

ORIGINAL RESEARCH

CARDIAC INTENSIVE CARE

Comparison of neutrophil-lymphocyte ratio and neutrophil-lymphocyte-platelet ratio in relation to acute kidney injury (AKI) in a cardiac surgery intensive care unit (CICU) patients

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ABSTRACT

Background & objective: Hypoperfusion, ischemia-reperfusion injury, intravascular hemolysis, neurohumoral activation, inflammation, oxidative stress, nephrotoxins, and mechanical factors contribute to the development of Acute Kidney Injury (AKI) following on-pump coronary artery bypass grafting (CABG). Inflammatory biomarkers such as the Neutrophil-Lymphocyte Ratio (NLR) and Neutrophil-Lymphocyte-Platelet Ratio (NLPR) have been proposed as potential markers for postoperative inflammation. Elevated NLR and NLPR values have been associated with AKI and 5-year mortality. This study aims to evaluate whether NLR and NLPR can serve as predictive tools in identifying patients at risk of developing AKI after cardiac surgery.

Methodology: This retrospective analytical study compares the NLR and NLPR with the incidence of AKI in patients post-cardiac surgery in the intensive care unit (ICU) at Adam Malik Hospital, Medan. The study includes all ICU patients who underwent cardiac surgery between January 1, 2023, and December 31, 2023. Data were analyzed using SPSS statistical software.

Results: A significant difference was found in NLR values between the AKI group (16.62 ± 10.2) and the non-AKI group (14.76 ± 12.6), with a p-value of 0.007. The sensitivity was 57%, and specificity was 44%, with a cutoff value of 17.10. Similarly, the NLPR values were significantly different between the AKI group (13.26 ± 8.40) and the non-AKI group (9.9 ± 5.79), with a p-value of 0.013. Sensitivity was 54%, and specificity was 50.8%, with a cutoff value of 18.42.

Conclusions: NLR and NLPR are significantly associated with the occurrence of AKI after cardiac surgery. Both ratios are valuable predictive tools for identifying patients at risk of AKI following surgery.

Abbreviations: ADQI: Acute Dialysis Quality Initiative AKI: Acute Kidney Injury, CABG: Coronary Artery Bypass Grafting, CAD: Coronary Artery Disease, ICU: Intensive Care Unit, NLR: Neutrophil-Lymphocyte Ratio, NLPR: Neutrophil-Lymphocyte-Platelet Ratio,

Keywords: Neutrophil-lymphocyte ratio; Neutrophil-lymphocyte-platelet ratio; Acute kidney injury; Cardiac surgery

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1. INTRODUCTION

Cardiovascular diseases have been associated with high morbidity and mortality rates worldwide. According to data from the World Health Organization (WHO), coronary artery disease (CAD) has been the leading cause of death in the past (2000-2015). In Indonesia, the prevalence of CAD based on medical diagnosis was 1.5% in the 2018 Basic Health Research (Riset Kesehatan Dasar) study. When pharmacological treatment and percutaneous interventions are insufficient for managing CAD, coronary artery bypass graft (CABG) surgery becomes a crucial treatment option for addressing the pathological conditions. Data from 2018 indicate that CABG is one of the most commonly performed thoracic surgeries in Indonesia, accounting for 1.7% of all thoracic surgeries performed.¹⁻³

Post-CABG complications can involve various organ systems, including the cardiovascular, hematologic, and renal systems. One significant renal complication that may arise is parenchymal kidney damage, specifically within the tubular system, which can lead to acute kidney injury (AKI). AKI is characterized by an increase in serum creatinine levels within 48 h or a reduction in urine output within 6 h following surgery.^{4,5}

In a cohort of 506 patients evaluated after CABG, 19.9% developed AKI, significantly increasing the risk of mortality, which can reach up to 60%. The primary cause of renal dysfunction after CABG is linked to the use of cardiopulmonary bypass (CPB) during the on-pump procedure. Prolonged CPB use, renal medullary hypoperfusion, and vasoconstriction during CABG increase the risk of AKI. This is due to the exposure of blood to non-physiological surfaces, hemodilution, and systemic stress response triggered during the procedure. Approximately 2 million patients undergo heart surgery annually, and AKI is a common complication characterized by a sudden decrease in renal function, which manifests as a rapid increase in creatinine levels, reduced urine output, or both. Despite efforts to improve patient outcomes through cardiac surgery, the development of AKI after heart surgery is significantly associated with higher hospitalization costs and elevated mortality rates, both short- and long-term. Studies have also shown that heart surgery-related AKI is closely linked to the development of chronic kidney disease, end-stage renal disease, heart failure, and severe cardiovascular complications in the future.⁶⁻⁸

