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Original Article

Neutrophil- and platelet-to-lymphocyte ratios in sepsis: mortality links in diabetic patients and hospital burden in acute kidney injury

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Abstract

Introduction: Timely identification of sepsis patients at elevated risk for in-hospital mortality or prolonged hospitalization remains a clinical imperative. This study aimed to assess the prognostic utility of two readily available hematological biomarkers, namely the neutrophil-to-lymphocyte count ratio (NLCR) and platelet-to-lymphocyte count ratio (PLCR), for their association with mortality and length of stay (LOS) among sepsis patients, including high-risk subgroups with acute kidney injury (AKI) or type 2 diabetes mellitus (T2DM).

Methodology: This retrospective 1-year cohort study included 202 adult sepsis patients. NLCR and PLCR were derived from admission complete blood counts. Receiver operating characteristic (ROC) curve analysis was used to evaluate discriminative performance, with optimal thresholds determined using Youden's index. Kaplan–Meier and log-rank tests assessed survival differences, while LOS comparisons were analyzed using Mann–Whitney and Chi-square tests.

Results: NLCR demonstrated limited overall prognostic value for mortality (AUC 0.560; sensitivity 53.68%; specificity 63.55%) but showed improved discrimination in patients with T2DM (AUC 0.603). PLCR was not associated with mortality in any subgroup (AUCs: 0.438–0.539). Diabetic patients with low NLCR had significantly higher survival (62.4% vs. 32.8%; $p = 0.039$). No significant survival differences were observed in the overall or AKI cohorts. Both NLCR and PLCR had poor association with LOS (AUC < 0.55). However, AKI patients with elevated NLCR had significantly prolonged hospitalization (11.5 ± 4.9 vs. 7.83 ± 4.5 days; $p = 0.039$). PLCR was not significantly associated with LOS.

Conclusions: NLCR may provide modest, preliminary prognostic value in specific sepsis subgroups, particularly those with T2DM or AKI, and may serve as a low-cost adjunct for early risk stratification.

Key words: sepsis; acute kidney injury; diabetes mellitus; neutrophil-to-lymphocyte ratio; platelet count.

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Introduction

Sepsis remains a major global health burden and is characterized by life-threatening organ dysfunction resulting from a dysregulated host response to infection [1]. In 2020, sepsis was estimated to account for 48.9 million cases and 11 million deaths worldwide, representing nearly 20% of all global mortality [2]. Timely risk stratification is critical for improving clinical outcomes, particularly in patients with underlying comorbidities or complications such as acute kidney injury (AKI). AKI affects up to 75% of critically ill patients with sepsis and is independently associated with increased mortality and prolonged hospitalization [3,4].

In low-resource and emergency care settings, there is a pressing need for accessible and cost-effective biomarkers to support early clinical decision-making. The neutrophil-to-lymphocyte count ratio (NLCR) and platelet-to-lymphocyte count ratio (PLCR), both derived from routine complete blood counts, have emerged as potential indicators of systemic inflammation. NLCR reflects the combined effects of neutrophilia and lymphopenia, hallmark features of acute infection and immune dysregulation, and has been associated with adverse outcomes in sepsis [5,6]. In contrast, PLCR may reflect platelet-mediated inflammatory activity and endothelial dysfunction, which contribute to tissue hypoperfusion and organ

failure [7].

Patients with type 2 diabetes mellitus (T2DM) constitute a particularly vulnerable subgroup, as they exhibit impaired innate immune responses and a chronic pro-inflammatory state that is often accompanied by elevated NLCR and PLCR values [8]. Despite their potential clinical relevance, the prognostic implications of these hematologic indices in sepsis, particularly among those with concomitant AKI or T2DM, remain insufficiently characterized. In this retrospective cohort study, the association of NLCR and PLCR with in-hospital mortality and length of hospitalization among patients admitted with sepsis was evaluated. Stratified analyses were performed in patients with diabetes and AKI to delineate subgroup-specific patterns. These findings aim to inform the utility of widely available inflammatory markers for risk assessment and early triage strategies in sepsis care.

Methodology

Study design

This single-center retrospective cohort study was conducted at the Department of Internal Medicine, Karsa Husada General Hospital, Batu City, East Java, Indonesia, and included patient admissions between September 2023 and October 2024. The primary objective was to evaluate the association between two readily accessible hematologic indices (NLCR and PLCR) and clinical outcomes in patients with sepsis, specifically in-hospital mortality and length of hospitalization. Subgroup analyses focused on patients with AKI and T2DM, given their distinct immunopathological profiles. Ethical approval was obtained from the Health Research Ethics Committee, Faculty of Medicine and Health Sciences, Maulana Malik Ibrahim State Islamic University, Malang, East Java, Indonesia, in accordance with applicable ethical guidelines (No. 100/03/EC/KEPK-FKIK/06/2025). Owing to the retrospective and observational nature of the study, the requirement for informed consent was waived.

