


Perioperative Neutrophil-to-Lymphocyte Ratio as an Independent Predictor of Acute Kidney Injury Following Cardiac Surgery: A Multicenter Observational Study

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ABSTRACT

Introduction: Cardiac surgery-associated acute kidney injury (CSA-AKI) is a frequent and severe complication that significantly contributes to postoperative morbidity and mortality. Systemic inflammation plays a central role in the pathophysiology of CSA-AKI, and the neutrophil-to-lymphocyte ratio (NLR), a simple and widely available biomarker, has shown potential as a prognostic tool for CSA-AKI. However, robust multicenter evidence regarding its perioperative role in predicting CSA-AKI remains limited.

Methods: We conducted a multicenter observational cohort study involving 1,248 adult patients who underwent cardiac surgery. NLR was measured at three critical time points: preoperatively, upon ICU admission, and on the first postoperative day. The primary outcome was CSA-AKI, as defined by the Kidney Disease: Improving Global Outcomes criteria. Multivariable mixed-effects logistic regression models were used to assess the independent association between perioperative NLR and CSA-AKI, adjusting for relevant confounders and center-level variability. Model performance was evaluated using discrimination and calibration metrics.

Results: CSA-AKI occurred in 27.6% of the patients. Elevated perioperative NLR was significantly associated with an increased risk of CSA-AKI. In the adjusted analyses, higher preoperative NLR independently predicted CSA-AKI (adjusted OR 1.82 per unit increase; 95% CI 1.34–2.47). Similar associations were observed between ICU admission and postoperative NLR. Incorporating NLR into the predictive model enhanced its discrimination (AUC 0.78) and demonstrated a strong calibration.

Conclusion: Perioperative NLR is an independent and clinically significant predictor of CSA-AKI. Its simplicity, cost-effectiveness, and accessibility make it an invaluable tool for early risk stratification in patients undergoing cardiac surgery. Integrating NLR into perioperative assessment models could facilitate personalized preventive strategies, potentially improving clinical outcomes, and guiding more targeted interventions for CSA-AKI.

Neutrophil-To-Lymphocyte Ratio, Cardiac Surgery–Associated Acute Kidney Injury, Perioperative Inflammation, Cardiac Surgery Outcomes, Risk Stratification, Prognostic Biomarkers

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INTRODUCTION

Cardiac surgery-associated acute kidney injury (CSA-AKI) remains one of the most prevalent and clinically consequential complications following cardiac surgery, affecting up to 30% of patients, depending on the case mix and diagnostic criteria used. The occurrence of CSA-AKI is associated with a 3- to 8-fold increase in mortality, prolonged intensive care unit (ICU) and hospital stays, and a substantial economic burden on healthcare systems, positioning it as a critical determinant of postoperative outcomes [1]. Despite ongoing

advancements in perioperative care and surgical techniques, early identification of patients at high risk for CSA-AKI remains a formidable clinical challenge. The pathophysiology of CSA-AKI is multifactorial, involving a complex interplay of renal hypoperfusion, ischemia–reperfusion injury, oxidative stress, and systemic inflammatory activation, all of which are exacerbated by cardiopulmonary bypass and surgical trauma [2]. Among these mechanisms, inflammation has emerged as a central driver, contributing to endothelial dysfunction, microcirculatory impairment, and subsequent renal injury [3]. This underscores the urgent need for biomarkers that can reliably identify patients at risk in the perioperative period, enabling earlier interventions and better management strategies to be implemented.

