

NLR, PLR, and SII Do Not Predict In-Hospital Mortality in Oldest-Old Male Patients with Acute Coronary Syndrome and Type 2 Diabetes: A Head-to-Head Comparative Study

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Abstract

Background

The neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and systemic immune-inflammation index (SII) have been associated with adverse outcomes in various cardiovascular populations. However, their comparative prognostic value in oldest-old (≥ 80 years) patients with acute coronary syndrome (ACS), coronary heart disease (CHD), and type 2 diabetes mellitus (T2DM) remains unexplored. We aimed to compare the predictive performance of NLR, PLR, and SII for in-hospital all-cause mortality in this population.

Methods

This single-center retrospective cohort study included 372 male patients aged ≥ 80 years with documented CHD, T2DM, and ACS. NLR, PLR, and SII were calculated from admission blood tests. The primary outcome was in-hospital all-cause mortality. Univariate and multivariable logistic regression models were used to assess the associations, and receiver operating characteristic (ROC) curves were generated to compare discriminative ability.

Results

The overall in-hospital mortality rate was 80.9% (301/372). None of the three indices was significantly associated with mortality in univariate analysis (NLR: OR = 0.99, 95% CI 0.95–1.03, $P = 0.589$; PLR: OR = 1.00, 95% CI 1.00–1.00, $P = 0.641$; SII: OR = 1.00, 95% CI 1.00–1.00, $P = 0.994$). After multivariable adjustment for age, heart failure, chronic kidney disease, serum creatinine, and HbA1c, all three indices remained non-significant (NLR: OR = 0.98, $P = 0.461$; PLR: OR = 1.00, $P = 0.281$; SII: OR = 1.00, $P = 0.890$). ROC analysis showed AUC values of 0.555, 0.526, and 0.540 for NLR, PLR, and SII, respectively, indicating negligible discriminative ability.

Conclusion

NLR, PLR, and SII do not provide independent prognostic information for in-hospital mortality in oldest-old male patients with CHD, T2DM, and ACS. Routine use of these indices for risk stratification in this population is not supported by our data.

1. Introduction

The global population is aging rapidly, and the proportion of individuals aged ≥ 80 years is projected to increase substantially in the coming decades [1]. In the oldest-old, the coexistence of coronary heart disease (CHD) and type 2 diabetes mellitus (T2DM) is particularly common, affecting up to 20% of this

population [2]. The oldest-old exhibit unique age-related physiological changes, including sarcopenia, adipose tissue redistribution, pancreatic β -cell senescence, and heightened inflammatory tone, which may alter the prognostic significance of traditional risk factors [3–5]. These patients are at extremely high risk of mortality and major adverse cardiovascular events, yet they are often underrepresented in clinical trials [6–7]. Moreover, the complex interplay of multiple comorbidities, polypharmacy, and age-related physiological changes makes risk stratification particularly challenging in this group [8].

Traditional cardiovascular risk factors, such as hypertension, dyslipidaemia, and smoking, have well-established prognostic value in middle-aged and younger elderly populations [9]. However, their predictive utility diminishes with advancing age, where competing risks and frailty become more influential [10–11]. In recent years, composite indices derived from routine laboratory tests have gained attention as potential biomarkers. The neutrophil-to-lymphocyte ratio (NLR), calculated from neutrophil and lymphocyte counts, reflects the balance between systemic inflammation and adaptive immune response [12]. Numerous studies have demonstrated that elevated NLR is independently associated with adverse outcomes across a wide spectrum of cardiovascular conditions, including acute and chronic coronary syndromes, heart failure, atherosclerotic disease, and cardiac arrhythmias [13–14]. A meta-analysis of patients with myocardial infarction confirmed that elevated NLR significantly predicts major adverse cardiovascular events and all-cause mortality [15]. Similarly, in patients with diabetes, NLR has been shown to be a reliable prognostic marker for mortality outcomes [16].

The platelet-to-lymphocyte ratio (PLR) is another inflammation-based index that integrates platelet count – a marker of thrombosis and inflammation – with lymphocyte count. Emerging evidence suggests that PLR is also associated with cardiovascular prognosis. A recent meta-analysis of 18 studies demonstrated that higher PLR significantly predicts increased mortality and major adverse cardiovascular events in patients with myocardial infarction [17]. In hypertensive individuals, elevated PLR independently predicts heightened risks of both all-cause and cardiovascular mortality [18]. Furthermore, studies have revealed V-shaped or J-shaped relationships between PLR and mortality in patients with cardio-cerebrovascular disease and asymptomatic coronary artery disease, highlighting the complexity of its prognostic role [19–20]. However, the evidence regarding PLR's utility in heart failure populations remains less conclusive, with some meta-analyses suggesting that PLR should be used with caution for prognosis assessment in heart failure patients [21].

The systemic immune-inflammation index (SII), first proposed by Hu et al. in 2014, is a more comprehensive biomarker calculated as platelet count $\times$ neutrophil count / lymphocyte count, thereby integrating three distinct immune-inflammatory pathways [22]. Compared with NLR and PLR, SII may offer a more holistic reflection of the host's inflammatory and immune status. An umbrella review of meta-analyses found that high SII levels are significantly associated with an increased risk of cardiovascular diseases (OR = 1.67, 95% CI: 1.06–2.61) and major adverse cardiovascular events [23]. In patients with heart failure with preserved ejection fraction, SII has been shown to outperform conventional inflammatory markers in predicting cardiovascular outcomes and rehospitalization [24]. Among patients with diabetes or prediabetes, SII exhibits a U-shaped relationship with all-cause

mortality and a J-shaped association with cardiovascular mortality [25]. Furthermore, in critically ill patients with atrial fibrillation, NLR, PLR, and SII have all been independently associated with increased risk of all-cause mortality [26].

