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Research Brief

Comparison of neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and systemic immune-inflammation index (SII) as marker of adverse prognosis in patients with infective endocarditis

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ABSTRACT

Infective Endocarditis (IE) remains a life-threatening condition and early risk stratification helps us to predict mortality and the need for aggressive treatment. We compared NLR, PLR, and SII, on admission to predict in-hospital mortality. Consecutive IE patients, who met inclusion criteria were analysed. Receiver operating characteristic curve (ROC) analysis was conducted for NLR, PLR, and SII to predict in-hospital mortality. The median value of NLR was 19.6 (10.1–27) in patients with mortality, and 5.4 (3.2–8.5) in alive patients. The median value of PLR and SII were comparable in both groups. The area under the ROC curve of NLR showed a significant value of 0.83 ($p = 0.001$). A Kaplan Meier survival analysis for patients taking a cut-off value of NLR (9.8) was statistically significant ($p < 0.001$). In multivariate regression model, only NLR was statistically significant predictor of mortality. So NLR, which is a simple, readily available, and inexpensive parameter has a better association with in-hospital mortality in IE patients.

1. Introduction

Early risk prediction is important in improving outcomes in Infective endocarditis (IE). Various association studies have focused on identifying widely available and inexpensive inflammatory markers to predict prognosis in IE.[1] The platelet-to-lymphocyte ratio (PLR) and neutrophil-to-lymphocyte ratio (NLR) are used as a biomarker to predict the degree of inflammation.[2,3] NLR and PLR are found to be independent predictors of worse prognosis in IE.[4] Systemic immune-inflammation index (SII), which integrates three types of inflammatory cells (platelet, neutrophil, and lymphocytes), is a promising predictor of adverse events in many immune-related, inflammatory, and infectious diseases.[5] Recently two studies have found that high SII levels are independently associated with mortality and embolic events in IE.[6,7] NLR has been shown to have a high predictive value for many cardiovascular diseases. However, data are scarce on its predictive value in IE patients. This study aimed to see if the NLR, PLR, and SII, assessed on admission, had any relationship with IE patients and compare how well these indexes could predict mortality.

2. Materials and methods

The IE cases admitted at our centre, who met inclusion criteria were recruited for the study. Patients for whom complete laboratory data available were only enrolled. Patients who did not meet Duke's criteria, age <18 years, patients with inflammatory, autoimmune diseases and cancers were excluded. Haematological tests done on first day of the patient's stay in the hospital were taken. The neutrophil-lymphocyte ratio (NLR) was computed by dividing the absolute neutrophil count by the absolute lymphocyte count. The platelet-to-lymphocyte ratio

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(PLR) was computed by dividing platelet count by absolute lymphocyte count. The Systemic immune-inflammation index (SII) was calculated as: SII = platelet count × neutrophil count/lymphocyte count. The adverse clinical events in the study endpoints included hospital death, heart failure, embolic events, recurrence and renal failure.

The effects of variables on in-hospital mortality were calculated by bivariate analysis. The variables for which the *p*-value <0.1 in the bivariate analysis were included in the binary logistic regression model. Chi-square or Fischer exact tests were used to compare categorical variables. Mann–Whitney *U* test was used to compare quantitative variables with an abnormal distribution, whereas the Student *t*-test was used to compare the means of two groups with a normal distribution. Receiver operating characteristic curve (ROC) analysis was conducted for NLR, PLR, and SII to predict mortality in terms of sensitivity and specificity and survival analysis was conducted by the Kaplan–Meier curve.

3. Results

A total of 73 patients admitted with IE were screened and 61 patients satisfied the inclusion criteria. The 11 patients who were dead were taken as the study group, and 50 patients who were discharged alive were taken as the control group. Baseline demographic variables were comparable in both groups except for age and atrial fibrillation. The median age of the population with mortality was higher (65 range 57–77) than patients who survived (57 range 49–66). Atrial fibrillation was seen more commonly in patients who had mortality than those alive. Neutrophil counts were significantly higher, and lymphocyte and platelet counts were significantly lower in patients with adverse outcomes. C reactive protein levels were comparable in both groups, while NLR was higher in patients with mortality than in the control group.