An additional meta-analysis of 91 observational studies on heart surgery patients published between 2004 and 2014 revealed a similar incidence of AKI, approximately 22.3%. Specifically, patients undergoing coronary artery bypass grafting (CABG) had a lower AKI incidence (19.0%) than those undergoing valve surgery (27.5%) or

aortic surgery (29.0%). A large epidemiological study found that the type of surgery itself significantly impacts the incidence of AKI requiring dialysis after heart surgery, with combined CABG and mitral valve surgery, as well as mitral valve surgery alone, presenting the highest risk. Patients with AKI also had longer hospital stays (15.4 vs. 10.5 days) and extended stays in the intensive care unit (ICU) (2.2 vs. 1.0 days).^{8,9}

Postoperative AKI after CABG can result from hypoperfusion, ischemia-reperfusion injury, hemolysis, neurohormonal activation, inflammation, oxidative stress, nephrotoxins, and mechanical factors. Many studies have discussed the inflammatory biomarkers associated with CABG. Parlar and Saskin (2018) suggested that the neutrophil-lymphocyte ratio (NLR) may serve as an early biopredictor of inflammation after CABG.⁷ Further research has shown that higher NLR quartiles post-surgery have the greatest impact on AKI incidence. Studies by Parlar et al. (2021) and others support the idea that a threefold increase in NLR correlates with the development of AKI after CABG.^{4,7} The NLR reflects two essential immune pathways, with neutrophils acting as markers of non-specific inflammation and lymphocytes regulating the immune response. Given the roles of these leukocyte subtypes, the NLR can be a useful predictive factor in patients undergoing CABG.^{9,10}

In this context, Adam Malik Hospital Medan, a leading heart surgery referral center in North Sumatra, provides valuable insights. In 2022, 44 heart surgeries, including CABG, were performed. Among these, 54.2% underwent CPB. In this study, approximately 83.3% of patients had normal renal function after surgery. Given this context, this study aimed to investigate the relationship between the neutrophil-lymphocyte ratio (NLR) and neutrophil-lymphocyte-platelet ratio (NLPR) and the incidence of AKI in patients undergoing cardiac surgery at Adam Malik Hospital, Medan.¹⁰

2. METHODOLOGY

This retrospective analytical study aimed to compare the neutrophil-lymphocyte ratio (NLR) and the neutrophil-lymphocyte-platelet ratio (NLPR) with the occurrence of Acute Kidney Injury (AKI) in post-cardiac surgery intensive care unit (ICU) patients at Adam Malik Hospital, Medan. The study was conducted at Adam Malik Hospital, Medan, utilizing data from the medical records of patients admitted to the ICU following cardiac surgery between January 1, 2023, and June 30, 2024. The research commenced after receiving approval from the Research Ethics Committee of the Faculty of Medicine, Universitas Sumatera Utara and Adam Malik Hospital, Medan.

Table 1: Comparative Demographic Data and Preoperative Characteristics

Variable		AKI (n = 72)	No AKI (n = 128)	P-value
Gender	Male	30 (41.7)	66 (51.6)	0.179
	Female	42 (58.3)	62 (48.4)	
Age (Yr)		51.78 ± 9.91	49.25 ± 11.18	0.313
Systolic BP (mmHg)		164.39 ± 24.68	163.71 ± 24.22	0.918
Diastolic BP (mmHg)		92.64 ± 13.76	92.64 ± 14.11	1.000
Heart Rate (bpm)		97.75 ± 20.60	101.28 ± 17.66	0.493
Creatinine (mg/dL)		1.55 ± 1.168	1.29 ± 0.90	0.342
Urea (mg/dL)		70.26 ± 53.63	21.25 ± 8.06	0.000
NLR		4.14 ± 4.10	4.07 ± 3.15	0.40
NLPR		9.76 ± 6.7	5.14 ± 4.1	0.27

Data presented as n (%) or Mean ± SD; P < 0.05 considered as significant

The study population consisted of all ICU patients who underwent cardiac surgery during the specified period. The samples were selected based on the inclusion and exclusion criteria. The inclusion criteria were patients aged 18-65 years, who underwent elective cardiac surgery and postoperative ICU care, underwent Cardiopulmonary Bypass (CPB), and had complete medical records. Patients with pre-existing kidney dysfunction or those undergoing hemodialysis prior to surgery, as well as those already receiving intensive care unit (ICU) care before surgery were excluded from the study.

