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Differential Associations of Neutrophil-To-Lymphocyte Ratio, Systemic Immune-Inflammation Index, and Serum Albumin with In-Hospital Mortality and Prolonged Length of Stay Among Patients with Heart Failure

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ABSTRACT: Heart failure (HF) involves inflammatory and systemic disturbances that may influence short-term hospital outcomes. This retrospective cohort study examined the associations of neutrophil-to-lymphocyte ratio (NLR), systemic immune-inflammation index (SII), and serum albumin with in-hospital mortality and prolonged length of stay (LOS) among 147 adults hospitalized with HF. Admission complete blood counts were used to calculate NLR and SII, while serum albumin was obtained at admission or within 24–48 hours. Eight patients (5.4%) died and 38 (25.9%) had prolonged LOS (≥9 days). Median NLR and SII were higher in patients who died than in survivors (16.97 vs 3.32 and 3,617.50 vs 790.00, respectively; both $p<0.001$), whereas albumin did not differ significantly ($p=0.100$). NLR and SII yielded mortality AUCs of 0.942 and 0.895, respectively; the combined NLR–SII–albumin model yielded an AUC of 0.946. For prolonged LOS, albumin was lower in affected patients (3.30 vs 3.60 g/dL; $p=0.001$), correlated inversely with numerical LOS ($r_s=-0.220$; $p=0.007$), and remained independently associated after adjustment (adjusted OR 0.230; 95% CI 0.104–0.511). Albumin showed the strongest individual discrimination for prolonged LOS (AUC 0.675). NLR and SII were more closely related to in-hospital mortality, whereas albumin was more consistently related to prolonged hospitalization. These findings, particularly the mortality discrimination estimates, require external validation.

1. INTRODUCTION

Heart failure (HF) remains associated with substantial hospitalization and mortality despite major advances in evidence-based therapy [1,2]. Hospitalized patients are clinically heterogeneous, prompting interest in inexpensive biomarkers that may complement conventional assessment of short-term risk [3,4].

Inflammatory activation contributes to HF progression through neurohormonal signaling, oxidative stress, endothelial dysfunction, and adverse myocardial remodeling [4,5]. The neutrophil-to-lymphocyte ratio (NLR) reflects relative neutrophilia and lymphopenia, whereas the systemic immune-inflammation index (SII) additionally incorporates platelet count [6,7]. Meta-analyses have associated elevated NLR with higher mortality in HF, including acute decompensated HF, while higher SII has likewise been associated with increased mortality risk [6-8].

Serum albumin provides complementary information because hypoalbuminemia in HF may reflect chronic congestion, inflammation, malnutrition, and renal dysfunction rather than nutritional status alone [3]. Meta-analytic evidence links

hypoalbuminemia with higher in-hospital and long-term mortality; in ICU-based HF cohorts, lower albumin has also been associated with short-term mortality and longer hospitalization [9-11].

Recent studies have generally evaluated NLR, SII, and albumin separately or within other composite inflammatory indices; the incremental value of combining these specific markers across both mortality and length-of-stay outcomes is less well characterized [6,7,12]. This study therefore examined their associations with in-hospital mortality and prolonged length of stay and compared the discriminative performance of individual biomarkers with their combined model.

2. MATERIALS AND METHODS

2.1 Study Design and Participants

This single-center retrospective cohort study included adult patients hospitalized with heart failure (HF) at Dr. Wahidin Sudirohusodo General Hospital, a tertiary referral hospital in Makassar, Indonesia. Medical records corresponding to hospitalizations between January 2023 and December 2025 were reviewed. Data extraction was conducted from May to June 2026 after ethical approval had been obtained. The study evaluated the associations of the neutrophil-to-lymphocyte ratio (NLR), systemic immune-inflammation index (SII), and serum albumin with in-hospital mortality and prolonged length of stay (LOS).

Patients were eligible if they were aged ≥18 years, had a documented diagnosis of HF based on the clinical diagnosis and/or International Classification of Diseases coding recorded in the medical record, had complete blood count data required to calculate NLR and SII at admission, had serum albumin measured at admission or within the first 24–48 hours of hospitalization, and had complete information on hospital disposition and LOS. All eligible patients during the study period were included using total sampling.