Despite the substantial body of evidence supporting the prognostic value of NLR, PLR, and SII in various cardiovascular populations, several important knowledge gaps remain. First, the vast majority of existing studies have been conducted in middle-aged or relatively younger elderly populations, with very limited data specifically addressing the oldest-old (≥ 80 years) — a group in which immunosenescence and chronic inflammation may fundamentally alter the relationship between inflammatory biomarkers and outcomes [27]. Second, while these indices have been individually validated across diverse settings, head-to-head comparisons of NLR, PLR, and SII within the same cohort — particularly in the oldest-old population with ACS — are scarce. It remains unclear which of these three readily available indices, if any, provides the most clinically useful prognostic information in this specific group. Third, the prognostic value of these indices in oldest-old patients with the triple burden of CHD, T2DM, and ACS has not been systematically examined. Given that these patients represent a particularly high-risk subgroup with unique pathophysiological features — including heightened inflammatory tone, advanced atherosclerotic burden, and multi-organ dysfunction — the predictive performance of these indices may differ substantially from that observed in younger or less comorbid populations [28–29]. Finally, in the era of contemporary standardized medical therapy, the independent prognostic value of these indices may be attenuated by the widespread use of cardioprotective medications that directly modulate inflammatory pathways [30].

Therefore, the present study was designed to address these gaps by: (1) evaluating the associations of NLR, PLR, and SII with in-hospital all-cause mortality in a cohort of oldest-old (≥ 80 years) male patients with CHD, T2DM, and ACS; and (2) comparing the predictive performance of these three indices using a head-to-head design.

2. Methods

2.1 Study design and participants

This was a single-center retrospective cohort study conducted at the Department of Geriatric Cardiology, General Hospital of Southern Theater Command, Guangzhou, China. We included male patients aged ≥ 80 years who were hospitalized between January 2011 and December 2022 with documented diagnoses of CHD, T2DM, and ACS.

CHD was defined as a history of myocardial infarction, coronary revascularization (percutaneous coronary intervention or coronary artery bypass grafting), or angiographically documented stenosis $\geq 50\%$ in at least one major epicardial coronary artery [31]. T2DM was defined according to the American Diabetes Association criteria: fasting glucose ≥ 7.0 mmol/L, HbA1c $\geq 6.5\%$, or use of glucose-lowering medications [32]. ACS was defined based on the Fourth Universal Definition of Myocardial Infarction,

encompassing ST-segment elevation myocardial infarction (STEMI), non-ST-segment elevation myocardial infarction (NSTEMI), and unstable angina [33].

Exclusion criteria were: (1) age < 80 years; (2) female sex; (3) absence of CHD, T2DM, or ACS; (4) missing data on key variables (age, sex, death status, neutrophil count, lymphocyte count, or platelet count). A total of 372 patients were finally included in the analysis.

2.2 Data collection

Demographic characteristics, clinical history, vital signs, laboratory parameters, and in-hospital mortality data were extracted from electronic medical records using a standardized case report form. The following variables were collected: age, sex, body mass index (BMI), systolic and diastolic blood pressure, comorbidities (hypertension, heart failure, chronic kidney disease [CKD], and stroke), and laboratory parameters (neutrophil count, lymphocyte count, platelet count, serum creatinine, blood urea nitrogen, and HbA1c). All laboratory measurements were obtained within 24 hours of admission.

2.3 Definition of indices

The three inflammation-based indices were calculated from admission complete blood count results as follows:

$NLR = \text{neutrophil count} / \text{lymphocyte count}$

$PLR = \text{platelet count} / \text{lymphocyte count}$

$SII = (\text{platelet count} \times \text{neutrophil count}) / \text{lymphocyte count}$

These indices were analyzed both as continuous variables and categorized into tertiles based on their distribution in the study population.

2.4 Outcome

The primary outcome was all-cause in-hospital mortality. Death status was ascertained from hospital electronic medical records and discharge summaries. All deaths occurring during the index hospitalization were recorded, regardless of the underlying cause.

2.5 Statistical analysis

Continuous variables were presented as mean $\pm$ standard deviation (SD) or median with interquartile range (IQR), depending on the distribution. Categorical variables were presented as frequencies (n) and percentages (%). For each index, patients were divided into tertiles (low, medium, high) based on the distribution of index values.

Baseline characteristics were compared across tertiles using one-way analysis of variance (ANOVA) for continuous variables and chi-square tests for categorical variables. Comparisons of mortality rates across tertiles were performed using the chi-square test.

Univariate logistic regression was first performed to assess the association of each index and other covariates (age, BMI, heart failure, CKD, stroke, serum creatinine, blood urea nitrogen, and HbA1c) with in-hospital mortality. Variables with $P < 0.10$ in univariate analysis were candidates for multivariable adjustment; clinically important variables (age, heart failure, CKD) were also included regardless of statistical significance.

Three separate multivariable logistic regression models were constructed for NLR, PLR, and SII, respectively. Each model adjusted for the same set of covariates: age (continuous), heart failure (yes vs. no), CKD (yes vs. no), serum creatinine (continuous), and HbA1c (continuous). Results were reported as odds ratios (OR) with 95% confidence intervals (CI).

The discriminative ability of each index for predicting in-hospital mortality was evaluated using receiver operating characteristic (ROC) curves, and the area under the curve (AUC) was calculated.

All statistical analyses were performed using R version 4.6.0 (R Foundation for Statistical Computing, Vienna, Austria). A two-sided P -value < 0.05 was considered statistically significant.

2.6 Ethical approval

The study protocol was reviewed and approved by the Institutional Review Board of the General Hospital of Southern Theater Command (approval number: pending). Because of the retrospective design and the use of anonymized data extracted from electronic medical records, the requirement for written informed consent was waived. All data were anonymized before analysis, and patient confidentiality was strictly maintained throughout the study.

3. Results

3.1 Baseline characteristics

A total of 372 oldest-old male patients with documented CHD, T2DM, and ACS were included in this analysis. The mean age was 85.1 ± 4.2 years (range 80–99 years). Overall in-hospital mortality was 80.9% (301/372). The distributions of NLR, PLR, and SII are summarized in Table 1. The mean values were 6.97 ± 5.86 for NLR, 165.13 ± 88.38 for PLR, and 1802.6 ± 1556.8 for SII. Missing data were minimal for all three indices (six cases, 1.6%).

Baseline characteristics of the study population stratified by NLR tertiles are presented in Table 1. Patients in the low NLR tertile had a significantly higher prevalence of heart failure (10.7% vs. 1.6% vs. 4.1%, $P = 0.006$) and higher BMI ($P = 0.001$) compared with those in the medium and high tertiles. No significant differences were observed for age, blood pressure, renal function, or HbA1c across NLR tertiles. Baseline characteristics stratified by PLR tertiles are presented in Supplementary Table S1. Baseline characteristics stratified by SII tertiles are presented in Supplementary Table S2.