Study population

Eligible participants were adult patients (aged ≥ 18 years) admitted with a clinical diagnosis of sepsis and with available complete blood count data sufficient for calculation of NLCR and PLCR. AKI was defined according to the Kidney Disease: Improving Global Outcomes (KDIGO) criteria, including any of the following conditions: (a) an increase in serum creatinine of ≥ 0.3 mg/dL within 48 hours; (b) an increase in serum creatinine to ≥ 1.5 times baseline value, presumed to have occurred within the preceding 7 days; or (c) urine output < 0.5 mL/kg/hour for at least six hours. Patients were excluded if they met any of the following criteria: age under 18 years; diagnosis of chronic kidney disease (CKD) irrespective of hemodialysis status; known autoimmune disease; active hematologic disorder; or malignancy. In addition, patients receiving systemic corticosteroids, chemotherapy, or other immunosuppressive therapies at the time of admission were excluded due to the potential influence of these treatments on leukocyte and platelet counts.

Data collection and variables

Clinical and laboratory data were extracted from institutional medical records using a standardized data abstraction form. Collected variables included demographic data (age and sex), laboratory parameters (absolute neutrophil count, lymphocyte count, platelet count, serum creatinine, and random blood glucose), and calculated indices (NLCR and PLCR). In addition, qSOFA scores, presence of AKI, duration of hospitalization, and in-hospital mortality status were collected.

Outcomes and statistical analysis

The primary outcomes were all-cause in-hospital mortality and total length of hospitalization. Secondary outcomes included subgroup analyses of these endpoints among patients with comorbid T2DM and/or AKI. Receiver Operating Characteristic (ROC) curve analysis was performed to evaluate the discriminative performance of NLCR and PLCR for mortality, AKI, and T2DM. Optimal cut-off values for each biomarker were determined using Youden's Index, which maximizes the combined sensitivity and specificity. Survival analysis was conducted using Kaplan–Meier estimators, and between-group comparisons were assessed using the log-rank test.

Length of stay (LOS) was analyzed both as a continuous variable, using the Mann–Whitney U test for non-normally distributed data, and as a dichotomized variable (short vs. long stay) based on the median value, evaluated using the Chi-square test. Univariate analyses were performed to assess the association between individual variables and study outcomes. Results are reported as odds ratios (ORs) with corresponding 95% confidence intervals (CIs). Statistical significance was defined as a two-sided $p < 0.05$. All statistical analyses were performed using Jamovi software (version 2.3.28).

Results

Patients' selection

A total of 362 patients diagnosed with sepsis were initially screened for eligibility. Patients were excluded because of CKD requiring hemodialysis (n = 85), hematologic disorders (n = 35), autoimmune diseases under active therapy (n = 22), and age younger than 18 years (n = 18). Ultimately, 202 patients met the inclusion criteria and were included in the final analysis. The patient selection process is illustrated in the flow diagram shown in Figure 1.

Clinical and demographic characteristics

The demographic and clinical characteristics of the study population are summarized in Table 1. The median age of the cohort was 59 years (range, 19–89). Non-survivors were significantly older than survivors, with a median age of 64 years (range, 26–89) compared with 59 years (range, 19–82) among survivors (p = 0.002). The sex distribution was nearly equal (50.5% male, 49.5% female), and no significant difference in mortality was observed between sexes (23.8% in females vs. 23.3% in males; p = 0.784). Vital signs at admission demonstrated that patients who died had a significantly lower median systolic blood pressure (114 mmHg vs. 124 mmHg; p = 0.022), and lower Glasgow Coma Scale (GCS) scores (similar median 15 vs. 15 with a wider distribution and lower mean values of 12 vs. 13.7; p < 0.001). Respiratory rates were higher among non-survivors (median 25 vs. 24 breaths/min), although this difference did not reach statistical significance (p = 0.100). Higher qSOFA scores were significantly associated with mortality, with 63.3% of

Figure 1. Flow diagram illustrating patient selection and inclusion.

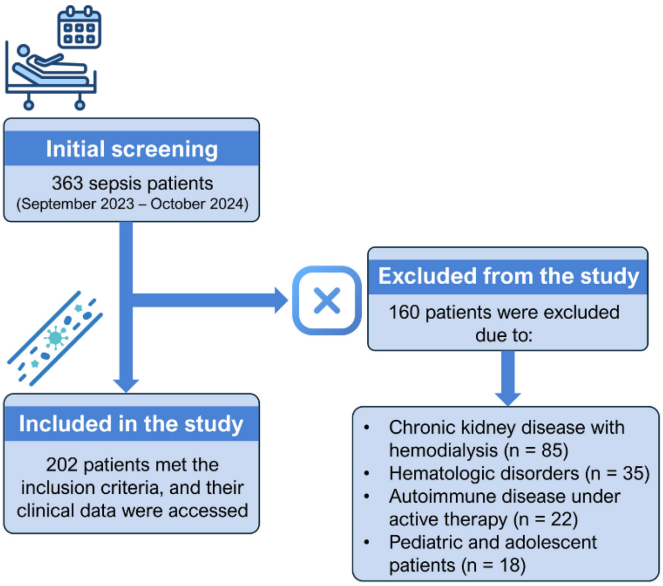


Table 1. Demographic and clinical characteristics of sepsis patients by hospital mortality.