Patients with active severe infection or sepsis, primary hematologic disorders, metastatic malignancy, active chemotherapy, or other conditions expected to substantially alter peripheral blood counts or serum albumin concentrations were excluded. Records with missing data for the principal biomarkers or study outcomes were also excluded. The final analytic cohort comprised 147 patients.

2.2 Data Collection and Clinical Variables

Data were retrospectively extracted from medical records using a structured data collection form. Recorded variables included age, sex, body mass index (BMI), HF diagnosis, left ventricular ejection fraction (LVEF), comorbidities, relevant treatment characteristics, laboratory parameters, hospital disposition, and LOS. Documented comorbidities included hypertension, diabetes mellitus, chronic kidney disease, coronary artery disease, stroke, and congenital heart disease.

The earliest available complete blood count obtained at admission was used to calculate NLR and SII. Serum albumin measured at admission or within the first 24–48 hours of hospitalization was used for analysis. Laboratory measurements were obtained from the hospital laboratory, and extracted data were checked for completeness and consistency before statistical analysis.

2.3 Biomarker and Outcome Assessment

NLR was calculated by dividing the neutrophil percentage by the lymphocyte percentage. SII was calculated as platelet count × neutrophil percentage/lymphocyte percentage. Serum albumin was expressed in g/dL. All three biomarkers were primarily analyzed as continuous variables to preserve information across their full distributions.

For categorical analyses, NLR was classified as low (≤3) or high (>3), SII as low ($\leq 600 \times 10^9$/L) or high ($>600 \times 10^9$/L), and serum albumin as normal (≥3.5 g/dL) or hypoalbuminemia (<3.5 g/dL). These predefined categories were used for categorical comparisons and were distinct from the optimal cut-off values subsequently derived from receiver operating characteristic (ROC) analyses.

The study outcomes were in-hospital mortality and prolonged LOS. In-hospital mortality was defined as death from any cause during the index hospitalization, with patients discharged alive constituting the comparison group.

LOS was defined as the number of days from hospital admission to hospital disposition. LOS was analyzed both as a continuous variable and as a binary outcome. A hospital stay of ≥9 days was classified as prolonged LOS, whereas a stay of ≤8 days was classified as non-prolonged LOS [13].

2.4 Statistical Analysis

Continuous variables were summarized as mean ± standard deviation when normally distributed and as median with minimum–maximum values when non-normally distributed. Categorical variables were presented as frequencies and percentages. Differences in continuous variables between two independent groups were assessed using the Mann–Whitney U test when appropriate. Categorical variables were compared using Pearson's chi-square test or Fisher's exact test according to expected cell counts. Spearman's rank correlation was used to assess the associations of continuous NLR, SII, and serum albumin values with numerical LOS.

The discriminative performance of individual biomarkers for in-hospital mortality and prolonged LOS was assessed using ROC analysis. Areas under the ROC curve (AUCs) with 95% confidence intervals (CIs) were calculated for NLR, SII, and serum albumin. Optimal cut-off values were identified using the Youden index, and the corresponding sensitivity and specificity were reported. Because lower serum albumin concentrations represented greater clinical risk, its direction was reversed for ROC interpretation.

For exploratory assessment of combined biomarker discrimination, binary logistic regression models incorporating NLR, SII, and serum albumin simultaneously were used to generate predicted probabilities for each participant. These predicted probabilities were subsequently evaluated using ROC analysis as a combined biomarker score. SII was scaled per 1000 units in regression-based analyses.

Potential factors associated with prolonged LOS were initially evaluated using bivariable analyses. The principal biomarkers and clinical-demographic variables with $p<0.25$ in bivariable analysis were considered for multivariable binary logistic regression using the backward likelihood-ratio method. Because NLR and SII were strongly correlated, they were entered into separate multivariable models to reduce collinearity. Adjusted associations were reported as odds ratios (ORs) with 95% CIs. Model calibration was assessed using the Hosmer–Lemeshow goodness-of-fit test.