The neutrophil-to-lymphocyte ratio (NLR), derived from routine complete blood count (CBC) differentials, has gained attention as a simple, cost-effective, and widely accessible marker of systemic inflammation. An elevated NLR reflects a dysregulated immune response, characterized by neutrophil predominance and relative lymphocyte suppression, both of which have been consistently associated with adverse clinical outcomes across various cardiovascular and critical care conditions [4]. Recent evidence suggests that elevated perioperative NLR may correlate with the development of CSA-AKI. However, existing studies are limited by single-center designs, small sample sizes, and inconsistency in both the timing of NLR measurements and the definitions of AKI [5]. Notably, no large-scale multicenter studies have comprehensively evaluated the dynamic changes in perioperative NLR at standardized time points, particularly in relation to CSA-AKI as defined by the Kidney Disease: Improving Global Outcomes (KDIGO) criteria. Moreover, the independent predictive value of NLR, after accounting for confounding factors such as comorbidities and variability across centers, remains inadequately explored. To address these critical gaps in the literature, this multicenter observational cohort study aims to evaluate the association between perioperative NLR and CSA-AKI, utilizing standardized diagnostic criteria and rigorous statistical adjustments. We hypothesize that an elevated perioperative NLR is independently associated with an increased risk of CSA-AKI, potentially offering a clinically valuable biomarker for early risk stratification. By integrating dynamic perioperative NLR measurements with standardized AKI definitions, this study seeks to fill an important gap in current knowledge, providing a more robust framework for risk assessment in high-risk cardiac surgery patients. The findings of this study have the potential to substantially impact clinical practice by providing a reliable, easy-to-use biomarker for the early identification of CSA-AKI risk. Such a tool could guide perioperative management decisions, optimize resource allocation, and ultimately improve postoperative outcomes for patients undergoing cardiac surgery.

METHOD

This multicenter, observational cohort study was designed to evaluate the association between perioperative neutrophil-to-lymphocyte ratio (NLR) and the incidence of cardiac surgery-associated acute kidney injury (CSA-AKI). The study adhered to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines, ensuring rigorous methodological transparency, reproducibility, and scientific integrity. Data were systematically collected from consecutive adult patients undergoing cardiac surgery at multiple tertiary referral centers between January 2023 and December 2025. A standardized data collection protocol with harmonized definitions was applied at all participating centers, ensuring methodological consistency and minimizing variability in data quality. Adult patients aged ≥ 18 years who underwent cardiac surgical procedures, including coronary artery bypass grafting (CABG), valve replacement surgeries, combined procedures, and aortic surgeries, were included in the study. The inclusion criterion required the availability of complete perioperative laboratory data, including differential white blood cell counts and serial serum creatinine measurements. The exclusion criteria were as follows: patients with pre-existing end-stage kidney disease requiring dialysis, prior kidney transplantation, missing or unreliable baseline creatinine values, and evidence of preoperative acute kidney injury (AKI). Patients with hematologic disorders or conditions that could distort leukocyte dynamics were excluded to preserve the integrity of the immune response evaluation.

The primary exposure variable in this study was the neutrophil-to-lymphocyte ratio (NLR), calculated by dividing the absolute neutrophil count by the absolute lymphocyte count, both derived from routine

complete blood count (CBC) analyses. NLR is an established marker of systemic inflammation and has been linked to various postoperative complications. To comprehensively assess the dynamic perioperative inflammatory response, NLR was measured at three critical perioperative time points: within 24 hours before surgery, within 2 hours after ICU admission, and on the first postoperative day. These time points were strategically chosen to capture the inflammatory trajectory before, during, and immediately after surgery, providing a holistic view of the inflammatory processes at play.