Variable	Median (min-max)			*p*
	Total (n = 202)	Dead (n = 95)	Survived (n = 107)	
Age (years)	59 (19 - 89)	64 (26 - 89)	59 (19 – 82)	0.002*
Gender, n (%)				
Male	102 (50.5)	47 (23.3)	55 (27.2)	0.784
Female	100 (49.5)	48 (23.8)	52 (25.7)	
Vital signs				
Respiratory rate	24 (19 - 56)	25 (13 - 99)	24 (14 – 35)	0.100
Systolic blood pressure (mmHg)	124 (25 - 203)	114 (64 – 203)	124 (25 – 192)	0.022*
Glasgow comma scale	15 (2 - 15)	15 (2 – 15)	15 (3 – 15)	< 0.001*
qSOFA, n (%)				
0–1	123 (60.9)	45 (36.6)	78 (63.4)	< 0.001*
2–3	79 (39.1)	50 (63.3)	29 (36.7)	
Kidney function				
Creatinine (mg/dL)	1.24 (0.24 - 13.2)	1.3 (0.24 – 10.7)	1.24 (0.35 – 13.2)	0.102
EGFR (mL/min /1.73 m^2)	58.4 (3.87 - 396)	57.6 (4.85 – 396)	58.4 (3.87 -241)	0.089
Blood parameter				
WBC (103/µL)	18 (2.3 - 69.1)	16.6 (2.94 – 52.1)	18 (2.33 – 69.1)	0.137
Neutrophil (103/µL)	15.5 (1.0 - 93.8)	14.2 (1.00 – 93.8)	15.5 (1.25 – 57.9)	0.193
Lymphocyte (103/µL)	1.23 (0.21 - 10.2)	1.25 (0.17 – 7.5)	1.23 (0.21 – 10.2)	0.049*
Platelet (103/µL)	292 (6 - 897)	258 (6 – 897)	292 (13 – 1491)	0.162
NLCR	10.91 (0.35-7671)	13.11 (0.35-65.29)	10.28 (0.53-76.18)	0.139
PLCR	233.33 (5.94-1777.78)	267.41 (5.94-1777.78)	210.36 (12.04-1365.15)	0.453
Monocyte	0.91 (0.03 - 85)	0.67 (0.04 – 4.4)	0.91 (0.03 – 85.0)	0.094
LOS, n (%)				
Short	111 (55)	61 (55)	50 (45)	0.013*
Long	91 (45)	34 (37.4)	57 (62.6)	
Type 2 diabetes mellitus, n (%)	77 (38.1)	36 (46.7)	41 (53.2)	0.951
Acute kidney injury, n (%)	76 (37.6)	41 (54)	35 (46)	0.126

*Significant at p < 0.05. SBP: systolic blood pressure; GCS: Glasgow Coma Scale; qSOFA: quick Sequential Organ Failure Assessment; eGFR: estimated glomerular filtration rate; WBC: white blood cell count; NLCR: neutrophil-to-lymphocyte count ratio; PLCR: platelet-to-lymphocyte count ratio; LOS: length of hospital stays.

patients with scores of 2–3 dying compared with 36.6% of those with scores of 0–1 ($p < 0.001$). Renal function parameters, including serum creatinine and estimated glomerular filtration rate (eGFR), did not differ significantly between survivors and non-survivors. Median serum creatinine levels were 1.30 mg/dL (range, 0.24–10.7) in non survivors and 1.24 mg/dL (range, 0.35–13.2) in survivors ($p = 0.102$), while median eGFR values were 57.6 and 58.4 mL/min/1.73 m², respectively ($p = 0.089$)

Hematologic profiles, mortality, and length of hospital stay

No statistically significant differences were observed in total leukocyte, neutrophil, or platelet counts between survivors and non-survivors. Lymphocyte counts were slightly lower among non-survivors (median 1.23 × 10³/μL) compared with survivors (median 1.25 × 10³/μL), and this difference reached marginal statistical significance ($p = 0.049$), potentially reflecting sepsis-associated immunoparalysis. Monocyte counts trended to be lower in non-survivors, although this difference did not reach statistical significance ($p = 0.094$). Although NLCR and PLCR were analyzed in the overall cohort, detailed stratified values are not presented here. LOS was dichotomized based on the cohort median. In the short LOS group, mortality was disproportionately higher (55% vs. 45%), whereas in the long LOS group, survivors predominated (62.6% vs. 37.4% mortality; $p = 0.013$). In subgroup analyses, among patients with T2DM (n = 77), mortality occurred in 46.7% (n = 36), while 53.2% (n = 41) survived; this difference was not statistically significant ($p = 0.951$). Similarly, among patients with AKI (n = 76), 41 patients (54%) died and 35 (46%) survived, with no statistically significant difference observed ($p = 0.126$).