Because only eight in-hospital deaths occurred, adjusted multivariable modeling of independent associations with mortality was not performed to reduce the risk of unstable estimates and overfitting. Accordingly, mortality analyses were interpreted primarily as between-group associations and exploratory assessments of biomarker discrimination. All statistical tests were two-sided, and $p<0.05$ was considered statistically significant. Statistical analyses were performed using IBM SPSS Statistics version 30 (IBM Corp., Armonk, NY, USA).

3. RESULTS AND DISCUSSION

3.1 Study Population and Baseline Characteristics

A total of 147 patients with heart failure met the eligibility criteria and were included in the analysis. The mean age was 52.14 ± 14.53 years, and 96 patients (65.3%) were male. Mean BMI was 22.88 ± 4.81 kg/m², while mean left ventricular ejection fraction (LVEF) was 33.42 ± 13.02%. Most patients had heart failure with reduced ejection fraction (HFrEF; 73.5%). Coronary artery disease was the most frequent comorbidity (49.0%), followed by diabetes mellitus (30.6%), hypertension (24.5%), and chronic kidney disease (15.6%). Mean hospital length of stay (LOS) was 7.20 ± 4.72 days; 38 patients (25.9%) experienced prolonged LOS, and 8 patients (5.4%) died during hospitalization. Median NLR and SII were 3.49 and 806.00 $\times 10^9$/L, respectively, while mean serum albumin was 3.55 ± 0.56 g/dL. Baseline characteristics are summarized in Table 1.

Table 1. Baseline Characteristics and Clinical Outcomes of the Study Population (n=147)

Characteristic	Value
Age, years	52.14 ± 14.53
Male sex	96 (65.3)
Female sex	51 (34.7)
BMI, kg/m²	22.88 ± 4.81
LVEF, %	33.42 ± 13.02

HFrEF (LVEF ≤40%)	108 (73.5)
HFmrEF (LVEF 41–49%)	20 (13.6)
HFpEF (LVEF ≥50%)	19 (12.9)
Coronary artery disease	72 (49.0)
Diabetes mellitus	45 (30.6)
Hypertension	36 (24.5)
Chronic kidney disease	23 (15.6)
NLR	3.49 (1.13–53.67)
NLR >3	90 (61.2)
SII, $\times 10^9$/L	806.00 (93.00–13,631.00)
SII >600 $\times 10^9$/L	93 (63.3)
Serum albumin, g/dL	3.55 ± 0.56
Hypoalbuminemia (<3.5 g/dL)	56 (38.1)
Length of stay, days	7.20 ± 4.72
Prolonged LOS (≥9 days)	38 (25.9)
Discharged alive	139 (94.6)
In-hospital death	8 (5.4)

Note: Data are presented as mean ± standard deviation, median (minimum–maximum), or n (%), as appropriate. BMI, body mass index; HFmrEF, heart failure with mildly reduced ejection fraction; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction; LOS, length of stay; LVEF, left ventricular ejection fraction; NLR, neutrophil-to-lymphocyte ratio; SII, systemic immune-inflammation index.

3.2 Associations of NLR, SII, and Serum Albumin with Clinical Outcomes

Patients who died during hospitalization had substantially higher NLR and SII values than those discharged alive. Median NLR was 16.97 in patients who died compared with 3.32 among survivors ($p<0.001$), while median SII was 3,617.50 versus 790.00, respectively ($p<0.001$). Serum albumin was numerically lower among patients who died, but the difference was not statistically significant ($p=0.100$). Using the predefined categorical thresholds, all eight in-hospital deaths occurred among patients with NLR >3 and SII >600 $\times 10^9$/L. These associations were significant for NLR ($p=0.023$) and SII ($p=0.027$), whereas the association between hypoalbuminemia and mortality was not significant ($p=0.260$). These findings are presented in Table 2, Panel A.