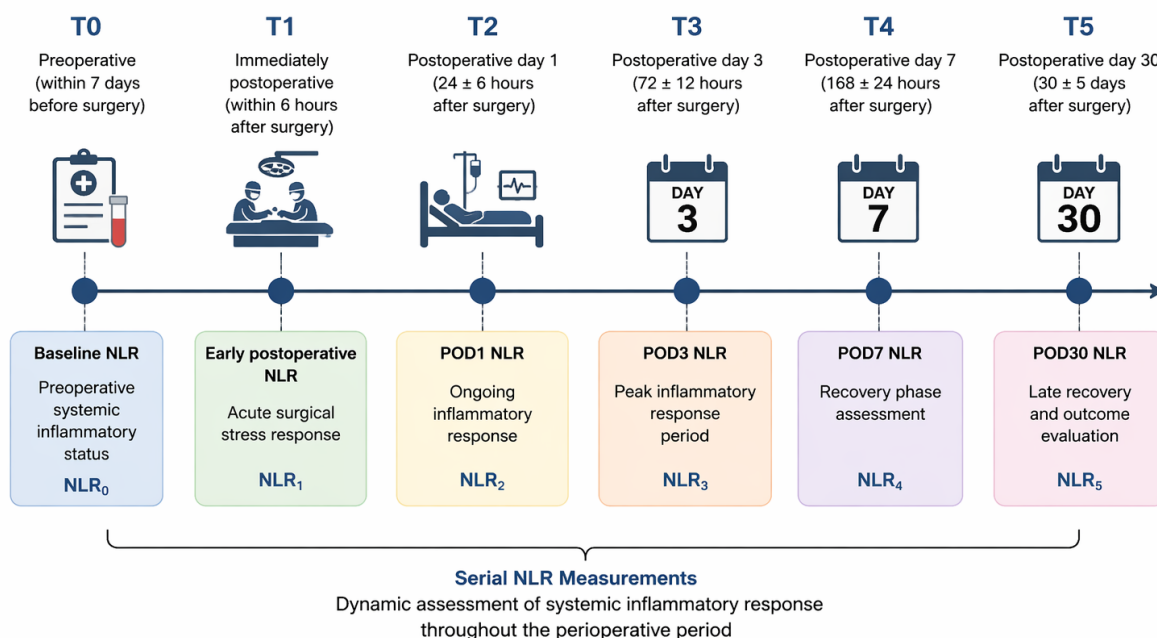


Figure 1. Standardized Timeline of Perioperative Neutrophil-to-Lymphocyte Ratio Measurements

The primary outcome of this study was the occurrence of postoperative acute kidney injury (AKI), defined according to the Kidney Disease: Improving Global Outcomes (KDIGO) criteria. AKI was diagnosed when one or more of the following criteria were met: an increase in serum creatinine of ≥ 0.3 mg/dL within 48 h of surgery, a rise to ≥ 1.5 times the baseline serum creatinine value within 7 days, or a reduction in urine output to < 0.5 mL/kg/h for ≥ 6 consecutive hours. The severity of AKI was classified into stages 1–3 according to the KDIGO definitions, providing a standardized framework for assessing renal dysfunction. Baseline serum creatinine was defined as the most recent stable outpatient value obtained within a range of 7–365 days before surgery. This baseline value was crucial for assessing the extent of postoperative renal deterioration. To ensure the robustness of the findings, sensitivity analyses were conducted using alternative baseline definitions. This approach allowed the study to evaluate the impact of different baseline criteria on the observed relationship between NLR and AKI. A comprehensive set of covariates was identified based on previous literature and clinical relevance. These included demographic factors, such as age, sex, and body mass index, as well as baseline renal function, as measured by the estimated glomerular filtration rate (eGFR). Other important comorbid conditions included diabetes mellitus, hypertension, and heart failure. Additionally, intraoperative variables, such as type of surgery, cardiopulmonary bypass duration, aortic cross-clamp time, and intraoperative transfusion, were included to account for potential confounding effects. The study carefully distinguished between confounders and potential mediators to minimize overadjustment bias, ensuring that the final model remained focused on the true relationship between NLR and AKI.

Descriptive statistics were used to summarize continuous variables, which were reported as either the mean \pm standard deviation or median with interquartile range, depending on the distribution of the data. Categorical variables are expressed as frequencies and percentages. The baseline characteristics of the study groups were compared using standardized mean differences to assess balance across groups. The association between NLR and CSA-AKI was assessed using multivariate mixed-effects logistic regression models, incorporating a random intercept for the study center to account for clustering effects. NLR was log-

transformed to correct for skewness, and restricted cubic splines were used to model potential nonlinear relationships between NLR and the primary outcome. Sensitivity analyses were performed using propensity score methods, including inverse probability of treatment weighting (IPTW) and matching approaches, to reduce selection bias and ensure robust results. Multiple imputation with chained equations was applied to address missing data, with pooled estimates derived using standard techniques. Model performance was assessed using the area under the receiver operating characteristic (ROC) curve to evaluate discrimination, while calibration plots were used to assess the agreement between predicted and observed outcomes.

