

## Original Research Article

# Neutrophil, lymphocyte and platelet ratio as a predictor of acute kidney injury after major noncardiac surgery

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## ABSTRACT

**Background:** Acute kidney injury (AKI) is a common complication after major surgery associated with increased morbidity and mortality. Inflammation plays a key role in the pathogenesis of postoperative AKI. This study evaluated the neutrophil-lymphocyte-platelet ratio (NLPR) as a predictor of AKI after major noncardiac surgery.

**Methods:** In a retrospective analysis, we studied 300 patients who underwent major noncardiac surgery. The NLPR was calculated from the complete blood count obtained within 12 hours postoperatively. AKI was defined by the KDIGO criteria. Multivariable logistic regression was used to evaluate the association between NLPR and AKI.

**Results:** AKI occurred in 46 patients (15.3%). The mean NLPR was significantly higher in patients who developed AKI compared to those who did not. On multivariable analysis, NLPR remained an independent predictor of AKI. The area under the receiver operating characteristic curve for NLPR to predict AKI was 0.804.

**Conclusions:** The neutrophil-lymphocyte-platelet ratio is an independent predictor of acute kidney injury after major noncardiac surgery. This simple, widely available biomarker can help identify patients at high risk for this complication.

**Keywords:** Acute kidney injury, Neutrophil-lymphocyte-platelet ratio, Retrospective analysis

## INTRODUCTION

Acute kidney injury (AKI) is a sudden deterioration in renal function that is highly prevalent in surgical patients. It is estimated to occur in 6-12% of patients undergoing major noncardiac surgery.<sup>1</sup> Patients who develop AKI have significantly increased risk of short and long-term morbidity and mortality, even when renal function recovers.<sup>2</sup> Due to its association with adverse outcomes, prompt identification of AKI is essential to institute supportive care and mitigate ongoing renal damage. However, serum creatinine rises late after established renal injury, precluding its use as an early biomarker. The pathogenesis of postoperative AKI is multifactorial and incompletely understood. Major surgery provokes a

systemic inflammatory response that contributes to renal tubular injury through hemodynamic instability, microvascular dysfunction and direct tubular damage mediated by oxidative stress and cytokines.<sup>3</sup> Inflammatory mediators and cells such as neutrophils, lymphocytes and platelets have been implicated as key drivers and perpetuators of AKI.<sup>4</sup>

The neutrophil-to-lymphocyte ratio (NLR) has emerged as a marker of systemic inflammation that predicts outcomes in cardiovascular disease, cancer and chronic kidney disease.<sup>5,6</sup> More recently, NLR has been associated with AKI in various settings including cardiac surgery, contrast administration and sepsis.<sup>7,8</sup> Accounting for platelets in the NLR, as a neutrophil-lymphocyte-platelet ratio (NLPR),

has been found to increase the predictive ability for AKI compared to NLR alone.<sup>9</sup>

While the utility of postoperative NLPR has been demonstrated in cardiac surgery, data on its performance in noncardiac surgery is lacking. The aim of this study was to evaluate the association of NLPR with AKI in patients undergoing major noncardiac surgery. We hypothesized that higher NLPR would be an independent predictor of postoperative AKI in this cohort.

## METHODS

We conducted a current study was hospital based prospective observational study conducted in the Department of Nephrology, Sri Aurobindo institute of medical sciences and hospital, Indore from April 2022 to May 2024.

We included patients aged 18 years or older who underwent elective or urgent noncardiac surgery under general anesthesia with an expected length of stay >48 hours. Major noncardiac surgery was defined as abdominal, orthopedic, thoracic, vascular or head and neck procedures. Authors excluded patients with preexisting end stage renal disease or kidney transplant, those with missing laboratory or outcome data and those who underwent cardiac or minor surgery.

Demographic and clinical data were collected from electronic medical records. The primary outcome was AKI, defined according to kidney disease: improving global outcomes (KDIGO) criteria as an increase in serum creatinine  $\geq 0.3$  mg/dL within 48 hours or  $\geq 50\%$  within 7 days. Baseline serum creatinine was defined as the creatinine measured closest to the date of surgery. Estimated glomerular filtration rate was calculated using the CKD-EPI equation.<sup>10</sup>

The maximum serum neutrophil and minimum lymphocyte and platelet counts measured within 12 hours after surgery were collected. Baseline characteristics were evaluated using descriptive statistics. Continuous variables were reported as means with standard deviations or medians with interquartile ranges based on normality. Categorical variables were reported as frequencies with proportions. Differences between groups were compared using Chi-square tests for categorical variables and t-tests or Wilcoxon rank sum tests for continuous variables.