Table 2. Associations of NLR, SII, and Serum Albumin with Clinical Outcomes

Panel A. Associations with In-Hospital Mortality

Biomarker	Discharged alive (n=139)	Died (n=8)	p-value
Continuous biomarker values			
NLR	3.32 (1.13–53.67)	16.97 (7.28–35.35)	<0.001*
SII ($\times 10^9$/L)	790.00 (93.00–13,631.00)	3,617.50 (940.00–7,953.00)	<0.001*

Albumin (g/dL)	3.60 (2.00–5.20)	3.40 (2.10–3.80)	0.100
Predefined biomarker categories			
NLR ≤3	57 (100.0)	0 (0.0)	
NLR >3	82 (91.1)	8 (8.9)	0.023*
SII ≤600 $\times 10^9$/L	54 (100.0)	0 (0.0)	
SII >600 $\times 10^9$/L	85 (91.4)	8 (8.6)	0.027*
Albumin ≥3.5 g/dL	88 (96.7)	3 (3.3)	
Albumin <3.5 g/dL	51 (91.1)	5 (8.9)	0.260

Note: Continuous biomarker values are presented as median (minimum–maximum), and categorical data as n (%). Continuous variables were compared using the Mann–Whitney U test, whereas categorical variables were compared using Fisher's exact test. Percentages in categorical rows are calculated within each biomarker category. NLR, neutrophil-to-lymphocyte ratio; SII, systemic immune-inflammation index. *Statistically significant at $p<0.05$.

For LOS, NLR and SII were numerically higher among patients with prolonged hospitalization, although neither difference reached statistical significance. Median NLR was 4.44 in patients with prolonged LOS compared with 3.32 in those with non-prolonged LOS (p=0.140), while median SII was 1,011.50 versus 790.00 (p=0.096). In contrast, serum albumin was significantly lower in patients with prolonged LOS (3.30 vs 3.60 g/dL, p=0.001). Albumin also showed a weak inverse correlation with numerical LOS (Spearman $r_s=-0.220$, p=0.007), whereas correlations with NLR ($r_s=0.128$, p=0.124) and SII ($r_s=0.112$, p=0.176) were weak and non-significant. These findings are summarized in Table 2, Panel B.

Panel B. Associations with Length of Stay

Biomarker	Non-prolonged LOS ≤8 days (n=109)	Prolonged LOS ≥9 days (n=38)	*p*-value (group comparison)	Spearman r_s with numerical LOS	*p*-value (correlation)
NLR	3.32 (1.13–35.35)	4.44 (1.35–53.67)	0.140	0.128	0.124
SII ($\times 10^9$/L)	790.00 (93.00–7,953.00)	1,011.50 (243.00–13,631.00)	0.096	0.112	0.176
Albumin (g/dL)	3.60 (2.50–5.20)	3.30 (2.00–4.30)	0.001*	−0.220	0.007*

Note: Biomarker values are presented as median (minimum–maximum). Between-group comparisons were performed using the Mann–Whitney U test. Spearman rank correlation was used to assess associations between continuous biomarker values and numerical LOS. NLR, neutrophil-to-lymphocyte ratio; SII, systemic immune-inflammation index; LOS, length of stay. *Statistically significant at $p<0.05$.

3.3 Discriminative Performance for In-Hospital Mortality and Prolonged Length of Stay

For in-hospital mortality, NLR showed the highest discriminative performance among the individual biomarkers, with an AUC of 0.942 (95% CI 0.892–0.991; $p<0.001$). At a cut-off of ≥7.38, NLR yielded a sensitivity of 87.5% and specificity of 80.6%. SII also demonstrated good discrimination, with an AUC of 0.895 (95% CI 0.803–0.986; $p<0.001$). Serum albumin showed lower discrimination, with an AUC of 0.673 (95% CI 0.520–0.825; $p=0.101$).

The combined NLR–SII–albumin model yielded the highest numerical AUC for mortality at 0.946 (95% CI 0.904–0.988), with 87.5% sensitivity and 87.1% specificity. The absolute difference in AUC between the combined model and NLR alone was 0.004.

For prolonged LOS, NLR and SII showed limited discrimination, with AUCs of 0.581 and 0.591, respectively. Serum albumin performed better, with an AUC of 0.675 (95% CI 0.570–0.780; $p=0.001$). At a cut-off of ≤3.35 g/dL, albumin had a sensitivity

of 52.6% and specificity of 78.0%. The combined model yielded an AUC of 0.678 (95% CI 0.573–0.783; p=0.001), representing an absolute AUC difference of 0.003 compared with albumin alone. The combined model showed higher specificity (87.2% vs 78.0%) but lower sensitivity (44.7% vs 52.6%) than albumin alone. Full ROC results are presented in Table 3, and the corresponding curves are shown in Figure 1.