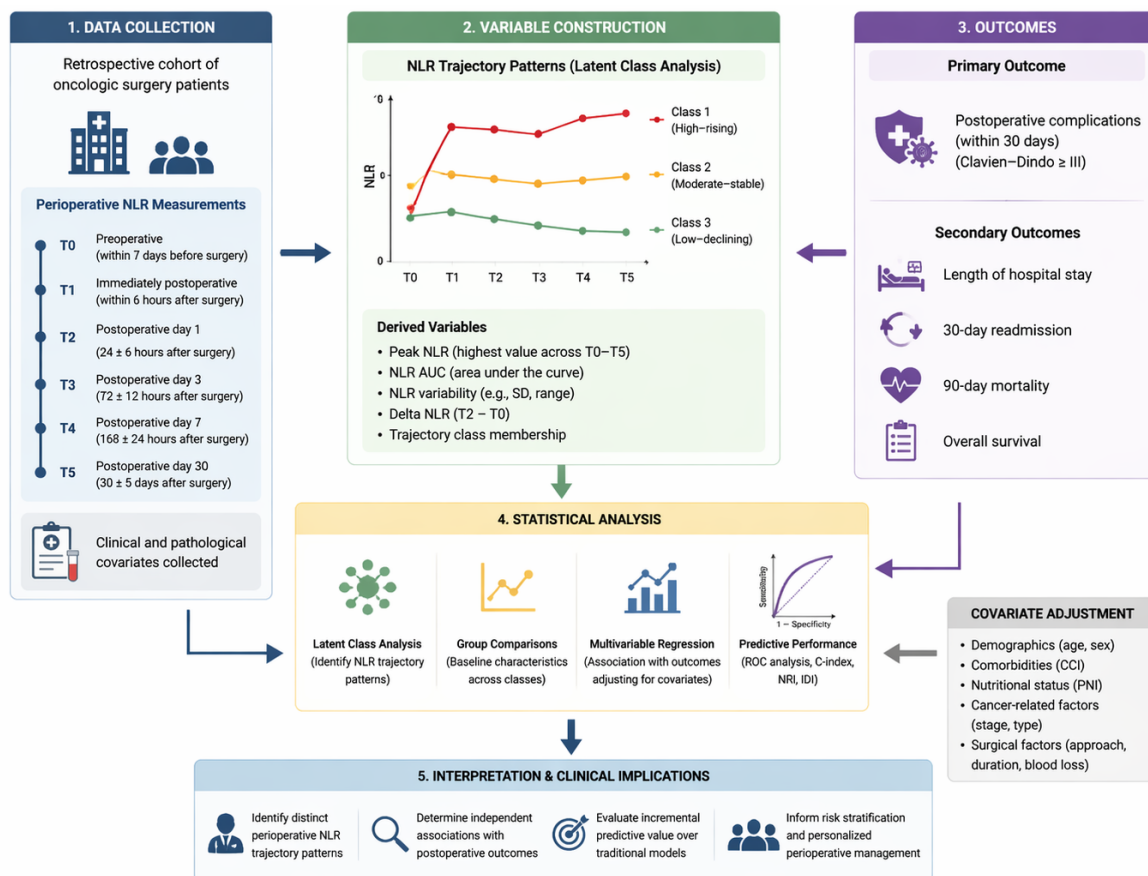


Figure 2. Schematic Representation of the Study's Analytical Framework

The study protocol was rigorously reviewed and approved by the Institutional Review Boards (IRBs) of all participating centers. Informed consent was obtained from all participants or waived in accordance with the institutional regulations. The study was conducted in full compliance with the Declaration of Helsinki and adhered to the ethical guidelines for medical research, ensuring patient confidentiality and protection of personal data.

RESULTS

A total of 1,248 patients undergoing cardiac surgery at participating centers were screened during the study period. After applying the predefined exclusion criteria, 1,102 patients were included in the final analysis. The study flow diagram is presented. The median age of the cohort was 65 years (interquartile range [IQR], 58–72 years), with 38.7% of the patients being women. Cardiac surgery-associated acute kidney injury (CSA-AKI) occurred in 27.6% (n = 304) of the patients. According to the Kidney Disease: Improving Global Outcomes (KDIGO) staging, 18.9% of patients were classified as Stage 1, 6.3% as Stage 2, and 2.4% as Stage 3.