3.2 Mortality rates by tertile

Table 2 presents the mortality rates across tertiles for each index. For NLR, mortality rates were 86.1% (105/122) in the low tertile, 78.7% (96/122) in the medium tertile, and 77.0% (94/122) in the high tertile. Similar patterns were observed for PLR (82.8%, 80.3%, and 78.7%, respectively) and SII (83.6%, 80.3%, and 77.9%, respectively). Although the lowest tertile paradoxically showed the highest mortality across all three indices, chi-square tests revealed no statistically significant differences across tertiles for any of the indices (NLR: $P = 0.165$; PLR: $P > 0.05$; SII: $P > 0.05$), as illustrated in Figure 1.

3.3 Logistic regression analysis

Univariate logistic regression showed that none of the three indices was significantly associated with in-hospital mortality (NLR: OR = 0.99, 95% CI 0.95–1.03, $P = 0.589$; PLR: OR = 1.00, 95% CI 1.00–1.00, $P = 0.641$; SII: OR = 1.00, 95% CI 1.00–1.00, $P = 0.994$). Heart failure showed a borderline association (OR = 5.79, 95% CI 1.19–104.50, $P = 0.088$), while age, BMI, CKD, stroke, creatinine, BUN, and HbA1c were not significantly associated with mortality (all $P > 0.05$).

In the multivariable logistic regression models, after adjusting for age, heart failure, CKD, serum creatinine, and HbA1c, NLR remained non-significant (OR = 0.98, 95% CI 0.94–1.03, $P = 0.461$). Similarly, PLR (OR = 1.00, 95% CI 1.00–1.00, $P = 0.281$) and SII (OR = 1.00, 95% CI 1.00–1.00, $P = 0.890$) showed no independent association with mortality, as shown in Table 3. None of the covariates achieved statistical significance in any of the three models.

3.4 ROC analysis

ROC analysis showed that all three indices had negligible discriminative ability for predicting in-hospital mortality. The AUC values were 0.555 for NLR, 0.526 for PLR, and 0.540 for SII, all close to 0.5, indicating no clinical utility (Figure 2).

3.5 Summary of findings

In summary, NLR, PLR, and SII were not associated with in-hospital mortality in this cohort of oldest-old male patients with CHD, T2DM, and ACS, either in univariate or multivariable analyses. The paradoxical inverse trends and the low AUC values suggest that routine inflammatory indices derived from admission blood counts have no prognostic value in this specific population.

4. Discussion

4.1 Main findings

In this retrospective cohort study of 372 oldest-old (≥ 80 years) male patients with CHD, T2DM, and ACS, we conducted a head-to-head comparison of three readily available inflammation-based indices – NLR, PLR, and SII – for predicting in-hospital all-cause mortality. The key findings are threefold. First, none of the three indices was significantly associated with mortality in univariate analysis, and this null association persisted after multivariable adjustment for age, heart failure, CKD, serum creatinine, and

HbA1c. Second, the ROC analysis confirmed the lack of discriminative ability for all three indices, with AUC values approximating 0.5 — essentially equivalent to random guessing. Third, we observed a paradoxical inverse trend across tertiles for all three indices, with the lowest tertile showing the highest mortality, further challenging the notion that these indices have prognostic utility in this population.

To the best of our knowledge, this is the first study to systematically compare NLR, PLR, and SII in the same cohort of oldest-old patients with the triple burden of CHD, T2DM, and ACS. Our findings suggest that routine inflammatory indices derived from admission blood counts have no independent prognostic value in this specific high-risk, multimorbid population.

4.2 Why did all three inflammatory indices fail to predict mortality in this population?

The consistent null findings across three different indices — each reflecting distinct but overlapping aspects of systemic inflammation and immune response — raise an important question: why do these well-established prognostic markers fail in this particular population? We propose several interconnected mechanisms that may explain these observations.

First, this cohort represents an extreme-age population with an exceptionally high short-term mortality rate (80.9%). In such a high-acuity setting — where patients are admitted with ACS and frequently complicated by acute decompensated heart failure, cardiogenic shock, or multi-organ dysfunction — the overwhelming impact of acute illness severity may completely eclipse the prognostic signal carried by baseline inflammatory indices [34]. Under these circumstances, the incremental prognostic value of admission NLR, PLR, or SII — which primarily reflect chronic inflammatory tone — is likely nullified by the acute-phase response [35].

Second, the oldest-old population is characterized by a state of immunosenescence — the age-related progressive dysregulation of the immune system, marked by chronic low-grade inflammation (often termed "inflammaging") and impaired adaptive immunity [36]. Previous studies have demonstrated that traditional risk factors lose their predictive power in the oldest-old [37-38], and our findings extend this observation to inflammation-based composite indices.

Third, all patients in this cohort were receiving contemporary standardized medical therapy, including statins, antiplatelet agents, beta-blockers, and glucose-lowering medications. Many of these agents have direct or indirect immunomodulatory effects [39-40], which may have attenuated the inflammatory signal captured by NLR, PLR, and SII at admission [41].

Fourth, the clinical heterogeneity within our cohort — including varying degrees of renal dysfunction, heart failure severity, and glycemic control — may have contributed to the null findings. Although we adjusted for these factors in our multivariable models, residual confounding from unmeasured factors (such as frailty, nutritional status, functional capacity, and acute illness severity) cannot be excluded [42-43].

4.3 Comparison with previous studies

Our findings contrast with the substantial body of literature supporting the prognostic value of NLR, PLR, and SII in various cardiovascular populations. In younger or middle-aged patients with ACS, elevated NLR has been consistently associated with adverse outcomes [13]. Similarly, PLR and SII have shown prognostic utility in patients with myocardial infarction, heart failure, and atrial fibrillation [17, 23]. However, these studies predominantly included patients with a mean age of 60–70 years, with relatively fewer comorbidities and longer follow-up durations. The generalizability of these findings to the oldest-old population has remained uncertain.