Table 3. Discriminative Performance of Individual and Combined Biomarkers for In-Hospital Mortality and Prolonged Length of Stay

Outcome / Biomarker	AUC	95% CI	p-value	Optimal cut-off	Sensitivity	Specificity
In-hospital mortality						
NLR	0.942	0.892–0.991	<0.001*	≥7.38	87.5%	80.6%
SII	0.895	0.803–0.986	<0.001*	≥941.50 $\times 10^9$/L	87.5%	59.7%
Albumin	0.673	0.520–0.825	0.101	≤3.75 g/dL	87.5%	37.4%
NLR + SII + albumin	0.946	0.904–0.988	<0.001*	≥0.0556†	87.5%	87.1%
Prolonged LOS						
NLR	0.581	0.475–0.686	0.140	≥4.21	55.3%	66.1%
SII	0.591	0.484–0.698	0.096	≥989.00 $\times 10^9$/L	52.6%	65.1%
Albumin	0.675	0.570–0.780	0.001*	≤3.35 g/dL	52.6%	78.0%
NLR + SII + albumin	0.678	0.573–0.783	0.001*	≥0.351†	44.7%	87.2%

Note: Optimal cut-offs were determined using the Youden index. Lower albumin concentrations were treated as indicating greater risk. †For the combined models, the cut-off represents the predicted probability generated from binary logistic regression incorporating NLR, SII, and albumin. SII was scaled per 1000 units in regression-based models. AUC, area under the receiver operating characteristic curve; CI, confidence interval; LOS, length of stay; NLR, neutrophil-to-lymphocyte ratio; SII, systemic immune-inflammation index. *Statistically significant at $p<0.05$.

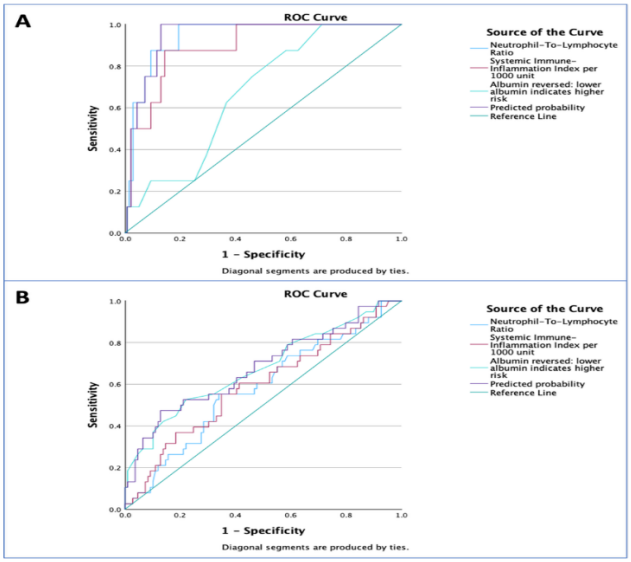

Figure 1. Receiver operating characteristic curves for clinical outcomes.

(A) Receiver operating characteristic curves of NLR, SII, serum albumin, and the combined NLR–SII–albumin model for in-hospital mortality. (B) Receiver operating characteristic curves of the same biomarkers and combined model for prolonged length of stay. For ROC analysis, the direction of serum albumin was reversed because lower concentrations indicated greater risk. NLR, neutrophil-to-lymphocyte ratio; SII, systemic immune-inflammation index; LOS, length of stay.

3.4 Multivariable Analysis of Factors Associated with Prolonged Length of Stay

In bivariable analyses of clinical and demographic factors, LVEF and sex were associated with prolonged LOS, while BMI met the prespecified criterion for consideration in multivariable modeling. Median LVEF was higher among patients with prolonged LOS than among those with non-prolonged LOS (36.00% vs 27.80%; p=0.006), and women represented a greater proportion of the prolonged-LOS group (50.0% vs 29.4%; p=0.021). BMI also showed a possible association (p=0.054), whereas age and the presence of at least one comorbidity were not associated with prolonged LOS.

Because NLR and SII were strongly correlated, separate multivariable models were fitted. In the NLR-based model, NLR did not remain in the final model after adjustment for albumin, LVEF, BMI, and sex. Similarly, SII was not retained in the final SII-based model. Both approaches converged on the same final model, in which serum albumin and LVEF remained independently associated with prolonged LOS.