Figure 2. Receiver operating characteristic (ROC) curves showing the discriminatory performance and optimal cut-off values of neutrophil-to-lymphocyte count ratio (NLCR) and platelet-to-lymphocyte count ratio (PLCR) for in-hospital mortality among (**a**) the overall sepsis cohort, (**b**) patients with acute kidney injury (AKI), and (**c**) patients with type 2 diabetes mellitus (T2DM), as well as for prolonged length of hospitalization among (**d**) all sepsis patients, (**e**) those with AKI, and (**f**) those with T2DM.

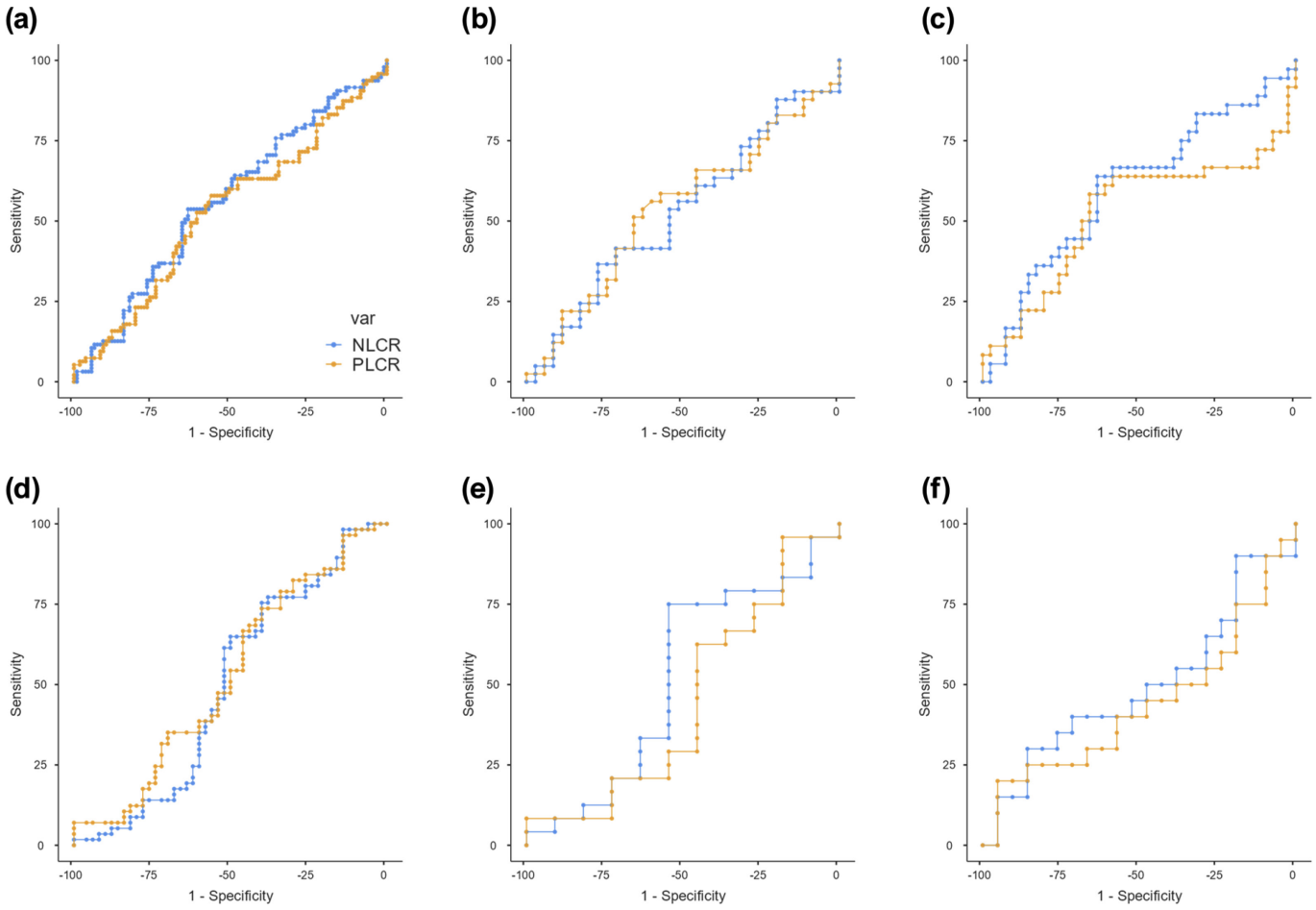


Table 2. Discriminative performance of NLCR and PLCR in association with mortality and length of hospitalization among patients with sepsis and relevant clinical subgroups.