Our study aligns with the emerging evidence that the prognostic value of conventional biomarkers diminishes with advancing age. De Ruijter et al. demonstrated that traditional cardiovascular risk factors failed to predict cardiovascular mortality in 85-year-olds [37]. Dalton et al. similarly reported that these risk factors had little to no association with cardiovascular events in individuals aged ≥ 85 years [38]. Our findings extend these observations to a more acutely ill population – oldest-old patients with ACS – and demonstrate that not just SII, but also the simpler indices NLR and PLR, lack prognostic utility.

4.4 Paradoxical inverse trend across tertiles

An unexpected observation in our study was the paradoxical inverse trend across tertiles for all three indices: patients in the lowest tertile paradoxically had the highest mortality, while those in the highest tertile had the lowest mortality. Although this trend did not reach statistical significance, it warrants discussion.

One possible explanation is the phenomenon of "reverse epidemiology" or "obesity paradox," which has been described in various chronic disease populations, including heart failure, CKD, and the elderly [44–45]. In these populations, traditional risk factors – including inflammatory markers – may exhibit inverse associations with outcomes due to the competing effects of malnutrition, frailty, and catabolic states.

4.5 Clinical implications

Our findings have several important clinical implications. First, they suggest that routine calculation of NLR, PLR, or SII from admission blood tests is not useful for prognostication in oldest-old male patients with ACS. Clinicians should not rely on these indices for risk stratification in this population, and should instead focus on more relevant clinical factors such as acute illness severity, cardiac function, renal function, and functional status.

Second, our results caution against the indiscriminate extrapolation of prognostic findings from younger or healthier populations to the oldest-old. The oldest-old represent a distinct physiological phenotype, and biomarkers validated in general populations may not perform similarly in this age group.

Third, the consistent null findings across three different indices highlight the need for novel risk stratification tools specifically designed for the oldest-old population. Given the high mortality rate and the unique pathophysiology of this group, traditional biomarkers may be insufficient, and alternative

approaches — such as frailty assessment and functional capacity evaluation — may be more informative [42-43].

4.6 Strengths and limitations

This study has several strengths. First, to our knowledge, it is the first head-to-head comparison of NLR, PLR, and SII in oldest-old patients with CHD, T2DM, and ACS. Second, the relatively large sample size ($n = 372$) for a study focusing exclusively on ≥ 80 -year-old patients provides adequate statistical power for multivariable adjustment. Third, we used in-hospital all-cause mortality as the outcome, which is a robust and unbiased endpoint.

Several limitations should be acknowledged. First, this was a single-centre retrospective study, which may introduce selection bias and limit generalizability [46]. Second, we only had baseline measurements of the inflammatory indices; dynamic changes during hospitalization may carry additional prognostic information that was not captured [47]. Third, we lacked data on nutritional status (e.g., serum albumin) and functional capacity (e.g., activities of daily living), which have been shown to be important prognostic factors in older populations [48-49]. Fourth, despite adjusting for key clinically relevant covariates, residual confounding from unmeasured variables cannot be excluded. Fifth, our cohort consisted exclusively of male patients, reflecting the sex distribution of our hospital's geriatric cardiology unit; whether these findings extend to female patients requires further investigation. Sixth, our outcome was in-hospital mortality, which may differ from long-term mortality in terms of risk factor associations. Finally, the high mortality rate (80.9%) may have limited our ability to detect associations between the indices and mortality, although this high event rate actually provided substantial statistical power for our analyses.

4.7 Future directions

Future research should focus on several areas. First, prospective studies with longer follow-up are needed to confirm whether these null findings extend to post-discharge mortality and long-term outcomes. Second, studies that incorporate dynamic measurements of inflammatory indices — rather than relying solely on single admission values — may better capture the prognostic information contained in these biomarkers [47]. Third, the inclusion of comprehensive geriatric assessments, including frailty indices, cognitive function, and nutritional status, may help identify more robust prognostic factors in the oldest-old population [48-49]. Fourth, investigations in female patients and in different ethnic groups are needed to assess the generalizability of our findings.

4.8 Conclusion

In this cohort of 372 oldest-old male patients with CHD, T2DM, and ACS, none of the three inflammation-based indices — NLR, PLR, or SII — was independently associated with in-hospital all-cause mortality. The ROC analysis confirmed their lack of discriminative ability, with AUC values approximating 0.5. These findings suggest that routine calculation of these indices from admission blood counts is not

useful for risk stratification in this specific population. Clinicians should not rely on NLR, PLR, or SII for prognostication in oldest-old patients with ACS, and future research should focus on developing age-specific risk assessment tools that incorporate geriatric domains beyond traditional biomarkers.

List of abbreviations

ACS: Acute coronary syndrome

AUC: Area under the curve

BMI: Body mass index

BUN: Blood urea nitrogen

CHD: Coronary heart disease

CI: Confidence interval

CKD: Chronic kidney disease

DBP: Diastolic blood pressure

HbA1c: Glycated hemoglobin

IQR: Interquartile range

NLR: Neutrophil-to-lymphocyte ratio

OR: Odds ratio

PLR: Platelet-to-lymphocyte ratio

ROC: Receiver operating characteristic

SBP: Systolic blood pressure

SCr: Serum creatinine

SD: Standard deviation

SII: Systemic immune-inflammation index

T2DM: Type 2 diabetes mellitus

Abbreviations

ACS

Acute coronary syndrome
AUC
Area under the curve
BMI
Body mass index
BUN
Blood urea nitrogen
CHD
Coronary heart disease
CI
Confidence interval
CKD
Chronic kidney disease
DBP
Diastolic blood pressure
HbA1c
Glycated hemoglobin
IQR
Interquartile range
NLR
Neutrophil-to-lymphocyte ratio
OR
Odds ratio
PLR
Platelet-to-lymphocyte ratio
ROC
Receiver operating characteristic
SBP
Systolic blood pressure
SCr
Serum creatinine
SD
Standard deviation
SII
Systemic immune-inflammation index
T2DM
Type 2 diabetes mellitus

Declarations

Ethics approval and consent to participate

The study protocol was reviewed and approved by the Institutional Review Board of the General Hospital of Southern Theater Command (approval number: pending). Because of the retrospective design and the use of anonymized data extracted from electronic medical records, the requirement for written informed consent was waived. All data were anonymized before analysis, and patient confidentiality was strictly maintained. The study was conducted in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki Declaration and its later amendments.

