpoints were analyzed based on PSM that allocated the patients to two groups with SIRI (log) = 2.23. The hospital stay was shorter in the low SIRI group ($p = 0.034$), but ICU stay was similar between the two groups ($p = 0.949$; Table 5). The incidence of AKI ($p = 0.900$) and the use of RRT ($p = 0.842$) were not notably different (Table 5).

Subgroup Analysis

Increased SIRI showed a prominent link with a heightened risk of in-hospital mortality in subgroups with age >60 years (HR [95% CI]: 1.602 [1.309–1.96]), female (HR [95% CI]: 1.851 [1.437–2.383]), absence of COPD (HR [95% CI]: 1.924 [1.503–2.463]), presence of AKI (HR [95% CI]: 1.701 [1.379–2.097]), SaO_2 >97% (HR [95% CI]: 2.077 [1.532–2.814]), respiratory rate ≤20 times/min (HR [95% CI]: 1.855 [1.409–2.443],), lactate ≤2.0 mmol/L (HR [95% CI]: 2.091 [1.604–2.726]), and use of mechanical ventilation (HR [95% CI]: 2.195 [1.686–2.858]) (all $p < 0.001$). There were apparent interactions in the lactate ($p = 0.012$) and mechanical ventilation ($p = 0.026$) subgroups (Figure 5).

Discussion

This study concluded that high levels of SIRI increased the incidence of in-hospital mortality and hospital stay in critically ill HF patients, and the prognostic value of SIRI was better than that of SII. Compared to traditional assessment indicators of HF such as N-terminal probrain natriuretic peptide (NT-proBNP) or echocardiography, SIRI and SII offer a more accessible, rapid, and cost-effective means of evaluation. Not to mention that a proportion of patients with HFpEF do not have abnormal NT-proBNP,[28] and echocardiography requires significant expertise from the operator.

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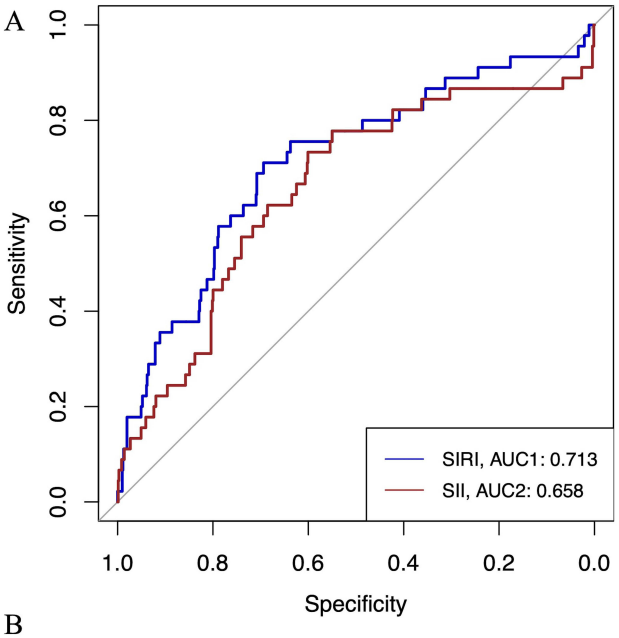
A



B

Indices	Threshold	Sensitivity	Specificity	Youden index
SIRI (log)	2.807	0.711	0.694	0.405
SII (log)	10.375	0.733	0.601	0.334

Figure 4 Receiver operating characteristic (ROC) curves of SIRI and SII for in-hospital mortality. (**A**) ROC curves and AUCs; (**B**) the sensitivity, specificity and Youden indices of SIRI (log) and SII (log).
Abbreviation: AUC, area under the curve.