The data collected included serum creatinine levels, complete blood count results, and urine output before and after the surgery. Additionally, the neutrophil-lymphocyte ratio (NLR) and lymphocyte-platelet ratio were calculated to assess the occurrence of AKI based on the Injury, Failure RiskLoss, and End-stage classification. The sampling method used was consecutive sampling, in which subjects were selected from the medical records of patients who met the study criteria.

The study began after receiving ethical approval from the Research Ethics Committee of the Faculty of Medicine, Universitas Sumatera Utara and Adam Malik Hospital, Medan. The researcher then conducted a comprehensive data compilation of patients who received post-cardiac surgery ICU care at Adam Malik Hospital in Medan. Data retrieval involved accessing and reviewing the medical records from the hospital's medical records department. The key data collected included serum creatinine levels, complete blood count results, and urine output before and after surgery. The researcher then calculated the neutrophil-lymphocyte ratio (NLR) and

lymphocyte-platelet ratio (LPR) to assess the occurrence of Acute Kidney Injury (AKI) based on the RIFLE criteria. Finally, the data were tabulated for further analysis.

Data analysis was conducted using SPSS software after data collection. The Shapiro-Wilk test was used to check the normality of the data, with numeric data presented as the mean (SD) and median (range). Categorical data are presented as frequencies and percentages, and statistical analysis for categorical data was performed using the chi-square test. The confidence interval used in this study was 95%, with a P < 0.05 considered statistically significant.

The study was conducted after obtaining ethical approval and followed standard clinical procedures routinely applied in patient care at the hospital. All procedures involved in this study were part of normal medical practice and were ethically conducted in accordance with established guidelines.

3. RESULTS

This study investigated the relationship between the neutrophil-lymphocyte ratio (NLR) and the occurrence of Acute Kidney Injury (AKI) in intensive care unit (ICU) patients following cardiac surgery at Adam Malik Hospital, Medan. Data collection was performed on all ICU patients who underwent cardiac surgery between January 1, 2023, and December 31, 2023, yielding a total sample size of 200. The characteristics of the research subjects are displayed in the Table 1.

The distribution of AKI incidence revealed that 72

Table 2: Comparison of NLR and NLPR Postoperatively

AKI Incidence	AKI (n = 72)	No AKI (n = 128)	P-value
Platelet ()	231.64 ± 121.30	367.11 ± 164.45	0.001
Neutrophil ()	12.44 ± 6.16	12.16 ± 11.07	0.040
Lymphocyte ()	0.735 ± 0.545	3.80 ± 2.72	0.001
Creatinine (mg/dL)	1.78 ± 1.068	1.29 ± 0.90	0.342
Urea (mg/dL)	80.46 ± 73.83	21.25 ± 20.96	0.001
NLR ()	16.62 ± 10.2	14.76 ± 12.6	0.007
NLPR ()	13.26 ± 8.40	9.9 ± 5.79	0.001
CPB Duration (min)	153.22 ± 43.2	92.32 ± 10.31	0.001

Data presented as Mean ± SD; P < 0.05 considered as significant

Table 3: Comparative NLR and NLPR values before and after surgery

Group		AKI	No AKI
NLR	Before surgery	4.14 ± 4.10	8.1 ± 4.07
	After surgery	8.1 ± 4.07	14.76 ± 12.6
NLPR	Before surgery	9.76 ± 6.7	5.14 ± 4.1
	After surgery	13.26 ± 8.40	9.9 ± 5.79

Data presented as Mean ± SD; P < 0.05 considered as significant

Table 4: Sensitivity and specificity of NLR and NLPR in predicting AKI

Variable	Cut-off Value	AUC	P-value	Sensitivity	Specificity
NLR	17.10	57.7%	0.007	57%	44%
NLPR	18.42	54.1%	0.001	54%	50.8%

(36%) participants developed AKI; 128 (64%) did not experience AKI.