Variable	Cut-off (ng/mL)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Youden's index	AUC (95% CI)
Mortality							
PLCR							
Overall	233.33	57.89	56.07	53.92	60	0.140	0.531 (0.444–0.618)
AKI	247.62	51.22	65.71	63.64	53.49	0.169	0.539 (0.390–0.688)
T2DM	58.33	63.41	65.85	60	64.29	0.242	0.524 (0.383–0.665)
NLCR							
Overall	12.70	53.68	63.55	56.67	60.71	0.172	0.560 (0.474–0.646)
AKI	20.85	36.59	77.14	65.22	50.94	0.137	0.527 (0.377–0.677)
T2DM	13.50	63.89	63.41	60.53	66.67	0.273	0.603 (0.465–0.741)
LOS							
PLCR							
Overall	161.01	73.68	40	58.33	57.14	0.137	0.526 (0.438–0.614)
AKI	48.41	95.83	18.18	71.88	66.67	0.140	0.447 (0.299–0.595)
T2DM	603.79	20	95.24	80	55.56	0.152	0.438 (0.297–0.579)
NLCR							
Overall	7.66	77.19	38	58.67	59.38	0.152	0.496 (0.408–0.584)
AKI	9.86	75	54.55	78.26	50	0.295	0.515 (0.367–0.663)
T2DM	20.4	25	85.71	66.67	56.25	0.157	0.493 (0.350–0.636)

AKI: acute kidney injury; AUC: area under the curve; T2DM: type 2 diabetes mellitus; LOS: length of stay; NLCR: neutrophil-to-lymphocyte count ratio; NPV: negative predictive value; PLCR: platelet-to-lymphocyte count ratio; PPV: positive predictive value.

Prognostic performance based on mortality

Receiver operating characteristic (ROC) analyses evaluating the association of NLCR and PLCR with in-hospital mortality among patients with sepsis are presented in Figure 2, with corresponding performance metrics summarized in Table 2. In the overall sepsis cohort, NLCR demonstrated limited discriminative ability, with an area under the curve (AUC) of 0.560, a sensitivity of 53.68%, and a specificity of 63.55%. PLCR showed a lower performance, with an AUC of 0.531 and corresponding sensitivity and specificity of 57.89% and 56.07%, respectively. Within the AKI subgroup, NLCR exhibited poor discriminative ability (AUC: 0.527), with a sensitivity of 36.59% and a specificity of 77.14%. PLCR showed a comparable and similarly limited performance in this subgroup (AUC: 0.539).

In contrast, among patients with T2DM, NLCR showed a relatively stronger association with mortality. In this subgroup, NLCR achieved an AUC of 0.603, with a sensitivity of 63.89% and specificity of 63.41%, representing the highest discriminative performance observed across all analyses. PLCR remained weakly associated with mortality in the T2DM subgroup (AUC: 0.524).

Kaplan–Meier survival analysis further supported the association between elevated NLCR and poorer prognosis (Figure 3). Patients with lower NLCR values had a higher survival probability of 62.4% (95%CI: 47.0–82.8) compared with 32.8% (95% CI: 18.6–58.0) among those with higher NLCR values (log-rank p = 0.039) (Table 3). No statistically significant survival differences were observed between high and low NLCR or PLCR strata in the overall sepsis cohort or within the AKI subgroup.