The definition and classification of HF based on left ventricular ejection fraction is widely accepted and used, with the prevalence of HFpEF rising to nearly 50% of all cases.[1,5] Notably, HFpEF is correlated with aging and female gender, and it exhibits distinct circulatory biomarkers compared to HFrEF.[1,5,28] Our study demonstrated a similar correlation between HF prognosis and age or gender. Subgroup analysis revealed that increased SIRI had a stronger association with mortality in patients older than 60 years, consistent with Wang et al.[10] However, recent epidemiological studies have reported a trend toward younger ages at HF onset and an increase in HF diagnosis, which may obscure the connection between age and outcomes.[1,2] In addition, the positive prognostic value of SIRI in mortality was pronounced in the female subgroup. There is a notable scarcity of studies to adequately address this phenomenon, which may be influenced by hormones and etiological heterogeneity.

As another novel predictive index, SII was examined in many overlapping areas of SIRI and compared with SIRI, Xia et al and Zhu et al showed that SIRI and SII had similar predictive capabilities for all-cause and cardiovascular mortality.[13,15] Lin et al reported an equivalent effect of SIRI and SII in AF-related stroke.[29] However, SIRI was superior

Table 5 Association of SIRI and secondary outcomes. AKI, acute kidney injury; RRT, renal replacement therapy

Secondary Outcomes	SIRI (log) ≤2.23, n = 217[1]	SIRI (log) >2.23, n = 217[1]	*p*-value
Length of hospital stay, day	9 [6, 13]	10 [7, 15]	0.034
Length of ICU stay, day	2.09 [1.21, 3.70]	2.11 [1.22, 3.33]	0.949
AKI	178 (82%)	179 (82%)	0.9
RRT	14 (6.5%)	13 (6.0%)	0.842

Notes: [1] Continuous variables were described as median and interquartile range (IQR) (median [IQR]), categorical variables were described as frequencies and percentages (n (%).

Variable	Count	HR [95%CI]	p–value	p for interaction
Overall	754	1.669 [1.364–2.042]	<0.001	
Age, years				0.744
<=60	164	1.966 [0.623–6.207]	0.249	
> 60	590	1.602 [1.309–1.96]	<0.001	
Gender				0.181
Female	309	1.851 [1.437–2.383]	<0.001	
Male	445	1.385 [0.981–1.955]	0.064	
Race				0.659
Non–white	280	1.533 [1.078–2.181]	0.017	
White	474	1.747 [1.37–2.228]	<0.001	
COPD				0.103
No	601	1.924 [1.503–2.463]	<0.001	
Yes	153	1.251 [0.822–1.903]	0.296	
Respiratory failure				0.382
No	586	1.745 [1.309–2.327]	<0.001	
Yes	168	1.427 [1.056–1.927]	0.021	
AKI				0.505
No	125	1.909 [0.816–4.462]	0.136	
Yes	629	1.701 [1.379–2.097]	<0.001	
CKD				0.743
No	536	1.711 [1.33–2.201]	<0.001	
Yes	218	1.783 [1.189–2.673]	0.005	
Hypertension				0.44
No	661	1.603 [1.28–2.008]	<0.001	
Yes	93	2.27 [1.315–3.918]	0.003	
Ischemic heart disease				0.287
No	538	1.526 [1.168–1.993]	0.002	
Yes	216	1.851 [1.341–2.554]	<0.001	
Diabetes				0.608
No	467	1.756 [1.344–2.294]	<0.001	
Yes	287	1.556 [1.138–2.128]	0.006	
SaO2, %				0.084
<=97	333	1.402 [1.034–1.902]	0.03	
>97	421	2.077 [1.532–2.814]	<0.001	
Heart rate, beats/min				0.646
<=90	505	1.694 [1.251–2.295]	0.001	
>90	249	1.577 [1.191–2.09]	0.001	
Respiratory rate, times/min				0.108
<=20	506	1.855 [1.409–2.443]	<0.001	
>20	248	1.351 [0.994–1.836]	0.055	
MAP, mmHg				0.879
<=70	195	1.656 [1.164–2.357]	0.005	
>70	559	1.677 [1.307–2.152]	<0.001	
White blood cell count, 10^9/L				0.111
<=10.0	418	2.191 [1.522–3.152]	<0.001	
>10.0	336	1.489 [1.117–1.986]	0.007	
Glucose, mg/dL				0.871
<=120	308	1.664 [1.151–2.405]	0.007	
>120	446	1.717 [1.329–2.218]	<0.001	
Lactate, mmol/L				0.012
<=2.0	551	2.091 [1.604–2.726]	<0.001	
>2.0	203	1.193 [0.85–1.675]	0.308	
Mechanical ventilation				0.026
No	554	1.427 [1.073–1.898]	0.014	
Yes	200	2.195 [1.686–2.858]	<0.001	
RRT				0.214
No	710	1.749 [1.373–2.229]	<0.001	
Yes	44	1.319 [0.892–1.949]	0.165	
Cardiac assistance				0.137
No	719	1.5 [1.186–1.897]	0.001	
Yes	35	1.715 [1.231–2.388]	0.001	