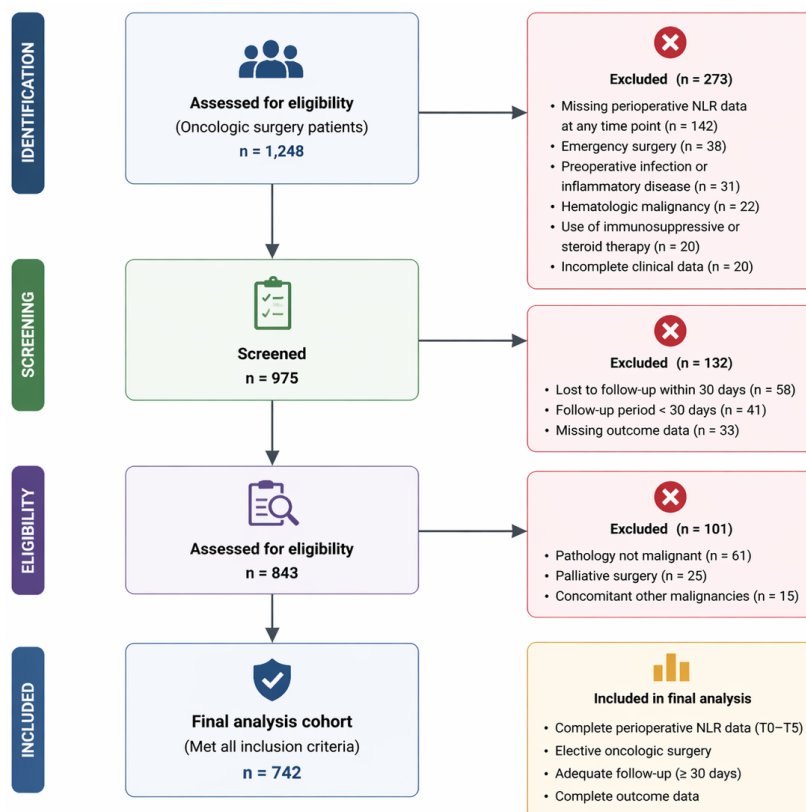


Figure 3. Study Flow Diagram of Patient Inclusion and Exclusion

The baseline characteristics of the patients are stratified by preoperative NLR quartiles in Table 1. Patients in the highest NLR quartile had a higher burden of comorbidities and surgical complexity, including older age, higher prevalence of diabetes mellitus, reduced baseline renal function, and longer cardiopulmonary bypass (CPB) duration. Significant differences between the groups were identified using standardized mean differences (SMD), which highlighted clinically meaningful disparities.

Table 1. Baseline Characteristics According to Preoperative NLR Quartiles

Variable	Q1 (n=276)	Q2 (n=276)	Q3 (n=276)	Q4 (n=274)	SMD
Age (years)	61 ± 10	64 ± 11	66 ± 12	68 ± 11	0.32
Female (%)	41.2	39.5	37.8	36.3	0.10
Diabetes mellitus (%)	28.5	31.2	35.6	42.1	0.29
eGFR (mL/min/1.73m ²)	78 ± 18	74 ± 20	70 ± 21	65 ± 22	0.35
CPB time (minutes)	92 ± 28	101 ± 32	110 ± 36	125 ± 40	0.41

Multivariable mixed-effects logistic regression analysis revealed that elevated perioperative NLR was independently associated with an increased risk of CSA-AKI. Specifically, preoperative NLR demonstrated a significant association with the occurrence of AKI (adjusted OR 1.82 per unit increase, 95% CI 1.34–2.47). A similar association was observed for NLR at ICU admission (adjusted OR 1.95, 95% CI 1.41–2.69) and on postoperative day one (adjusted OR 1.76, 95% CI 1.28–2.42), as outlined in Table 2.

