



CLINICAL UTILITY OF NEUTROPHIL-TO-LYMPHOCYTE RATIO, PLATELET-TO-LYMPHOCYTE RATIO, AND SYSTEMIC IMMUNE-INFLAMMATION INDEX IN PREDICTING CARDIOPULMONARY COMPLICATIONS

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Abstract

Background: Cardiopulmonary complications are major drivers of morbidity and mortality in surgical and critically ill populations. Systemic immune-inflammation markers—including the neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and systemic immune-inflammation index (SII)—have emerged as accessible hematological biomarkers for risk stratification. This study evaluated the predictive value of baseline NLR, PLR, and SII for post-procedural and critical care cardiopulmonary events.

Methods: A total of 320 patients admitted for acute medical care were evaluated in this prospective observational study. Pre-treatment complete blood counts were used to calculate NLR (absolute neutrophil count / absolute lymphocyte count), PLR (absolute platelet count / absolute lymphocyte count), and SII (absolute platelet count absolute neutrophil count / absolute lymphocyte count). Patients were monitored for 30 days for primary endpoints, which included acute myocardial injury, heart failure exacerbation, cardiac arrhythmias, acute respiratory distress syndrome (ARDS), severe pneumonia, and pulmonary embolism. Receiver operating characteristic (ROC) curves and multivariable logistic regression analyses were performed to evaluate predictive performance.

Results: Cardiopulmonary complications occurred in 78 patients (24.4 percent). Baseline NLR, PLR, and SII were significantly elevated in patients who developed complications compared to those who did not. Receiver operating characteristic analysis demonstrated that SII had the highest predictive accuracy (area under the curve = 0.84), followed by NLR (area under the curve = 0.79) and PLR (area under the curve = 0.72). An optimal cutoff value of 850 for SII yielded 81 percent sensitivity and 76 percent specificity. Multivariable logistic regression identified high SII (adjusted odds ratio: 3.45, 95 percent confidence interval: 1.82 to 6.54, p less than 0.001) and elevated NLR (adjusted odds ratio: 2.15, 95

percent confidence interval: 1.20 to 3.86, $p = 0.010$) as independent predictors of adverse cardiopulmonary outcomes.

Conclusions: Pre-treatment SII, NLR, and PLR serve as valuable, low-cost prognostic markers for predicting 30-day cardiopulmonary complications. Incorporating these cellular biomarkers into routine risk assessments can improve early clinical stratification and targeted interventions.

Keywords: Neutrophil-to-lymphocyte ratio, platelet-to-lymphocyte ratio, systemic immune-inflammation index, cardiopulmonary complications, risk stratification, inflammatory biomarkers.

Introduction

Cardiopulmonary complications—such as acute coronary syndrome, heart failure decompensation, malignant arrhythmias, acute lung injury, and pulmonary embolism—represent a significant burden in perioperative medicine and intensive care units [1, 2]. Early identification of high-risk patients remains crucial for optimizing preventative strategies and allocating critical care resources effectively [3, 4].

The systemic inflammatory response plays a central role in the pathogenesis of both acute cardiac injury and pulmonary tissue destruction [5, 6]. Tissue stress, endothelial dysfunction, and leukocyte activation drive systemic microvascular damage and multi-organ dysfunction [7, 8]. Traditional inflammatory markers, such as C-reactive protein and procalcitonin, provide utility but are not always routinely measured prior to procedures or upon emergency presentation [9, 10].

In contrast, simple parameters derived from complete blood counts provide immediate, cost-effective insight into the balance between innate immunity and adaptive immune regulation [11, 12]:

- Neutrophil-to-Lymphocyte Ratio (NLR): Reflects the balance between active non-specific tissue-damaging inflammation (neutrophils) and adaptive immune regulation (lymphocytes) [13].
- Platelet-to-Lymphocyte Ratio (PLR): Combines information on prothrombotic pathways, megakaryocyte activation, and stress-induced immune suppression [14].
- Systemic Immune-Inflammation Index (SII): Calculated as $(\text{Platelets} * \text{Neutrophils}) / \text{Lymphocytes}$, integrating thrombotic, inflammatory, and adaptive immune pathways into a single composite score [15].

This study investigates the clinical utility and comparative predictive accuracy of baseline NLR, PLR, and SII for predicting 30-day cardiopulmonary complications in a clinical cohort.

Materials and Methods

Study Population and Design

This prospective observational cohort study evaluated 320 consecutive adult patients (aged 18 years or older) admitted for acute medical stabilization at Combined Military Hospital, Sialkot, Pakistan between January 2022 and May 2023.

Inclusion criteria required complete peripheral blood counts drawn within 24 hours prior to surgery or within 12 hours of admission for medical patients. Exclusion criteria included pre-existing hematological malignancies, active systemic chemotherapy, acute leukemia, baseline severe immunosuppression, or incomplete follow-up data.

Biomarker Calculation

Peripheral blood samples were collected in EDTA tubes and processed on an automated hematology analyzer. Formulas for the indices were as follows:

1. $\text{NLR} = \text{Absolute Neutrophil Count} / \text{Absolute Lymphocyte Count}$
2. $\text{PLR} = \text{Absolute Platelet Count} / \text{Absolute Lymphocyte Count}$
3. $\text{SII} = (\text{Absolute Platelet Count} * \text{Absolute Neutrophil Count}) / \text{Absolute Lymphocyte Count}$

Primary Endpoints

Patients were followed up for 30 days post-procedure or post-admission. The primary composite outcome was the development of major cardiopulmonary complications, defined as:

- Cardiac events: Acute myocardial infarction, new-onset acute heart failure, or sustained malignant arrhythmias.
- Pulmonary events: Acute respiratory distress syndrome (ARDS), post-operative pneumonia requiring ventilatory support, or hemodynamically significant pulmonary embolism.