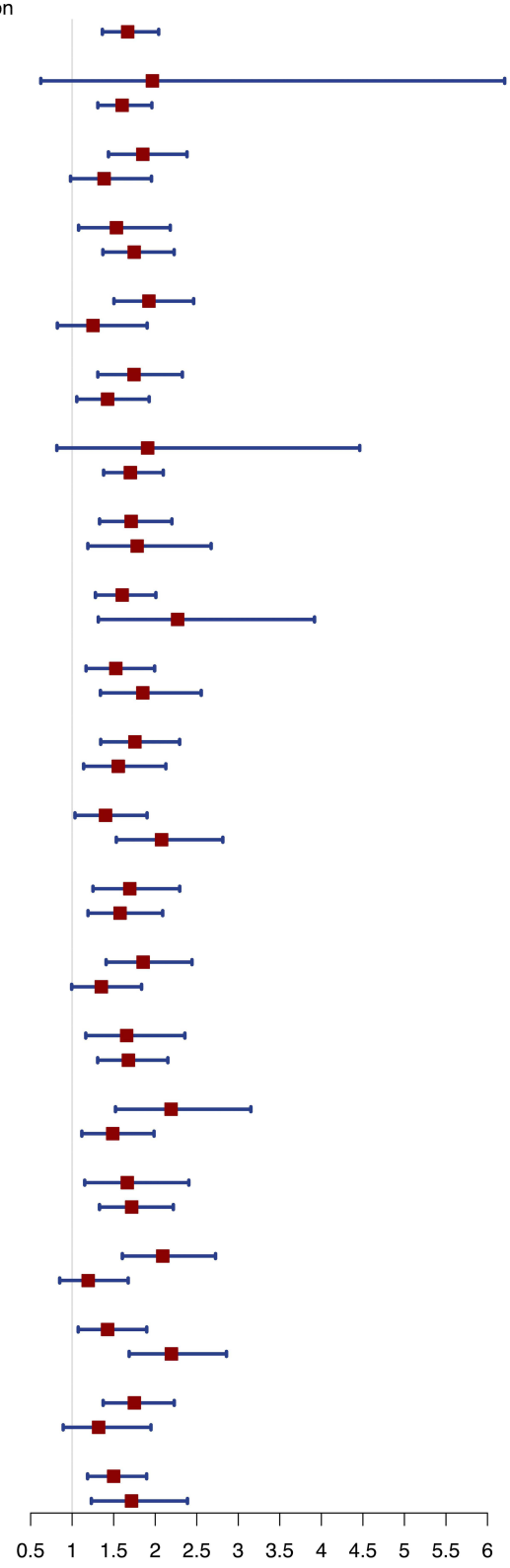


Figure 5 Forest plots of patients in subgroups.

Abbreviations: COPD, chronic obstructive pulmonary disease; AKI, acute kidney injury; CKD, chronic kidney disease; SaO_2, oxygen saturation; MAP, mean arterial pressure; RRT, renal replacement therapy; HR, hazard ratio; CI, confidence intervals.