Prognostic performance based on length of stay

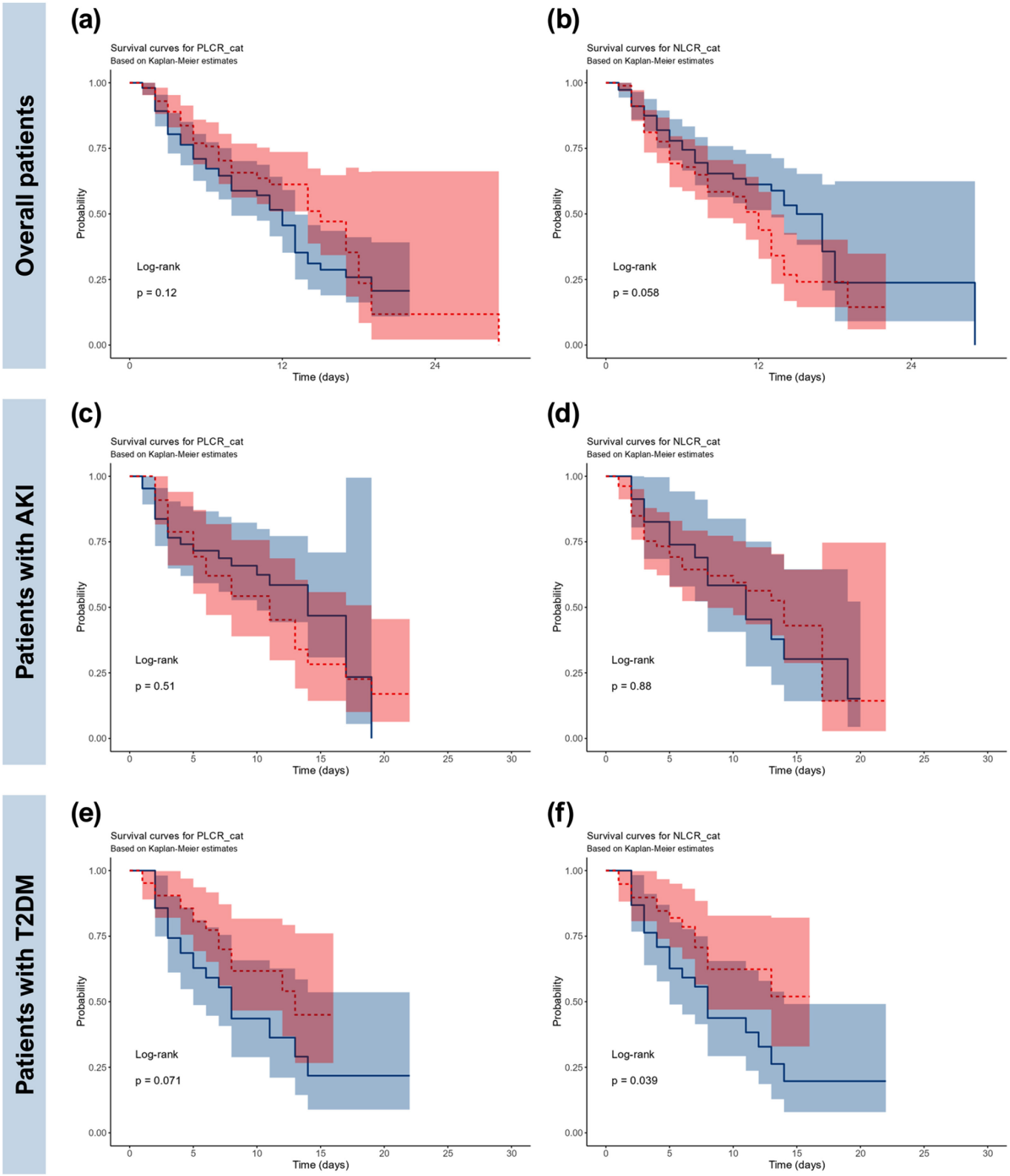
The discriminative performance of the NLCR and PLCR for stratifying sepsis patients according to length of hospitalization was limited across all analyses, as reflected by AUC values consistently below 0.55 (Table 2). In the overall cohort, PLCR demonstrated a sensitivity of 73.68% and specificity of 40.0% at an optimal cut-off value of 161.01, corresponding to an

Table 3. Results of Kaplan–Meier survival analysis evaluating the association between PLCR and NLCR values and mortality outcomes in the overall sepsis population, and in clinical subgroups with AKI and T2DM.

Group	PLCR		NLCR	
	Survival (95% CI) (%)	Log-rank p	Survival (95% CI)	Log-rank p
Overall				
High	45.6 (35.2 to 59. 1)	0.12	43.8 (32.9 to 58.4)	0.058
Low	61.3 (51.0 to 73.6)		61.2 (51.4 to 72.9)	
Acute kidney injury				
High	45.2 (29.8 to 68.7)	0.51	45.4 (27.5 to 75.1)	0.88
Low	58.5 (44.3 to 77.2)		56.3 (43.5 to 72.9)	
T2DM				
High	36.3 (21.0 to 62.7)	0.071	32.8 (18.6 to 58.0)	0.039*
Low	54.0 (36.8 to 79.3)		62.4 (47.0 to 82.8)	

*Significant at $p < 0.05$. NLCR: neutrophil-to-lymphocyte count ratio; PLCR: platelet-to-lymphocyte count ratio; T2DM: type 2 diabetes mellitus.

Figure 3. Kaplan–Meier survival curves illustrating the association of platelet-to-lymphocyte count ratio (PLCR) (left panels) and neutrophil-to-lymphocyte count ratio (NLCR) (right panels) with in-hospital mortality in the overall sepsis cohort (**a, b**), patients with acute kidney injury (AKI) (**c, d**), and those with type 2 diabetes mellitus (T2DM) (**e, f**).