The preoperative characteristics of the study population are summarized in Table 1, showing variables such as age, sex, systolic and diastolic blood pressure, heart rate, creatinine level, urea level, NLR, and NLPR. The average age of patients in the AKI group was 51.78 ± 9.91 years, while the non-AKI group had an average age of 49.25 ± 11.18 years. A review of the literature suggests that older age is associated with a reduced ability of the kidneys to adapt to hemodynamic disturbances. Additionally, women are more likely to develop AKI than men, according to the KDIGO guidelines.

Systolic blood pressure was similar between the AKI (164.39 ± 24.68 mmHg) and non-AKI groups (163.71 ± 24.22 mmHg), as was the diastolic blood pressure

(92.64 ± 13.76 mmHg vs. 92.64 ± 14.11 mmHg).

These results align with those of Kim et al., who showed that hypertension and cardiovascular diseases are strong predictors of AKI. Platelet count, and lymphocyte counts were significantly lower in AKI group groups (P < 0.05). Creatinine levels were equivalent in both groups (P = 0.342). Urea levels in the AKI group were significantly higher than those in the non-AKI group, indicating that elevated urea levels are associated with an increased risk of AKI (Table 1).

Postoperative data revealed that platelet counts were significantly lower in the AKI group than in the non-AKI group (P = 0.001). This finding supports the study by Jansen et al., which showed platelet dysfunction in patients with AKI. Neutrophil counts were significantly higher in the AKI group (P = 0.04), while lymphocyte counts were significantly lower in the AKI group (P = 0.001). The NLR and NLPR were also significantly higher in the AKI group, indicating stronger inflammatory responses in patients with AKI than in those without (Table 2).

Table 3 shows that the NLR increased more significantly in the AKI group than in the non-AKI group after surgery, reflecting a stronger inflammatory response in patients who developed AKI postoperatively. This suggests that NLR may serve as a potential biomarker for monitoring AKI risk after cardiac surgery.

Similarly, Table 3 shows a more significant increase in NLPR in the AKI group after surgery, suggesting that the combination of neutrophils, lymphocytes, and platelets may be a more comprehensive indicator of AKI risk than NLR alone.

The cut off values for NLR and NLPR were 17.1 and 18.42, respectively. NLR showed higher sensitivity (57%) than NLPR (54%), whereas NLPR had a higher specificity (50.8%) than NLR (44%). These findings suggest that both NLR and NLPR have potential as biomarkers for predicting AKI after cardiac surgery, with NLPR offering a more comprehensive view of the inflammatory and hemostatic responses involved in AKI pathogenesis than NLR (Table 4).

4. DISCUSSION

Acute Kidney Injury (AKI) is a critical syndrome characterized by a sudden decline in the glomerular filtration rate. It is a common and significant health issue worldwide, affecting both developed and developing countries, regardless of economic status. AKI is associated with high morbidity, mortality, and healthcare costs. The Acute Dialysis Quality Initiative (ADQI) defines AKI within the consensus framework of Risk, Injury, Failure, Loss, and End-Stage Kidney Disease (RIFLE). This condition is particularly prevalent in hospitalized patients, affecting approximately 10-15% of all hospitalized individuals and exceeding 50% in ICU patients, highlighting its clinical significance and the need for effective early detection and management strategies.^{11,12}

In this study, we compared the neutrophil-lymphocyte ratio (NLR) and the neutrophil-lymphocyte-platelet ratio (NLPR) as early predictors of AKI in post-surgical patients in the ICU following heart surgery at Adam Malik Hospital, Medan. The pathophysiology of postoperative AKI is multifactorial, involving hypoperfusion, ischemia-reperfusion injury (IR injury), oxidative stress, inflammation, and neurohormonal activation. Surgical trauma, particularly during laparotomy and cardiac surgeries, induces inflammatory responses and increases the activity of the renin-angiotensin-aldosterone and sympathetic nervous systems, resulting in vasoconstriction and impaired renal perfusion.¹³⁻¹⁵