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to SII for prognostic prediction in pulmonary arterial hypertension, acute ischemic stroke, and asthma.[11,30,31] It is hypothesized that the discrepancies may be attributed to the bidirectional regulatory effects of PLT in different situations, except for the specific populations studied. Thrombocytopenia is closely related to all-cause mortality in HF patients,[24,26] and synchronous decreases in PLT and LC in certain immunosuppressive situations may offset the ratio fluctuation and result in delayed changes in SII. Combined with Cox analysis, Kaplan-Meier survival analysis, AUC values and Youden indices, SIRI was a more stable and distinct index to predict prognosis in critically ill HF patients. Besides, the RCS of SII showed a U- or S-shaped non-linear relationship with in-hospital mortality, lacking stability and consistency compared with SIRI.

HF is a clinical syndrome rather than a single disease, with most patients presenting multiple complications.[1,3,32] In this study, AKI, a prevalent comorbidity of HF, was considered as a secondary outcome, but the incidence showed no positive association with SIRI levels. The use of RRT was significantly more pronounced among non-survivors but exhibited a negative association with SIRI levels. Nevertheless, previous reports disclosed that higher SIRI predicted AKI incidence and mortality in patients with abdominal trauma and those receiving percutaneous coronary intervention.[33,34] The discrepancies may be attributed to the causative factors of AKI, and the association of SIRI with AKI secondary to HF requires further investigation.

Respiratory system disorders such as COPD were intimately linked to cardiac function and represented major causes of HF except for ischemic heart disease and hypertension. However, our subgroup analysis revealed that higher SIRI was more strongly associated with HF patients without COPD, and this positive trend was also found in subgroups with normal respiratory status (lower respiratory rate and higher oxygen saturation) and lactate. We speculated that COPD and factors leading to abnormal respiratory status and hyperlactatemia were predominantly linked to poor prognosis, and the causal effect was far greater than low-grade inflammation represented by SIRI. Although patients with sepsis or SIRS were excluded to minimize the impact of severe inflammatory conditions, other pathological conditions may still significantly affect the result in certain scenarios. Furthermore, subgroup analysis unveiled an interaction between mechanical ventilation and SIRI and a link of SIRI with mortality in patients with or without mechanical ventilation, but the association was more pronounced in patients with mechanical ventilation. Considering that mechanical ventilation can alleviate HF, especially left ventricular HF to a certain extent, a sustained inflammatory response under mechanical ventilation may indirectly indicate severe disease and an elevated risk of mortality.

Strengths and Limitations

This study presents several notable strengths: (1) We included patients admitted with a primary diagnosis of HF and excluded patients with severe inflammation to eliminate the underlying confounding factors of SIRI or SII, which minimize the bias; (2) Critically ill HF patients were enrolled without limitation of age, gender, or cause, and SIRI was a stable predictor of poor prognosis, suggesting its potential for widespread clinical application; (3) SIRI outperformed SII in prognostic value among critically ill HF patients, with a novel conclusion from previous studies.

Several limitations also exist: (1) This is a single-center retrospective cohort study, which inherently introduces selection bias; (2) The excessive missing variables in the database precludes the examination of some indices of interest, such as echocardiographic measurements and cardiac output; (3) The mechanism of the association between SIRI and HF is not studied.

Conclusion

This cohort study concluded that SIRI was strongly associated with in-hospital mortality and had more promising prognostic power than SII in HF patients. In addition, a higher SIRI level was related to longer hospital stays but showed no significance with ICU stay, the incidence of AKI, and the use of RRT.

Data Sharing Statement

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Ethics Approval and Consent to Participate

All data were legally extracted from the MIMIC-IV database without prejudice to public conduct, and patient identity information was anonymized. Therefore, ethical approval and informed consent were waived for this study.

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Disclosure

The authors report no conflicts of interest in this work.

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