The median value of NLR was 6.17 (3.5–10.7), which was 19.6 (10.1–27) in patients with mortality, while 5.4 (3.2–8.5) in patients who survived (Table 1). The median value of PLR was 156.8 (96.1–197.8), and the SII value was 1317.4 (813–2091), which were comparable in both groups. The area under the ROC curve of NLR (Fig. 1) showed a significant value of 0.83 (95 %CI 0.683–0.982, $p = 0.001$). When we listed the coordinates of the ROC curve of NLR, 9.81 had maximum sensitivity (81.8%, 95%CI 52.3–94.9) and specificity (80%, 95%CI 67–88.8) with a positive predictive value of 47.4% and negative predictive value of 95.2%. ROC analysis made for SII AUC 0.451 (95% CI 0.241–0.66) and PLR AUC 0.473 (95% CI 0.229–0.716) were not significant. A comparison of the ROC curve for NLR, SIII, and PLR is given in Fig. 1.

Twenty patients had undergone surgery which was comparable in both groups. Heart failure, renal failure, sepsis, multiple organ dysfunction syndrome (MODS), and peripheral embolism were significantly higher in patients who died than in alive patients. A Kaplan Meier survival analysis was made for patients taking a cut-off value of NLR 9.8 was statistically significant with a log-rank *p*-value <0.001 (Fig. 2). On bivariate analysis, age, renal failure, diabetes mellitus (DM), and atrial fibrillation (AF) were associated with in-hospital mortality. In the multivariate analysis, only NLR was a statistically significant predictor of mortality (Table 2).

Table 1
Comparison of Laboratory variables in IE patients with mortality and no mortality.

Variable	Total (N = 61)	Mortality		*p*-value*
		Yes (n = 11)	No (n = 50)	
Hb (g/dL), median (IQR)	10.2 (9.3–11.3)	10.8 (8.9–12.3)	9.8 (9.3–11.0)	0.493
CRP (mg/L), median (IQR)	88.6 (41.3–173.9)	88.6 (16.2–286.1)	83.7 (42.3–169.3)	0.871
Urea (mg/dL), median (IQR)	32.3 (18.7–55.2)	103 (37–124)	25 (17.8–46.3)	0.001
Serum Creatinine (mg/dL), median (IQR)	1.1 (0.8–1.7)	1.5 (1.1–3)	1 (0.73–1.7)	0.03
PCV (%), median (IQR)	30.8 (28.2–34.4)	33.7 (26.0–35.8)	30.5 (28.3–33.7)	0.542
TLC (K/μL), median (IQR)	11.9 (8.1–15.8)	11.5 (8.5–19.4)	12.0 (8.0–15.5)	0.447
Monocyte count(K/μL), median (IQR)	0.4 (0.2–0.69)	0.3 (0.2–0.5)	0.4 (0.28–0.7)	0.292
Neutrophil count(K/μL), median (IQR)	9.3 (6.0–12.9)	10.4 (8.1–15.5)	9.2 (5.7–12.3)	0.119
Lymphocyte count (K/μL), median (IQR)	1.5 (0.89–2.04)	0.6 (0.5–1.63)	1.6 (1.2–2.1)	0.003
Platelet count(K/μL), median (IQR)	222.0 (159.0–282.5)	110 (38–165.0)	229 (177.2–296.7)	0.001
NLR, median (IQR)	6.17 (3.5–10.7)	19.6 (10.1–27.0)	5.4 (3.2–8.5)	0.001
PLR, median (IQR)	156.8 (96.1–197.8)	127.9 (62.5–235.7)	156.9 (102.6–192.5)	0.778
SII (K/μL), median (IQR)	1317.4 (813.17–2091.6)	1112.7 (675.0–3234.0)	1439.4 (843.9–2043.3)	0.613

NLR, Neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; SII, systemic immune-inflammation index; IQR, interquartile range; CRP, C reactive protein; TLC, total leukocyte count; Hb, haemoglobin; PCV packed cell volume.
**p* value is between mortality yes and mortality no.