Clinical trial number

Not applicable.

Consent for publication

Not applicable. This manuscript does not contain any individual person's data in any form.

Availability of data and materials

The data that support the findings of this study are derived from electronic medical records at the General Hospital of Southern Theater Command. Due to ethical and privacy restrictions, the data are not publicly available. Access to the data may be requested from the corresponding author upon reasonable justification and with approval from the hospital's Institutional Review Board.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

TL and LX conceived and designed the study.

TL, ZG, ZY, SC, JB, HC, and ML contributed to data acquisition and analysis.

TL drafted the initial manuscript. LX, ZG, and ZY critically revised the manuscript for important intellectual content.

All authors read and approved the final manuscript.

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Authors' information

Not applicable.

References

1. WHO. World report on aging and health. Geneva: World Health Organization; 2015.
2. Chen HL, Yu XH, Yin YH, et al. Multimorbidity patterns and the association with health status of the oldest-old in long-term care facilities in China: a two-step analysis. *BMC Geriatr*. 2023;23(1):851.
3. Wang X, Xu M, Li Y. Adipose tissue aging and metabolic disorder, and the impact of nutritional interventions. *Nutrients*. 2022;14(15):3134.
4. Murakami T, Inagaki N, Kondoh H. Cellular senescence in diabetes mellitus: distinct senotherapeutic strategies for adipose tissue and pancreatic β cells. *Front Endocrinol (Lausanne)*. 2022;13:869414.
5. Sales WB, Silva PVS, Vital BSB, Câmara M. Sarcopenia and intrinsic capacity in older adults: a systematic review. *Arch Gerontol Geriatr*. 2025;136:105875.
6. Zuo X, Li X, Tang K, et al. Sarcopenia and cardiovascular diseases: a systematic review and meta-analysis. *J Cachexia Sarcopenia Muscle*. 2023;14(3):1183-1198.
7. Ahmed B, Farb MG, Gokce N. Cardiometabolic implications of adipose tissue aging. *Obes Rev*. 2024;26(6):e13806.
8. Bellary S, Kyrou I, Brown JE, Bailey CJ. Type 2 diabetes mellitus in older adults: clinical considerations and management. *Nat Rev Endocrinol*. 2021;17(9):534-548.
9. Teo KK, Rafiq T. Cardiovascular risk factors and prevention: a perspective from developing countries. *Can J Cardiol*. 2021;37(5):733-743.
10. van Bommel T, Gussekloo J, Westendorp RG, Blauw GJ. In a population-based prospective study, no association between high blood pressure and mortality after age 85 years. *J Hypertens*. 2006;24(2):287-292.
11. Kaneko H, Yano Y, Okada A, et al. Age-dependent association between modifiable risk factors and incident cardiovascular disease. *J Am Heart Assoc*. 2023;12(9):e027684.
12. Zahorec R. Ratio of neutrophil to lymphocyte counts—rapid and simple parameter of systemic inflammation and stress in critically ill. *Bratisl Lek Listy*. 2001;102(1):5-14.
13. Pruc M, Kubica J, Banach M, et al. Diagnostic and prognostic performance of the neutrophil-to-lymphocyte ratio in acute coronary syndromes: a meta-analysis of 90 studies including 45,990 patients. *Kardiol Pol*. 2024;82(3):276-284.
14. Shahsanaei F, Abbaszadeh S, Behrooj S, Rahimi Petrudi N, Ramezani B. The value of neutrophil-to-lymphocyte ratio in predicting severity of coronary involvement and long-term outcome of percutaneous coronary intervention in patients with acute coronary syndrome: a systematic review and meta-analysis. *Egypt Heart J*. 2024;76(1):39.

15. Banahene NO, Sinha T, Shaikh S, et al. Effect of elevated neutrophil-to-lymphocyte ratio on adverse outcomes in patients with myocardial infarction: a systematic review and meta-analysis. *J Am Heart Assoc.* 2023;12(15):e029387.
16. Dabaghi GG, Rad MR, Mortaheb M, et al. The neutrophil-to-lymphocyte ratio predicts cardiovascular outcomes in patients with diabetes: a systematic review and meta-analysis. *Cardiol Rev.* 2025;33(3):202-211.
17. Pruc M, Peacock FW, Rafique Z, et al. The prognostic role of platelet-to-lymphocyte ratio in acute coronary syndromes: a systematic review and meta-analysis. *J Clin Med.* 2023;12(21):6903.
18. Xu R, Chen L, Yan C, Xu H, Cao G. Elevated platelet-to-lymphocyte ratio as a predictor of all-cause and cardiovascular mortality in hypertensive individuals. *J Clin Hypertens (Greenwich).* 2025;27(3):e14980.
19. Li J, Zeng Y, Sun C, et al. V-shaped relationship between platelet-to-lymphocyte ratio and mortality in patients with cardio-cerebrovascular disease: an observational study. *Medicine (Baltimore).* 2025;104(39):e44802.
20. Zhao J, Li Z, Fu S, et al. Association between platelet-to-lymphocyte ratio and 28-day all-cause mortality in patients with asymptomatic coronary artery disease: a cohort study. *Eur J Med Res.* 2025;30(1):1251.
21. Vakhshoori M, Bondariyan N, Sabouhi S, et al. The impact of platelet-to-lymphocyte ratio on clinical outcomes in heart failure: a systematic review and meta-analysis. *Ther Adv Cardiovasc Dis.* 2024;18:17539447241227287.
22. Hu B, Yang XR, Xu Y, et al. Systemic immune-inflammation index predicts prognosis of patients after curative resection for hepatocellular carcinoma. *Clin Cancer Res.* 2014;20(24):6212-6222.
23. Agyeman KB, Shafi N, Contreras R, et al. The association between systemic immune-inflammation index and cardiovascular diseases: an in-depth umbrella review of meta-analyses with GRADE assessment. *Heliyon.* 2025;11(5):e42736.
24. Zhu S, Li H, Ou Z, Zheng M, Yuan W. Systemic immune-inflammation index outperforms conventional inflammatory markers in predicting cardiovascular outcomes in heart failure with preserved ejection fraction. *J Inflamm Res.* 2026;19:1-11.
25. Long Z, Du J, Hu J, Xiao Y, Hou C. The prognostic value of the systemic immunity–inflammation index for cardiovascular and all-cause mortality in cardiovascular disease patients with diabetes or prediabetes. *J Diabetes Investig.* 2024;15(12):1783-1793.
26. Li Q, Nie J, Cao M, Luo C, Sun C. Association between inflammation markers and all-cause mortality in critical ill patients with atrial fibrillation: analysis of the MIMIC-IV database. *IJC Heart & Vasculature.* 2024;51:101372.
27. Franceschi C, Campisi J. Chronic inflammation (inflammaging) and its potential contribution to age-associated diseases. *J Gerontol A Biol Sci Med Sci.* 2014;69 Suppl 1:S4-S9.
28. Badimon L, Bugiardini R, Cubedo J. Pathophysiology of acute coronary syndromes in the elderly. *Int J Cardiol.* 2016;222:1105-1109.