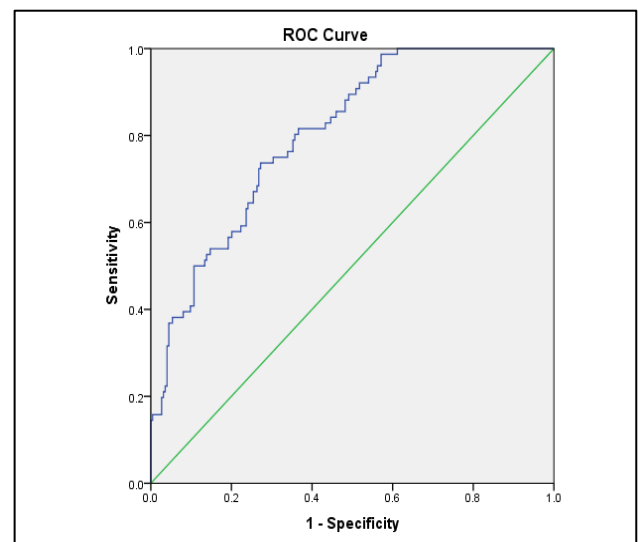
Separate univariable logistic regression models were used to identify factors associated with AKI. Covariates that were associated with AKI at  $p < 0.05$  were included in a multivariable logistic regression model to determine the independent association between NLPR and AKI, with results reported as adjusted odds ratios (aOR) and 95% confidence intervals (CI). Model calibration and fit were assessed using the Hosmer–Lemeshow goodness of fit test. To assess the capacity of the NLPR to discriminate between patients with and without AKI, a receiver

operating characteristic (ROC) curve was generated and the area under the curve (AUC) and its 95% CI were calculated. All analyses were performed using SPSS version 24.0. Two-sided  $p$  values  $< 0.05$  were considered statistically significant.

## RESULTS

Table 1 compares the demographic and clinical characteristics of patients with and without AKI. Patients with AKI were older ( $67 \pm 12$  years vs.  $61 \pm 13$  years,  $p = 0.002$ ) and had significantly lower preoperative eGFR ( $67 \pm 37$  vs.  $80 \pm 24$  ml/min/1.73 m<sup>2</sup>,  $p = 0.002$ ). Diabetes was more prevalent in the AKI group (39% vs. 24%,  $p = 0.03$ ). While hypertension and urgent surgery were slightly more common in the AKI group, these differences were not statistically significant ( $p = 0.09$  and  $p = 0.17$ , respectively). No significant differences were observed in surgery types between the groups.

Table 2 shows that patients with AKI had higher levels of inflammatory markers. Neutrophil count ( $10.2 \pm 4.1$  vs.  $8.3 \pm 3.7 \times 10^3/\mu\text{L}$ ,  $p = 0.002$ ), neutrophil-lymphocyte ratio ( $15.7 \pm 9.4$  vs.  $10.2 \pm 6.8$ ,  $p < 0.001$ ) and neutrophil-lymphocyte-platelet ratio ( $15.2 \pm 11.6$  vs.  $8.1 \pm 6.3$ ,  $p < 0.001$ ) were significantly elevated in the AKI group. Lymphocyte and platelet counts were lower in the AKI group, reflecting an inflammatory response.



**Figure 1: ROC curve (receiver operating characteristic curve).**

Univariate analysis highlights significant predictors of AKI. Older age (OR 1.04 per year,  $p = 0.003$ ), lower preoperative eGFR (OR 0.98 per ml/min/1.73 m<sup>2</sup>,  $p = 0.008$ ), diabetes (OR 2.04,  $p = 0.03$ ) and higher neutrophil count (OR 1.13 per  $10^3/\mu\text{L}$ ,  $p = 0.003$ ) were positively associated with AKI. Higher neutrophil-lymphocyte ratio (OR 1.09 per unit,  $p < 0.001$ ) and neutrophil-lymphocyte-platelet ratio (OR 1.10 per unit,  $p < 0.001$ ) were strongly predictive of AKI.

In multivariable analysis, NLP (neutrophil-lymphocyte-platelet ratio) remained the strongest independent predictor of AKI (adjusted OR 1.08 per unit,  $p < 0.001$ ). While age and preoperative eGFR showed trends toward significance, diabetes was not an independent predictor of AKI after adjustment for other variables. Table 3

summarizes the predictive accuracy of the NLP for detecting AKI. The AUC was 0.804, indicating good discrimination. The confidence interval ranged from 0.752 to 0.856, with a highly significant  $p$  value ( $p < 0.001$ ), emphasizing the robust predictive capability of NLP in identifying AKI.