4. Discussion

Our study focused on different inflammatory indexes and their potential to predict mortality in IE patients. Renal failure, heart failure, septic shock, high creatinine, low platelet count, and high NLR were associated with in-hospital mortality. In addition, high NLR and not PLR or SII at admission is a significant predictor of in-hospital mortality in IE patients.

Various inflammatory markers have been studied in IE to predict adverse outcomes. Turak et al[8] evaluated 121 patients with IE retrospectively and showed that elevated NLR (NLR > 7.1) is linked to poor prognosis, in-hospital mortality and embolic events. NLR has a stronger predictive value than a stand-alone leukocyte differential count. Bozbay et al[9] investigated 171 patients with IE and found that high NLR group has high mortality but NLR showed no predictive indicator of mortality on long-term follow-up. The study by Meshaal et al[4] found that NLR is an independent predictor of in-hospital mortality in IE and calculation of NLR at admission may assist in early risk stratification in patients with IE. The study conducted by Chen et al[10] found stronger evidence of NLR as a reliable predictor of in-hospital mortality and morbidity.

The predictive power of SII in Infective endocarditis has been studied by Agus et al and found that SII is an independent predictor of mortality in their cohort and performed better than NLR and PLR in predicting mortality in IE patients.[3]This was in contrast to our study, as NLR was a better mortality predictor than SII and PLR similar to previously mentioned studies.

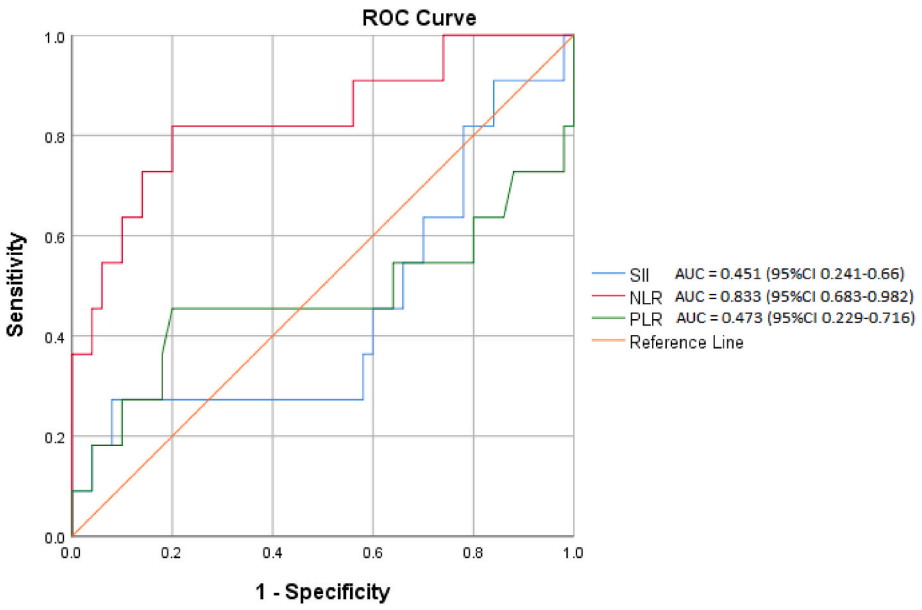

Fig. 1. The receiver-operating characteristic curve of NLR, PLR and SII for predicting in-hospital mortality in patients with infective endocarditis.