29. Kayani WT, Khan MR, Deshotels MR, Jneid H. Challenges and controversies in the management of ACS in elderly patients. *Curr Cardiol Rep.* 2020;22(7):51.
30. van Bussel EF, Richard E, Busschers WB, et al. A cardiovascular risk prediction model for older people: development and validation in a primary care population. *J Clin Hypertens (Greenwich).* 2019;21(8):1145-1152.
31. Thygesen K, Alpert JS, Jaffe AS, et al. Fourth universal definition of myocardial infarction (2018). *J Am Coll Cardiol.* 2018;72(18):2231-2264.
32. American Diabetes Association Professional Practice Committee for Diabetes*. 2. Diagnosis and Classification of Diabetes: Standards of Care in Diabetes—2026. *Diabetes Care.* 2026;49(Suppl 1):S27-S49.
33. Collet JP, Thiele H, Barbato E, et al. 2020 ESC guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation. *Eur Heart J.* 2021;42(14):1289-1367.
34. Harteloh P. From mono to multi-causality: towards a comprehensive perspective on understanding death. *Health Policy.* 2024;147:105121.
35. Nelson MR, McNeil JJ, Stocks N, Panjwani S, Shah RC. Adjudication of cause of death in older adults: learnings for death certification from the ASPIrin in Reducing Events in the Elderly study. *Clin Trials.* 2025;22(6):695-700.
36. Wikby A, Ferguson F, Forsey R, et al. An immune risk phenotype, cognitive impairment, and survival in very late life: impact of allostatic load in Swedish octogenarian and nonagenarian humans. *J Gerontol A Biol Sci Med Sci.* 2005;60(5):556-565.
37. de Ruijter W, Westendorp RG, Assendelft WJ, et al. Use of Framingham risk score and new biomarkers to predict cardiovascular mortality in older people: population based observational cohort study. *BMJ.* 2009;338:a3083.
38. Dalton JE, Rothberg MB, Dawson NV, et al. Failure of traditional risk factors to adequately predict cardiovascular events in older populations. *J Am Geriatr Soc.* 2020;68(4):754-761.
39. Oesterle A, Laufs U, Liao JK. Pleiotropic effects of statins on the cardiovascular system. *Circ Res.* 2017;120(1):229-243.
40. Aldafas R, Crabtree T, Alkharaiji M, Vinogradova Y, Idris I. Sodium-glucose cotransporter-2 inhibitors (SGLT2) in frail or older people with type 2 diabetes and heart failure: a systematic review and meta-analysis. *Age Ageing.* 2024;53(1):afad254.
41. Popoviciu MS, Ghittea TC. Age-stratified differences in cardio-reno-metabolic risk profiles. *Geriatrics (Basel).* 2026;11(1):18.
42. Fried LP, Tangen CM, Walston J, et al. Frailty in older adults: evidence for a phenotype. *J Gerontol A Biol Sci Med Sci.* 2001;56A(3):M146-M156.
43. Rockwood K, Mitnitski A. Frailty in relation to the accumulation of deficits. *J Gerontol A Biol Sci Med Sci.* 2007;62(7):722-727.

44. Lavie CJ, Milani RV, Ventura HO. Obesity and cardiovascular disease: risk factor, paradox, and impact of weight loss. *J Am Coll Cardiol*. 2009;53(21):1925-1932.

45. Kalantar-Zadeh K, Block G, Horwich T, Fonarow GC. Reverse epidemiology of conventional cardiovascular risk factors in patients with chronic heart failure. *J Am Coll Cardiol*. 2004;43(8):1439-1444.

46. Hachamovitch R, Peña JM, Xie J, Shaw LJ, Min JK. Imaging registries and single-center series. *JACC Cardiovasc Imaging*. 2017;10(3):276-285.

47. Ding X, Chen S, Zhu L, Zheng C, Mou H, Cai G, Shen Y. Dynamic inflammatory trajectories and 28-day mortality in patients in the intensive care unit: An exploratory observational study. *J Intensive Med*. 2026 Feb 28;6(2):166-174.

48. Li X, Cao X, Ying Z, et al. Associations of serum albumin with disability in activities of daily living, mobility and objective physical functioning regardless of vitamin D: cross-sectional findings from the Chinese Longitudinal Healthy Longevity Survey. *Front Nutr*. 2022;9:809499.

49. Corti MC, Guralnik JM, Salive ME, Sorkin JD. Serum albumin level and physical disability as predictors of mortality in older persons. *JAMA*. 1994;272(13):1036-1042.