AUC of 0.526. Within the AKI subgroup, PLCR exhibited high sensitivity (95.83%) but low specificity (18.18%), resulting in poor discriminative capacity (AUC: 0.447). Among patients with T2DM, PLCR showed high specificity (95.24%) but markedly low sensitivity (20.0%) at a cut-off of 603.79, with an associated AUC of 0.438. Similarly, NLCR demonstrated limited utility in discriminating the length of hospitalization across all subgroups. In the overall population, the NLCR yielded an AUC of 0.496, with sensitivity and specificity values of 77.19% and 38.0%, respectively, at a cut-off of 7.66. Within the AKI subgroup, performance was marginally improved (AUC: 0.515), whereas in the T2DM subgroup, discriminative ability remained low (AUC: 0.493) (Table 2).

Further analyses examined the association between inflammatory indices and length of hospitalization based on optimal cut-off values (Table 4). Among patients with AKI, elevated NLCR levels were associated with significantly prolonged hospitalization, with a mean length of hospitalization of 11.5 ± 4.9 days compared with 7.83 ± 4.5 days among those with lower NLCR value (p = 0.039). No significant association between NLCR and length of hospitalization were observed in the overall cohort (p = 0.063) or in the T2DM subgroup (p = 0.463). Likewise, PLCR was not significantly associated with length of hospitalization in the overall population (p = 0.155), the AKI subgroup (p = 0.075), or the T2DM subgroup (p = 0.817).

Discussion

Findings from the present study suggest that NLCR may provide modest and preliminary prognostic value as a clinical marker of mortality in patients with sepsis, with the most notable association observed in the subgroup with T2DM. Diabetic patients with lower NLCR values demonstrated significantly improved survival compared with those with elevated NLCR. In addition, NLCR was significantly associated with prolonged hospitalization among patients with AKI. In contrast, the PLCR did not show statistically significant associations with either mortality or length of hospitalization across any of the evaluated subgroups.

Recent advances in hematology have highlighted the role of platelets as active immune effectors in sepsis. Platelets interact directly with leukocytes and endothelial cells through receptors such as P-selectin and glycoprotein VI (GPVI), promoting the formation of platelet leukocyte aggregates, neutrophil extracellular traps (NETs), and microvascular immunothrombosis, all of which contribute to organ dysfunction [9]. Additional studies have demonstrated that platelet-mediated neutrophil activation and endothelial injury amplify sepsis severity, underscoring the importance of platelet–immune interactions beyond simple platelet count thresholds [10]. Moreover, emerging evidence suggests that qualitative platelet abnormalities—reflected by parameters such as platelet activation state, immature platelet fraction, and platelet leukocyte complexes—may offer greater prognostic value in sepsis than quantitative indices alone [11].

The findings from the present study are broadly consistent with previously published literature. A meta-analysis reported that elevated NLR was associated with increased sepsis-related mortality, with a pooled hazard ratio of 1.69 (95%CI: 1.43–1.99) [12]. Similarly, a retrospective analysis involving 3,043 patients with sepsis identified an NLCR threshold > 20.25 as predictive of 28-day mortality (AUC: 0.553), although with modest discriminatory performance [13]. Westerdijk *et al.*[14] also reported diagnostic utility for NLCR in intensive care unit patients with suspected sepsis (AUC: 0.61), particularly when measured at the time of initial presentation.

Biologically, NLCR reflects the balance between neutrophil-driven innate immune activation and lymphocyte-mediated adaptive immune suppression. During sepsis, systemic inflammation and catecholamine surges promote neutrophil

Table 4. Association of PLCR and NLCR with length of hospitalization among sepsis patients, stratified by optimal cut-off values derived from ROC analysis.

Group[a]	PLCR		NLCR	
	Length of stay (days)	*p*	Length of stay (days)	*p*
Overall				
High	8.5 (5.0, 14.0)	0.155	9.0 (5.0, 13.5)	0.063
Low	7.0 (5.0, 10.0)		7.0 (5.0, 10.0)	
Acute kidney injury[b]				
High	10.7 ± 4.9	0.075	11.5 ± 4.9	0.039*
Low	5.3 ± 3.5		7.83 ± 4.5	
Type 2 diabetes mellitus				
High	5.0 (5.0, 7.0)	0.817	6.0 (5.0, 9.75)	0.463
Low	8.0 (5.0, 10.3)		8.0 (5.0, 10.0)	

[a]Presented as median (1st, 3rd quartiles); otherwise, [b]mean ± standard deviation. *Statistically significant at $p < 0.05$.

demargination and lymphocyte apoptosis [5], resulting in elevated NLCR values that indicate immune dysregulation. In patients with diabetes mellitus, chronic inflammation, oxidative stress, and vascular injury may further impair immune competence, increasing susceptibility to organ failure [8]. Consequently, lower NLCR values in this cohort may reflect more preserved immune homeostasis, potentially accounting for the observed survival advantage. In patients with AKI, systemic inflammation contributes to renal vasodilation, endothelial dysfunction, and ischemic tubular injury, and elevated NLCR values may indicate a greater inflammatory burden, consistent with the observed prolongation of hospitalization [15].