Each 1-g/dL increase in serum albumin was associated with lower odds of prolonged LOS (adjusted OR 0.230; 95% CI 0.104–0.511; p<0.001). LVEF was positively associated with prolonged LOS in the final model (adjusted OR 1.037 per 1% increase; 95% CI 1.006–1.069; p=0.018). Model calibration was acceptable according to the Hosmer–Lemeshow test (p=0.555). The final multivariable model is presented in Table 4.

Table 4. Multivariable Factors Associated with Prolonged Length of Stay

Variable	β coefficient	Adjusted OR	95% CI	p-value
Serum albumin, per 1 g/dL increase	−1.468	0.230	0.104–0.511	<0.001*
LVEF, per 1% increase	0.036	1.037	1.006–1.069	0.018*

Note: Multivariable binary logistic regression was performed using backward likelihood-ratio elimination. The candidate variables were the principal biomarkers and clinical-demographic variables meeting the prespecified bivariable criterion of p<0.25. NLR and SII were analyzed in separate initial models because of their strong correlation; neither remained in the final model. Both models converged on the same final model comprising serum albumin and LVEF. Hosmer–Lemeshow goodness-of-fit test: p=0.555. CI, confidence interval; LVEF, left ventricular ejection fraction; OR, odds ratio. *Statistically significant at p<0.05.

3.5 Discussion

In this retrospective cohort of hospitalized patients with heart failure, NLR, SII, and serum albumin showed distinct relationships with short-term clinical outcomes. NLR and SII were higher among patients who died during hospitalization, whereas albumin was more consistently associated with prolonged length of stay (LOS). NLR provided the strongest individual discrimination for in-hospital mortality, while albumin showed the strongest individual discrimination for prolonged LOS and remained independently associated with this outcome after adjustment. Such divergence is clinically plausible because heart failure reflects interacting hemodynamic, inflammatory, metabolic, and extracardiac processes rather than a single biological pathway [1,2]. Inflammatory activation is particularly relevant during decompensation and may reflect systemic disease burden beyond conventional cardiac measures [4,5].

The mortality findings for NLR are consistent with contemporary evidence. NLR reflects the balance between neutrophil-predominant innate inflammation and relative lymphopenia, both of which may accompany physiological stress in heart failure. Meta-analytic evidence indicates higher NLR among patients with heart failure who die than among survivors, with similar prognostic associations reported in acute decompensated heart failure [6,8]. Admission NLR has also been associated with adverse cardiovascular outcomes in hospitalized acute heart failure [14]. In our cohort, all eight deaths occurred among patients with NLR >3, and NLR yielded an AUC of 0.942. The ROC-derived threshold of 7.38, however, was substantially higher than the predefined threshold of 3, emphasizing that these cut-offs serve different analytical purposes and should not be regarded as interchangeable or universally applicable.

SII showed a similar mortality pattern, although its discrimination was numerically lower than that of NLR. By incorporating platelet count alongside neutrophils and lymphocytes, SII captures an additional component of the inflammatory and thrombo-inflammatory response. A recent meta-analysis of 15 studies involving 77,917 patients found that elevated SII was associated with higher mortality in heart failure [7]. Associations with short-term mortality have also been reported in acute decompensated heart failure [15], while studies in broader congestive heart failure and HFrEF populations have demonstrated adverse prognostic associations [16,17]. These data support the direction of our findings, although they do not indicate superiority of SII over NLR; in the present cohort, NLR had a higher AUC and greater specificity.

Serum albumin behaved differently. Although concentrations were lower among patients who died, the difference was not statistically significant. This contrasts with larger evidence showing an association between hypoalbuminemia and mortality in heart failure. A meta-analysis of 48 studies linked hypoalbuminemia with both in-hospital and long-term mortality [9], while Chao et al. (2022) reported an inverse relationship between albumin and short-term mortality in critically ill patients with congestive heart failure [10]. More recent data in older patients hospitalized with acute heart failure similarly associated lower albumin with one-year mortality [18]. Given only eight deaths in our cohort, the non-significant mortality finding should not be interpreted as evidence against this relationship. Albumin is also biologically non-specific, reflecting inflammation, hepatic congestion, renal dysfunction, hemodilution, malnutrition, and protein loss [3,19].