Tables

Table 1. Baseline characteristics of the study population stratified by NLR tertiles

Variable	Low NLR (n=122)	Medium NLR (n=122)	High NLR (n=122)	P value
Age, years	85.58 ± 3.95	85.26 ± 2.93	85.11 ± 2.70	0.506
BMI, kg/m ²	25.24 ± 4.01	26.26 ± 3.06	24.58 ± 3.53	0.001
SBP, mmHg	126.38 ± 18.82	125.15 ± 18.87	123.08 ± 19.16	0.391
DBP, mmHg	76.72 ± 14.58	77.80 ± 15.91	77.51 ± 14.04	0.841
SCr, µmol/L	87.69 ± 21.35	88.86 ± 62.83	91.86 ± 79.96	0.856
BUN, mmol/L	4.62 ± 1.71	4.29 ± 1.30	4.80 ± 2.05	0.071
HbA1c, %	6.03 ± 1.41	5.86 ± 1.11	5.89 ± 1.42	0.609
Hypertension, n (%)				0.058
Normal	70 (57.4)	87 (71.3)	87 (71.3)	
Grade 1	7 (5.7)	8 (6.6)	9 (7.4)	
Grade 2	18 (14.8)	16 (13.1)	12 (9.8)	
Grade 3	27 (22.1)	11 (9.0)	14 (11.5)	
Heart failure, n (%)				0.006
No	109 (89.3)	120 (98.4)	117 (95.9)	
Yes	13 (10.7)	2 (1.6)	5 (4.1)	
CKD, n (%)				0.125
No	114 (93.4)	120 (98.4)	118 (96.7)	
Yes	8 (6.6)	2 (1.6)	4 (3.3)	

Footnotes:

Data are presented as mean ± SD or n (%). P values were calculated using one-way ANOVA (continuous variables) or chi-square test (categorical variables). Hypertension grade was defined according to the Chinese Hypertension Prevention and Treatment Guidelines (2018 revision): Grade 1: SBP 140–159 mmHg and/or DBP 90–99 mmHg; Grade 2: SBP 160–179 mmHg and/or DBP 100–109 mmHg; Grade 3: SBP ≥180 mmHg and/or DBP ≥110 mmHg. Stroke history was not reported as all patients had no documented history of stroke.

Abbreviations: NLR, neutrophil-to-lymphocyte ratio; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; SCr, serum creatinine; BUN, blood urea nitrogen; HbA1c, glycated hemoglobin; CKD, chronic kidney disease.

Table 2. Mortality rates by tertile of NLR, PLR, and SII

Index	Low tertile	Medium tertile	High tertile	P for trend
NLR	105/122 (86.1%)	96/122 (78.7%)	94/122 (77.0%)	0.1653
PLR	101/122 (82.8%)	98/122 (80.3%)	96/122 (78.7%)	0.7175
SII	102/122 (83.6%)	98/122 (80.3%)	95/122 (77.9%)	0.5238

Footnotes:

P for trend was calculated using the Cochran-Armitage trend test. NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; SII, systemic immune-inflammation index.

Table 3. Multivariable logistic regression models comparing NLR, PLR, and SII for predicting all-cause mortality

Variable	Model 1 (NLR)	Model 2 (PLR)	Model 3 (SII)
Index (per unit)	0.98 (0.94–1.03), P=0.461	1.00 (1.00–1.00), P=0.281	1.00 (1.00–1.00), P=0.890
Age (per year)	1.05 (0.95–1.16), P=0.350	1.05 (0.95–1.17), P=0.318	1.05 (0.95–1.16), P=0.343
Heart failure (yes vs no)	5.38 (0.80–118.05), P=0.156	5.71 (0.84–125.08), P=0.142	5.35 (0.80–117.15), P=0.157
CKD (yes vs no)	0.30 (0.05–1.77), P=0.164	0.31 (0.05–1.80), P=0.169	0.31 (0.05–1.78), P=0.167
Creatinine (per μmol/L)	1.00 (0.99–1.00), P=0.205	1.00 (0.99–1.00), P=0.168	1.00 (0.99–1.00), P=0.195
HbA1c (per %)	0.91 (0.75–1.13), P=0.371	0.90 (0.74–1.11), P=0.314	0.91 (0.75–1.13), P=0.376

Footnotes:

All models adjusted for age, heart failure, chronic kidney disease, serum creatinine, and HbA1c. Data are presented as odds ratio (95% confidence interval). NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; SII, systemic immune-inflammation index; CKD, chronic kidney disease; HbA1c, glycated hemoglobin.