The study found that patients with AKI had a significantly higher average NLR (16.62 ± 10.2) than those without non-AKI patients, suggesting that an elevated NLR may serve as a reliable marker of systemic stress and inflammation in AKI. This finding aligns with previous studies that demonstrated a positive correlation between high NLR values and AKI development. Bu X et al. found that AKI developed in 59% of patients

diagnosed with sepsis in the ICU, with an average NLR of 17 ± 4 , indicating a significant relationship between AKI and elevated NLR.^{16,17} Similarly, Hyun et al. observed significant increases in NLR among patients undergoing renal replacement therapy, further supporting the predictive value of NLR in critical care settings.^{18,19}

In addition to NLR, the NLPR, which includes platelet counts, was significantly higher in patients with AKI than in those without non-AKI patients. This increase in NLPR reflects not only the inflammatory response but also platelet activation, which plays a critical role in AKI pathogenesis. Platelets contribute to microvascular injury and are involved in leukocyte recruitment and endothelial dysfunction, which exacerbate renal damage.^{13,14} The findings of this study are consistent with those of Koo et al., who demonstrated that an elevated NLPR, especially following cardiac surgery, can predict AKI in postoperative patients.²⁰

Moreover, we observed that preoperative NLR values were higher in patients who subsequently developed AKI after surgery. This suggests that pre-existing inflammatory conditions and an elevated NLR may predispose patients to greater inflammatory responses, increasing the risk of AKI. These results are in line with previous studies, including those by Bu Xi et al., which highlighted the predictive value of NLR as an independent risk factor for AKI, particularly in sepsis and shock patients.¹² High preoperative NLR has been shown to be predictive of worse outcomes, including AKI and other complications, underscoring its role as a biomarker for monitoring patient risk.^{21,22}

The study also examined the relationship between RNL and AKI and found that the difference in NLR and NLPR between the AKI and non-AKI groups became more evident over time, particularly after the third day post-surgery, possibly due to the delayed apoptosis of lymphocytes. Neutrophils, which are part of the initial inflammatory response, increase rapidly after surgical trauma, leading to endothelial damage, leukocyte accumulation, and further exacerbation of the inflammatory response. This is supported by previous findings that emphasize neutrophils' role in the acute phase of inflammation and their potential as biomarkers for early detection of AKI.¹⁷

The data in this study suggest that both NLR and NLPR are useful tools for the early detection and monitoring of AKI in post-cardiac surgery patients. These ratios reflect a balance between pro-inflammatory and anti-inflammatory responses, with NLR increasing due to neutrophil proliferation and lymphocyte apoptosis during acute inflammation. An elevated NLR indicates a higher degree of systemic stress and inflammation, both of which are closely associated with AKI progression.

Furthermore, platelet activation, as evidenced by the increased NLPR, underscores the contribution of platelet-driven inflammation to the development of renal injury.

In conclusion, NLR and NLPR appear to be valuable biomarkers for predicting AKI, especially in patients undergoing major surgeries, such as cardiac surgery. An increase in these ratios indicates the extent of systemic inflammation and provides insight into the pathophysiology of AKI. However, further research is needed to validate these findings in a broader population and refine these markers to improve the sensitivity and specificity of AKI prediction.

5. CONCLUSION

This study concluded that both the neutrophil-lymphocyte ratio (NLR) and the neutrophil-lymphocyte-platelet ratio (NLPR) are significantly associated with the incidence of Acute Kidney Injury (AKI) in ICU patients following cardiovascular surgery at Adam Malik Hospital. The findings suggest that these ratios may serve as useful biomarkers for the early detection and monitoring of AKI in post-cardiac surgery patients, indicating the role of inflammation and immune responses in AKI pathophysiology.

6. Data availability

Numerical data generated in this study is available with the corresponding author, and can be provided on request

7. Ethical considerations

Ethics approval and consent to participate were obtained from the relevant authorities. Permission for this study was obtained from the Ethics Committee of Universitas Sumatera Utara and Haji Adam Malik General Hospital (No. 1450/KEPK/USU/2024).

8. Funding

No external or industry funding was involved in this study.

9. Competing interests

The authors declare no conflict of interest in this study.

10. Author contributions

DAGH, ELRS, HK: Conception and design.

ELRS, HK: Administrative support.

DAGH: Provision of study materials or patients.

All authors took part in collection and assembly of data, data analysis and interpretation, manuscript writing and final approval of the manuscript.

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