Additional mechanisms may further explain these associations. NLCR increases as a result of neutrophil demargination and lymphocyte apoptosis, which are hallmark features of dysregulated innate and adaptive immune response in sepsis [16]. In patients with diabetes mellitus, chronic low-grade inflammation, oxidative stress, and impaired lymphocyte-mediated immunity contribute to elevated baseline NLCR levels, which may be further exacerbated during sepsis. This amplified pro-inflammatory state, coupled with reduced pathogen clearance, may increase mortality risk [17]. In contrast, PLCR may be elevated in the context of AKI, where cytokine accumulation, endothelial dysfunction, and uremia-induced platelet activation promote both thrombocytosis and lymphocyte suppression [7]. This dysregulated hemostatic-inflammatory axis may contribute to microvascular injury, delayed tissue repair, and prolonged hospitalization. Collectively, these findings suggest that elevated NLCR and PLCR may represent distinct, comorbidity-specific surrogates of systemic immune stress, associated with increased mortality risk in patients with diabetes and increased healthcare burden in those with AKI.

Although the discriminative performance of the NLCR remained modest in the present study (AUCs < 0.65), its accessibility, low cost, and ease of calculation from routine complete blood counts support its potential utility as a practical adjunct for early risk stratification, particularly in resource-limited settings. In clinical practice, NLCR may serve as a preliminary triage indicator to identify patients who require closer monitoring or more intensive intervention. Supporting this concept, previous studies have shown that persistently elevated NLCR values beyond the third day of hospitalization are associated with significantly increased mortality [18-20]. Furthermore, combinatorial approaches have demonstrated improved prognostic performance, as the integration of NLCR with biomarkers such as procalcitonin (PCT) has enhanced mortality prediction [20,21], while incorporation into established clinical scoring systems, including qSOFA and SOFA, has improved risk stratification [19]. More recently, machine learning models incorporating NLCR alongside clinical and laboratory parameters (e.g., PCT, lactate, interleukin-6, and vital signs) have achieved robust discriminative performance, with reported AUCs exceeding 0.85 [19,22,23]. Although PLCR showed limited prognostic utility when evaluated in isolation, its potential additive value within multivariable or composite predictive models warrants further investigation.

Several limitations should be considered when interpreting the findings of the present study. First, the retrospective, single-center design may limit external validity and generalizability. Second, residual confounding cannot be excluded, as variables such as comorbid conditions, infection source, severity of organ dysfunction, and differences in therapeutic management (including timing and selection of antimicrobial therapy), were not fully adjusted for in the analyses. Third, NLCR and PLCR were measured only at hospital admission, precluding evaluation of longitudinal trends or dynamic changes, which may provide additional prognostic information. Fourth, the overall discriminative performance of both biomarkers was modest, indicating limited predictive utility when used as standalone measures. Finally, the absence of multivariable regression analysis prevented adjustment for potential confounders that may influence associations with mortality and length of hospitalization.

Conclusions

The NLCR appears to be a potentially informative biomarker with prognostic relevance in specific clinical subgroups of patients with sepsis. Notably, lower NLCR values were associated with improved survival among patients with T2DM and with shorter hospitalization among those with AKI. In contrast, the PLCR did not demonstrate meaningful associations with either mortality or length of hospitalization in the present cohort. The integration of NLCR and PLCR into multivariable prediction models or composite risk-scoring frameworks remains an area of interest and merits further investigation. Future research should prioritize prospective, multicenter studies to validate these findings. In addition, studies should assess generalizability across diverse healthcare settings and

evaluate the prognostic value of dynamic NLCR and PLCR trajectories during sepsis.

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Data sharing statement
All relevant data and materials supporting the findings of this study are available upon request from the corresponding author.

Authors' contributions
Conceptualization: NFA; Data curation: NFA, IRA, RRM; Formal Analysis: IRA, MI; Funding Acquisition: MH; Investigation: NFA, IRA; Methodology: MI, MH; Project Administration: NFA, MH; Resources: NFA, MI, RRM, RMSSSN, AZA, IRA; Software: MI, MH; Supervision: IRA, MI, MH; Validation: MI, MH;Visualization: MI, MH; Writing – draft preparation: NFA, MI, RRM, RMSSSN, AZA; Writing – review & editing: NFA, MI, RRM, RMSSSN, AZA, MH.

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Conflict of interest
No conflict of interest is declared.

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