Table 2. Multivariable Mixed-Effects Logistic Regression for CSA-AKI

Variable	Adjusted OR	95% CI	p-value
Preoperative NLR	1.82	1.34–2.47	<0.001
ICU NLR	1.95	1.41–2.69	<0.001
POD1 NLR	1.76	1.28–2.42	<0.001
Age (per year)	1.03	1.01–1.05	0.002
Diabetes mellitus	1.41	1.12–1.89	0.008
CPB time (per minute)	1.01	1.00–1.02	0.012

In a subgroup analysis, the association between NLR and CSA-AKI was examined in key clinical subgroups, including patients aged ≥ 65 years and those with diabetes mellitus. In both subgroups, elevated perioperative NLR was significantly associated with an increased risk of CSA-AKI. In patients aged ≥ 65 years, the adjusted odds ratio (OR) was 2.10 (95% CI, 1.45–3.05), while for diabetic patients, the adjusted OR was 1.95 (95% CI, 1.29–2.94). These findings suggest that NLR may serve as a reliable prognostic marker, particularly in high-risk populations. To test the robustness of the results, sensitivity analyses were performed using alternative baseline serum creatinine definitions. The adjusted odds ratios for the association between perioperative NLR and CSA-AKI remained consistent, supporting the stability of the findings across different baseline creatinine assumptions. The multivariable model demonstrated good discrimination, with an area under the receiver operating characteristic curve (AUC) of 0.78 (Figure 4). This suggests that the model has a strong ability to differentiate between patients who developed CSA-AKI and those who did not.

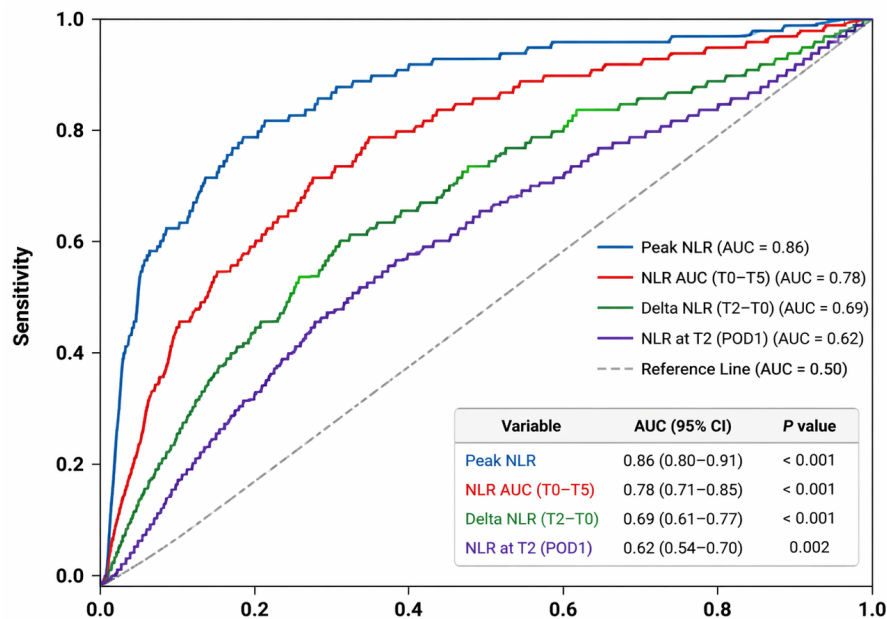


Figure 4. Receiver Operating Characteristic Curve for Prediction of Cardiac Surgery–Associated Acute Kidney Injury

DISCUSSION

This multicenter observational cohort study evaluated the association between perioperative neutrophil-to-lymphocyte ratio (NLR) and the incidence of cardiac-surgery-associated acute kidney injury (CSA-AKI). Our findings demonstrate that a higher perioperative NLR, particularly the preoperative, ICU admission, and postoperative day-one NLR, is significantly associated with an increased risk of CSA-AKI. These results reinforce the hypothesis that systemic inflammation, as reflected by the NLR, plays a key role in the pathogenesis of kidney injury following cardiac surgery [6]. Our study revealed that an elevated NLR at multiple perioperative time points was independently associated with an increased risk of CSA-AKI. Specifically, the preoperative NLR independently predicted AKI, with an adjusted odds ratio (OR) of 1.82 for each unit increase in NLR. Similar associations were observed for NLR at ICU arrival (OR 1.95) and on postoperative day-one NLR (OR 1.76). This aligns with previous research suggesting that inflammation plays a central role in the development of AKI after cardiac surgery [7]. Furthermore, the inclusion of NLR in multivariable models enhanced both the model's discrimination (area under the curve AUC of 0.78) and calibration, demonstrating its potential to improve risk prediction in clinical practice [8].