**Table 1: Baseline characteristics of patients with and without acute kidney injury.**

| Characteristics                              | No AKI (n=254) | AKI (n=46) | P value |
|----------------------------------------------|----------------|------------|---------|
| Age, (in years)                              | 61±13          | 67±12      | 0.002   |
| Male sex                                     | 138 (54%)      | 27 (59%)   | 0.59    |
| Preoperative eGFR, ml/min/1.73m <sup>2</sup> | 80±24          | 67±37      | 0.002   |
| Diabetes                                     | 61 (24%)       | 18 (39%)   | 0.03    |
| Hypertension                                 | 167 (66%)      | 36 (78%)   | 0.09    |
| Surgery type                                 |                |            |         |
| Abdominal                                    | 105 (41%)      | 21 (46%)   | 0.390   |
| Orthopedics                                  | 58 (23%)       | 8 (17%)    |         |
| Thoracic                                     | 55 (22%)       | 15 (33%)   |         |
| Head and neck                                | 26 (10%)       | 1 (2%)     |         |
| Vascular                                     | 10 (4%)        | 1 (2%)     |         |
| Urgent surgery                               | 22 (9%)        | 7 (15%)    | 0.17    |

**Table 2: Postoperative inflammatory markers in patients with and without acute kidney injury.**

| Markers                                     | No AKI (n=254) | AKI (n=46) | P value |
|---------------------------------------------|----------------|------------|---------|
| Neutrophil count, $\times 10^3/\mu\text{l}$ | 8.3±3.7        | 10.2±4.1   | 0.002   |
| Lymphocyte count, $\times 10^3/\mu\text{l}$ | 1.0±0.5        | 0.8±0.4    | 0.007   |
| Platelet count, $\times 10^3/\mu\text{l}$   | 182.6±58.4     | 158.9±63.1 | 0.011   |
| Neutrophil-lymphocyte ratio                 | 10.2±6.8       | 15.7±9.4   | <0.001  |
| Neutrophil-lymphocyte-platelet ratio        | 8.1±6.3        | 15.2±11.6  | <0.001  |

**Table 3: Accuracy of NLP to detect AKI.**

| Area  | Std. Error <sup>a</sup> | P value | Asymptotic 95% confidence interval |             |
|-------|-------------------------|---------|------------------------------------|-------------|
|       |                         |         | Lower bound                        | Upper bound |
| 0.804 | 0.027                   | 0.000   | 0.752                              | 0.856       |

## DISCUSSION

The current study demonstrates that the neutrophil-to-lymphocyte and platelet ratio (N/LP ratio) is a strong predictor of AKI in the postoperative period following major abdominal surgeries. The incidence of AKI in our cohort (22.4%) is comparable to the 22.4% reported by Gameiro et al, (2018) in their retrospective study on major abdominal surgeries.<sup>11</sup> Both studies underline the significant burden of AKI in surgical patients and highlight common risk factors such as advanced age, preoperative renal function and systemic inflammation. Gameiro et al, demonstrated that older age (71.1±13.2 years vs. 60.6±15.7 years,  $p < 0.0001$ ) and lower preoperative eGFR were strong predictors of AKI, findings that were mirrored in the current study (67±12 years vs. 61±13 years,  $p = 0.002$ , preoperative eGFR 67±37 vs. 80±24 mL/min/1.73m<sup>2</sup>,  $p = 0.002$ ).<sup>11</sup> These similarities reinforce the importance of baseline patient characteristics in

identifying high-risk individuals. Oezkur et al also identified systemic inflammation as a major driver of AKI following cardiac surgery, with elevated neutrophil counts and reduced lymphocyte counts being prominent marker.<sup>12</sup> The study extends these findings by incorporating platelet counts into the predictive model, showing that the N/LP ratio effectively captures the interplay between inflammation and coagulation.

Systemic inflammation is a well-recognized contributor to AKI pathogenesis. Zarbock et al emphasized that ischemia-reperfusion injury, endotoxemia and microvascular dysfunction are central to AKI development in critically ill patients.<sup>13</sup> These mechanisms align with the elevated neutrophil counts and NLR observed in AKI patients in both our study and prior research. For instance, Park et al, demonstrated that increased neutrophil counts and reduced lymphocyte counts were significant predictors of AKI in patients undergoing thoracic surgeries.<sup>14</sup>

Similarly, our study found a higher neutrophil count ( $10.2 \pm 4.1 \times 10^3/\mu\text{l}$  vs.  $8.3 \pm 3.7 \times 10^3/\mu\text{l}$ ,  $p=0.002$ ) and a lower lymphocyte count ( $0.8 \pm 0.4 \times 10^3/\mu\text{l}$  vs.  $1.0 \pm 0.5 \times 10^3/\mu\text{l}$ ,  $p=0.007$ ) in the AKI group.