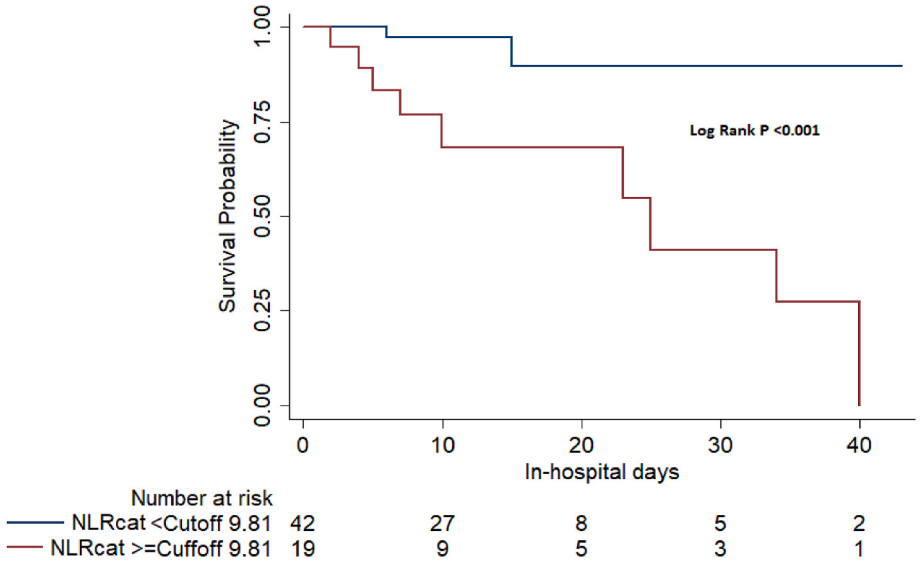

Fig. 2. Kaplan–Meier curve for in-hospital mortality according to the cut-off value of Neutrophil lymphocyte ratio in patients with infective endocarditis.

Table 2
Clinical and laboratory predictors of mortality by univariate and multivariate logistic regression analysis.

	Crude OR (95% CI)	*p* Value	Adjusted OR (95% CI)	*p* Value
Age≥55 years	10 (1.2–84.1)	0.017	7.2 (0.5–106.8)	0.15
Diabetes mellitus	3.4 (0.9–13.2)	0.093	1.9 (0.1–28.4)	0.63
Atrial fibrillation	9 (1.3–62.6)	0.037	1.1 (0–77.1)	0.977
Dyspnoea	3.7 (0.9–15.6)	0.096	2.9 (0.2–33.2)	0.399
Aortic valve vegetation	3.4 (0.9–13.1)	0.081	10.3 (0.7–162.3)	0.096
Platelet count <150 K/μL	12.8 (2.9–57.3)	0.001	8.4 (0.5–130.2)	0.128
Serum Creatinine >1.3 mg/dL	4.1 (1–16.1)	0.079	1.7 (0.1–20.1)	0.676
NLR Cuff off≥9.81	18 (3.3–96.7)	<0.001	37.5 (2.1–669.3)	0.014

NLR, Neutrophil-to-lymphocyte ratio; OR, odds ratio.

Our study's fundamental flaws are its retrospective design and limited sample size. The goal of this study was to see if there was a link between inflammatory levels at admission and in-hospital mortality. However, the findings of this study need to be verified in larger prospective cohorts.

5. Conclusion

The present study shows that a high NLR has better association with in-hospital mortality in IE than SII and PLR. NLR is a simple, readily available, and inexpensive parameter that can be used as a predictive marker to identify high-risk patients for mortality in IE.

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Contributory statement

SR: Conceptualization, Methodology, Writing and Editing; MC: Methodology, Analysis, Tables and figures, editing and reviewing; AW: Conceptualization, drafting and reviewing; MN: Reviewing and critical analysis; AK: Supervision, drafting, reviewing and critical analysis.

All authors critically revised the article for its intellectual content. All the authors have critically revised and agreed to the article for its contents before submission.

Ethical approval

The study has been approved by the scientific research committee and institutional ethics committee (Ref. AM/EC/203–2021).

Declaration of competing interest

All authors confirm that they have nothing to declare.

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