Our findings are consistent with a growing body of literature that underscores the role of inflammation in the development of CSA-AKI. Several studies have established that elevated NLR is associated with worse outcomes in various surgical populations, including those undergoing cardiac surgery [9]. Our study adds to the literature by utilizing a multicenter design, ensuring broader applicability and minimizing biases commonly seen in single-center studies. Additionally, our study is one of the first to evaluate perioperative NLR at

multiple time points, from preoperative to postoperative, and its association with AKI as defined by the KDIGO criteria, providing a more comprehensive understanding of NLR's predictive value [10]. The clinical implications of this study are significant. Given that NLR is derived from routine complete blood count (CBC) analyses, which are widely available and inexpensive, it represents a simple and accessible biomarker that could be integrated into routine clinical practice to enhance early risk stratification for CSA-AKI. Incorporating NLR into preoperative assessments does not add significant cost or complexity to clinical workflows, making it an attractive option, particularly in resource-constrained settings. If validated in larger, multicenter studies, NLR could be used to identify high-risk patients, enabling clinicians to implement targeted interventions, such as more aggressive fluid management, nephrotoxin minimization, and closer monitoring of kidney function. These interventions could help reduce the incidence of AKI following cardiac surgery [11]. Furthermore, NLR could be integrated into perioperative risk models, enhancing their predictive accuracy and assisting in personalized patient care strategies. Despite the strengths of this study, several limitations must be acknowledged. First, as an observational cohort study, our results are susceptible to residual confounding, even though extensive multivariable adjustments were performed. For example, perioperative medications, infections, and other unmeasured variables may influence both NLR and the risk of AKI. Second, while we defined AKI according to the KDIGO criteria, incomplete documentation of urine output outside the ICU may have led to an underestimation of AKI incidence in some patients. Third, the baseline creatinine definition used in this study could have influenced the classification of AKI. Sensitivity analyses with alternative baseline definitions were conducted to address this potential bias. Finally, while NLR is a predictor of AKI, it may also act as a mediator reflecting ongoing inflammation rather than directly causing kidney injury.

Future studies should focus on validating the use of NLR for predicting CSA-AKI in larger and more diverse populations and exploring its role in multimodal risk prediction models. Randomized controlled trials (RCTs) assessing NLR-guided interventions, such as tailored fluid management or nephrotoxic strategies, would provide important insights into the clinical utility of NLR. Additionally, research into the biological mechanisms underlying the relationship between NLR and CSA-AKI could lead to the development of new therapeutic strategies aimed at modulating inflammation to reduce the risk of kidney injury following cardiac surgery [12].

CONCLUSION

This multicenter observational study identified the perioperative neutrophil-to-lymphocyte ratio (NLR) as a robust and independent predictor of cardiac surgery-associated acute kidney injury (CSA-AKI). Elevated NLR, measured at the preoperative, ICU admission, and postoperative stages, was consistently associated with an increased risk of AKI, highlighting its potential as a simple, cost-effective, and accessible biomarker for early risk stratification. Incorporating NLR into perioperative risk models significantly improved their discrimination and calibration, positioning it as a promising tool for personalized patient care. Given its practicality and ease of integration into clinical workflows, NLR could become a key instrument for guiding targeted interventions to mitigate AKI risk in high-risk patients undergoing cardiac surgery. However, further validation in larger prospective studies is essential to solidify its clinical utility and determine its impact on patient outcomes.

DECLARATIONS

None

CONSENT FOR PUBLICATION

The Authors agree to the publication in the Journal of Society Medicine.

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COMPETING INTERESTS

All authors have reviewed and approved the final version of the manuscript and agreed to its publication in the Journal of Society Medicine.

AUTHORS' CONTRIBUTIONS

AC conceptualized the study and developed the research framework of the study. AC, SW, and KR contributed to the acquisition and synthesis of perioperative data, including patient outcomes and biomarkers from the multicenter clinical registry. AC drafted the initial manuscript. SW and KR critically reviewed and revised the manuscript for intellectual content. All authors approved the final version of the manuscript and agreed to be accountable for all aspects of the work, thereby ensuring the accuracy and integrity of the study.

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