The relationship between albumin and LOS was more consistent. Patients with prolonged LOS had lower albumin concentrations, albumin correlated inversely with numerical LOS, and higher albumin remained independently associated with lower odds of prolonged hospitalization. Liu et al. (2023) similarly found a negative association between serum albumin and prolonged LOS among 2,280 patients with acute heart failure [11]. Hospitalization duration is nevertheless multifactorial. Using the same ≥9-day definition, Ignatavičiūtė et al. (2023) identified renal dysfunction, NT-proBNP, blood pressure, treatment interruption, and valvular disease as relevant factors [13]. Nutritional impairment and altered body composition are also common in heart failure [20], while congestion may influence renal, hepatic, metabolic, and functional status throughout hospitalization [21]. Albumin in this setting may therefore capture broader systemic vulnerability rather than nutritional status alone.

The combined biomarker models produced only small numerical AUC differences from the strongest individual biomarkers: 0.946 versus 0.942 for mortality and 0.678 versus 0.675 for prolonged LOS. Because formal pairwise AUC comparisons were not performed, these differences cannot establish incremental discrimination. This distinction is important because studies assessing the added prognostic value of composite inflammatory indices have used formal measures such as changes in C-index, net reclassification improvement, and integrated discrimination improvement [12]. The positive association between higher LVEF and prolonged LOS was also unexpected. Given the HFrEF-predominant sample and incomplete adjustment for congestion, renal function, and treatment-related factors, residual confounding or sample-specific characteristics are plausible explanations [13,21].

These findings suggest complementary rather than interchangeable roles for routinely available biomarkers: NLR and SII were more closely related to in-hospital mortality, whereas albumin was more consistently related to hospitalization duration. Their use as standalone prognostic tools is not supported by the present data. The single-center retrospective design, reliance on single early-hospitalization biomarker measurements, absence of serial biomarker assessment, biomarker non-specificity, residual confounding, and lack of external validation limit generalizability. Most importantly, only eight deaths occurred; sparse outcome events can produce unstable estimates and increase the risk of overfitting in multivariable prediction models [22]. Accordingly, the mortality ROC thresholds and combined models should be regarded as exploratory and require external validation in larger, multicenter cohorts before clinical application.

4. CONCLUSION

NLR and SII were significantly associated with in-hospital mortality among patients hospitalized with heart failure, with NLR showing the strongest individual discrimination for this outcome. In contrast, serum albumin was more consistently associated with prolonged length of stay and remained independently associated with prolonged hospitalization after adjustment. Combining NLR, SII, and albumin produced only small numerical increases in AUC compared with the strongest individual biomarker for each outcome. Given the limited number of in-hospital deaths and the single-center retrospective design, the mortality cut-offs and combined biomarker models should be regarded as exploratory rather than clinically validated prediction

tools. Larger prospective, multicenter studies are needed to confirm these associations, assess incremental value beyond established clinical risk factors, and externally validate the identified thresholds.

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AUTHOR CONTRIBUTIONS

Rizka Mardiyati: Conceptualization, Investigation, Data Curation, Formal Analysis, and Writing – Original Draft.

Haerani Rasyid: Conceptualization, Methodology, Supervision, Validation, and Writing – Review & Editing.

Suryani As'ad: Methodology, Supervision, Validation, and Writing – Review & Editing.

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All authors critically reviewed the manuscript, approved the final version, and agreed to be accountable for the integrity and accuracy of the work.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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ETHICS STATEMENT

The study protocol was approved by the Research Ethics Committee of Hasanuddin University, Makassar, Indonesia (approval No. 560/UN4.6.4.5.31/PP36/2026; protocol No. UH26040466; 23 April 2026). The study used retrospective medical-record data without direct patient intervention. Patient confidentiality was maintained throughout the study, and personally identifying information was excluded from the analytic dataset.

DATA AVAILABILITY STATEMENT

The data supporting the findings of this study are available from the corresponding author upon reasonable request, subject to applicable ethical and institutional restrictions.

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