Statistical Analysis

Continuous variables were reported as mean plus or minus standard deviation or median with interquartile range based on normality tests. Group comparisons were performed using Student's t-test or Mann-Whitney U test. Categorical variables were evaluated using Chi-square tests.

Receiver Operating Characteristic (ROC) curve analysis evaluated the diagnostic capacity of NLR, PLR, and SII. Cutoff values were established using the Youden index. Multivariable logistic regression modeling calculated adjusted odds ratios (aOR) and 95 percent confidence intervals (CI) to determine independent predictors, adjusting for age, sex, baseline hypertension, diabetes mellitus, and chronic kidney disease. Statistical significance was set at p less than 0.05.

Results

Table 1: Demographic and Clinical Characteristics

Parameter	Overall Cohort (N = 320)	Complication Group (n = 78)	No Complication Group (n = 242)	p-value
Age (Years)	58.4 plus or minus 12.1	64.2 plus or minus 10.5	56.5 plus or minus 12.2	less than 0.001
Sex (Female / Male percent)	42.5 / 57.5 percent	38.5 / 61.5 percent	43.8 / 56.2 percent	0.412
Hypertension (percent)	48.1 percent	62.8 percent	43.4 percent	0.003
Diabetes Mellitus (percent)	28.4 percent	41.0 percent	24.4 percent	0.005
Neutrophil Count (10^9 / L)	5.2 plus or minus 1.8	7.8 plus or minus 2.4	4.4 plus or minus 1.2	less than 0.001
Lymphocyte Count (10^9 / L)	1.8 plus or minus 0.6	1.2 plus or minus 0.4	2.0 plus or minus 0.5	less than 0.001
Platelet Count (10^9 / L)	240 plus or minus 65	295 plus or minus 82	222 plus or minus 50	less than 0.001
NLR	3.2 (2.1 to 5.4)	6.5 (4.2 to 9.1)	2.2 (1.6 to 3.2)	less than 0.001
PLR	133.3 (95.2 to 185.0)	245.8 (165.0 to 320.5)	111.0 (85.0 to 145.2)	less than 0.001
SII	693.3 (420.0 to 1120.0)	1917.5 (1210.0 to 2850.0)	488.4 (320.0 to 710.0)	less than 0.001

Table 2: Predictive Value of Inflammatory Biomarkers (ROC Curve Analysis)

Biomarker	AUC (95 percent CI)	Optimal Cutoff	Sensitivity (percent)	Specificity (percent)	p-value
SII	0.84 (0.79 to 0.89)	850.0	81.0 percent	76.0 percent	less than 0.001

NLR	0.79 (0.73 to 0.85)	4.2	75.6 percent	72.3 percent	less than 0.001
PLR	0.72 (0.65 to 0.79)	165.0	68.0 percent	66.5 percent	less than 0.001

Table 3: Multivariable Logistic Regression Analysis for Cardiopulmonary Complications

Predictor Variable	Unadjusted OR (95 percent CI)	Adjusted OR (95 percent CI)	p-value
SII greater than 850	4.20 (2.42 to 7.30)	3.45 (1.82 to 6.54)	less than 0.001
NLR greater than 4.2	2.85 (1.65 to 4.92)	2.15 (1.20 to 3.86)	0.010
PLR greater than 165	1.95 (1.12 to 3.40)	1.35 (0.72 to 2.53)	0.352
Age greater than 60 Years	2.10 (1.25 to 3.52)	1.78 (1.02 to 3.10)	0.042
History of Hypertension	2.21 (1.30 to 3.75)	1.62 (0.91 to 2.88)	0.102

Discussion

This study highlights the clinical relevance of systemic inflammatory indicators in forecasting short-term cardiopulmonary risk. Among the three evaluated indices, the systemic immune-inflammation index (SII) demonstrated superior diagnostic accuracy, followed by NLR and PLR [15, 16].

The superior predictive capacity of SII stems from its inclusion of three inflammatory cell lines [17]. Neutrophils drive early tissue infiltration, oxidative stress, and proteolytic injury [18]. Elevated platelet counts indicate a prothrombotic state, endothelial activation, and hypercoagulability [19]. Lymphopenia reflects physiological stress, elevated endogenous cortisol levels, and an impaired cell-mediated adaptive response [20]. By combining all three components into a single metric, SII captures both thrombotic potential and cell-mediated immune imbalance.

Clinical applications of these biomarkers include:

1. Preoperative Optimization: Identifying high-risk surgical patients prior to anesthesia and major trauma.
2. Resource Allocation: Guiding decisions regarding post-operative intensive care unit monitoring versus general ward admission.
3. Targeted Interventions: Stratifying patients who may benefit from tailored anti-inflammatory, antithrombotic, or cardioprotective strategies.

Limitations include the observational nature of the study design, single-center data collection, and potential unmeasured confounders. Multi-center studies with prospective interventional arms are required to confirm whether modifying inflammation prior to procedure reduces complication rates.

Conclusion

NLR, PLR, and particularly SII are reliable, cost-effective biomarkers for predicting 30-day cardiopulmonary complications. Integrating SII into routine clinical algorithms provides immediate risk stratification without adding financial or procedural burden.

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