Figures

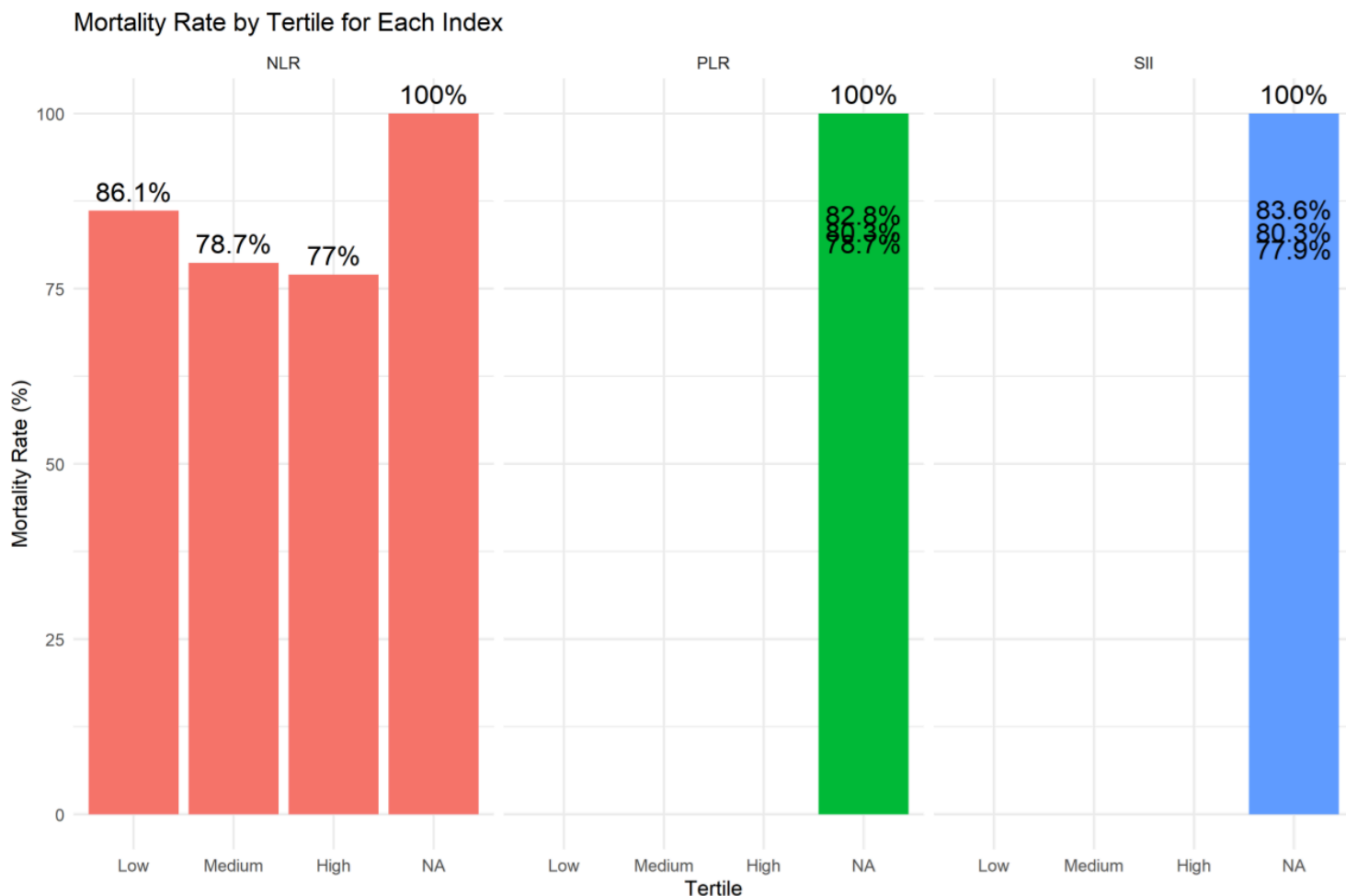


Figure 1

Mortality rates by tertile for NLR, PLR, and SII. Bars represent mortality rates with exact percentages shown above each bar.

Footnotes:

Chi-square tests showed no significant differences in mortality across tertiles for any of the three indices (all $P > 0.05$).

NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; SII, systemic immune-inflammation index.

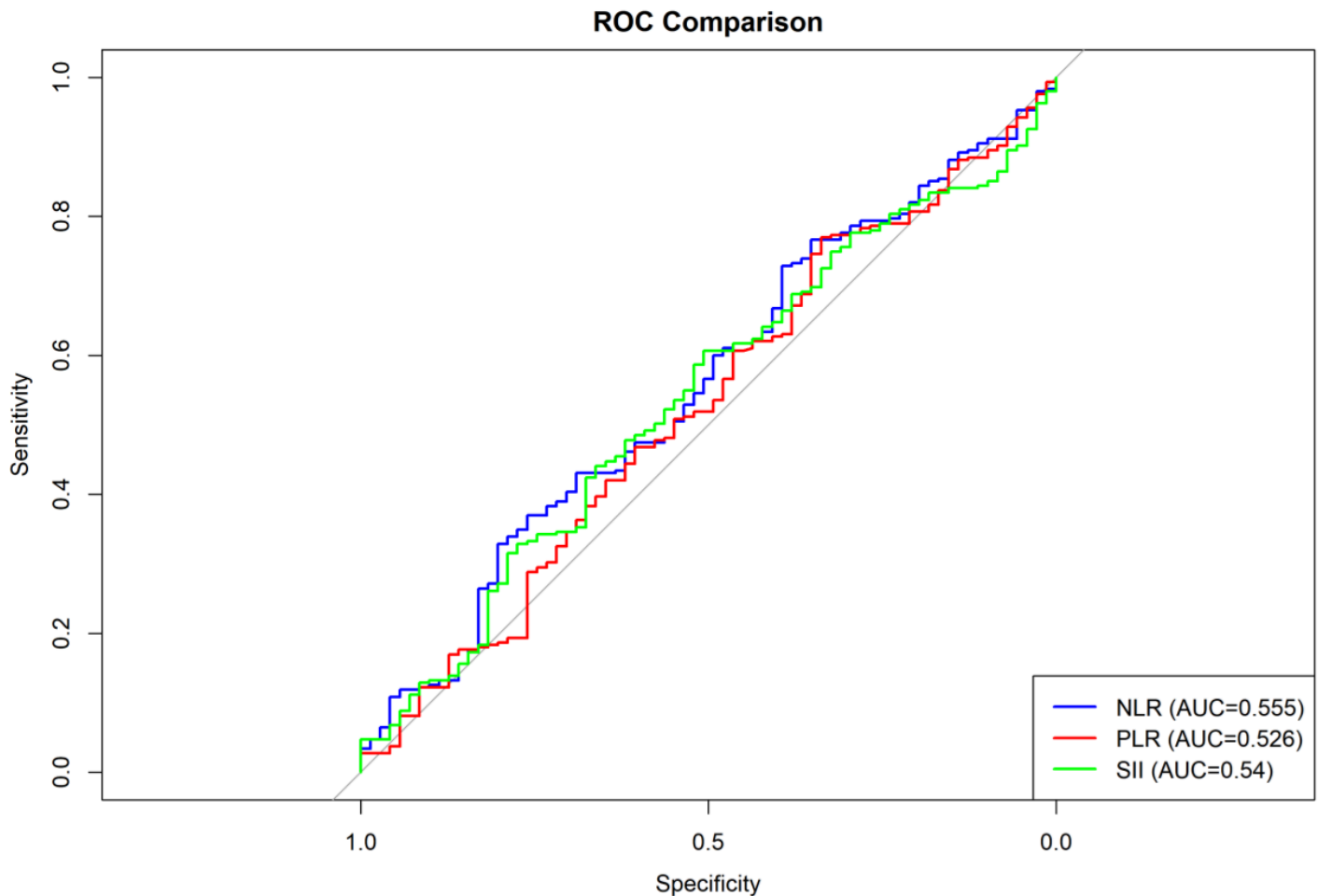


Figure 2

ROC curves of NLR, PLR, and SII for predicting all-cause mortality. Area under the curve (AUC) values were 0.555 for NLR, 0.526 for PLR, and 0.540 for SII.

Footnotes:

Pairwise comparisons using DeLong's test showed no significant differences between AUCs (all $P > 0.05$).

NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; SII, systemic immune-inflammation index.

Supplementary Files

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- [SupplementaryTableS1.docx](#)
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