The integration of platelet counts into the N/LP ratio further enhances its predictive value by incorporating a coagulation component. Hong et al demonstrated that platelet activation plays a pivotal role in microvascular congestion and renal ischemia during AKI.<sup>15</sup> The current study supports these findings, with AKI patients showing significantly lower platelet counts compared to non-AKI patients ( $158.9 \pm 63.1 \times 10^3/\mu\text{l}$  vs.  $182.6 \pm 58.4 \times 10^3/\mu\text{l}$ ,  $p=0.011$ ).

The predictive value of the N/LP ratio in AKI has been highlighted in multiple studies. Gameiro et al, identified the N/LP ratio as an independent predictor of AKI, with a significant association even after adjusting for confounders.<sup>11</sup> The study corroborates this finding, with a multivariate-adjusted odds ratio of 1.08 (95% CI 1.04–1.12,  $p<0.001$ ) for the N/LP ratio. Zhang et al conducted a meta-analysis on the NLR in AKI and found it to be a reliable predictor of renal injury.<sup>16</sup> The current study expands on this by incorporating platelet counts, which may provide a more comprehensive assessment of the inflammatory and coagulative responses driving AKI.

Malhotra et al further emphasized the utility of NLR in AKI prediction, particularly in cardiac surgery patients, where systemic inflammation is a significant contributor to renal injury.<sup>17</sup> Similar trends were observed in our study, where the N/LP ratio demonstrated a strong predictive ability with an AUC of 0.804 for AKI detection. This aligns with findings from other cohorts and reinforces the utility of the N/LP ratio in diverse surgical populations.

While the N/LP ratio emerged as the strongest independent predictor in the study, other variables such as age and preoperative eGFR also showed significant associations. Gameiro et al, similarly reported that age, eGFR and intraoperative transfusion were independent predictors of AKI.<sup>11</sup> In contrast, our study did not find intraoperative transfusion to be a significant factor, potentially due to differences in surgical protocols and patient populations. The role of diabetes in AKI prediction was also less pronounced in our study's multivariate analysis (adjusted OR 1.36,  $p=0.41$ ), compared to Gameiro et al who identified it as a significant risk factor (OR 2.04,  $p=0.03$ ).<sup>11</sup>

The AUC of 0.804 reported in our study indicates good predictive accuracy for the N/LP ratio, consistent with findings from prior research. Zhang et al reported a pooled AUC of 0.79 for NLR in their meta-analysis, highlighting its reliability across different clinical settings.<sup>16</sup> The incorporation of platelet counts in the current study may enhance the ratio's predictive accuracy by accounting for coagulation dynamics, as suggested by Hong et al.<sup>15</sup>

The findings of the current study and prior research collectively underscore the importance of systemic inflammation and coagulation in AKI development. The N/LP ratio, as a composite marker, offers several advantages, including simplicity, cost-effectiveness and accessibility in clinical practice. By integrating this marker into perioperative risk assessment protocols, clinicians can identify high-risk patients and implement timely interventions, such as optimizing hemodynamics, minimizing nephrotoxic exposures and ensuring adequate hydration.

However, several limitations need to be addressed. The current study conducted in single centers, which may limit generalizability. Future prospective, multicenter studies with standardized protocols for monitoring inflammatory markers are needed to validate these findings further. Additionally, exploring the utility of the N/LP ratio in other patient populations, such as those undergoing sepsis or trauma-related surgeries, could broaden its applicability.

## CONCLUSION

The current study highlights the significant role of systemic inflammation and coagulation in the development of postoperative AKI following major abdominal surgeries. The N/LP ratio emerged as a robust and independent predictor of AKI, demonstrating strong associations with inflammatory processes driving renal injury. Elevated N/LP ratios were consistently observed in patients with AKI. Other predictors, including advanced age and lower preoperative eGFR, were also significant contributors to AKI risk, further validating their role in perioperative risk stratification. While systemic inflammation, as reflected by elevated neutrophil counts and reduced lymphocyte and platelet counts, plays a central role in AKI pathophysiology, the integration of platelet counts into the N/LP ratio enhances its predictive utility by capturing coagulation dynamics.

The predictive accuracy of the N/LP ratio, with an AUC of 0.804 in our cohort, suggests that it is a reliable and cost-effective marker for identifying patients at risk of AKI. Incorporating the N/LP ratio into routine perioperative risk assessments could facilitate early identification of high-risk patients, enabling timely interventions to mitigate AKI-related complications.

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