RESEARCH PAPER

Risk Factors for Acute Kidney Injury Following Cardiac Surgery: A Retrospective Cohort Study

Yonarti[1]*, Haerani Rasyid[1], Jayarasti Kusumanegara[2], Andi Adil[3], Syakib Bakri[1], Idar Mappangara[1], Hasyim Kasim[1], Sitti Rabiul Zatalia Ramadhan[1], Nasrum Machmud[1], Akhyar Albaar[1], Khadijah Hasyim[1], Achmad Fikry[1] and Andi Alfian Zainuddin[4]

[1]*Department of Internal Medicine, Faculty of Medicine Hasanuddin University, Makassar, Indonesia*
[2]*Department of Thoracic, Cardiac, and Vascular Surgery, Faculty of Medicine Hasanuddin University, Makassar, Indonesia*
[3]*Department of Anesthesiology and Intensive Care, Faculty of Medicine Hasanuddin University, Makassar, Indonesia*
[4]*Department of Public Health and Community Medicine, Faculty of Medicine Hasanuddin University, Makassar, Indonesia*
Corresponding Author Mail: *yonartithamrin@gmail.com*

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ABSTRACT

Introduction: Cardiac surgery encompasses procedures such as coronary artery bypass grafting, valve repair or replacement, surgery for congenital heart defects, and heart transplantation. One frequent complication is acute kidney injury, which arises due to various factors.

Methods: This retrospective study at Wahidin Sudirohusodo Hospital, Makassar, Indonesia, began in October 2025, using data from January 2025. Patients who had open-heart surgery without prior renal replacement therapy were selected via consecutive sampling. Data analysis employed SPSS version 25 and the CART model, with significance at $p<0.05$.

Results: The study involved 89 participants, with around 30.3% experiencing acute kidney injury (AKI). Participants over 50 years old were 2.76 times more likely to develop AKI compared to those younger than 50, a result that was statistically significant ($p = 0.02$). Individuals with a previous history of CKD faced a 13.86 times greater risk of AKI than those without chronic kidney disease (CKD), which was also statistically significant ($p = 0.01$). Additionally, patients who had undergone CABG were 2.72 times more prone to developing AKI than those who had non-CABG surgeries, with this association being statistically significant ($p = 0.04$). Factors such as sex, history of hypertension, diabetes mellitus, use of IABP, and CPB duration did not show statistical significance. The CART model identified CKD as the primary risk factor for post-cardiac surgery AKI, with an accuracy score of 86.52% and AUC of 86.46%.

Conclusions: Through statistical analysis using the CART model, significant risk factors for AKI after cardiac surgery were identified. These include being over 50 years old ($p=0.02$), having a history of CKD ($p=0.01$), and undergoing coronary artery bypass grafting (CABG) ($p=0.04$). Consequently, patients with these risk factors who are undergoing CABG should be carefully monitored during the perioperative period to prevent AKI after cardiac surgery.

Keywords: Acute kidney injury, Cardiac surgery, Perioperative risk factors, Chronic kidney disease

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INTRODUCTION

Cardiac surgery encompasses a range of operations aimed at repairing, replacing, or restoring the function of the heart and its major blood vessels. These procedures include coronary artery bypass grafting (CABG), valve surgeries, operations for congenital heart defects, and heart transplants.[1] Since the success of the first open heart surgery by John Gibbon in 1953 with the assistance of a cardiopulmonary bypass (CPB) machine, various cardiac surgery techniques have continued to develop rapidly, both in procedural aspects, technology, and perioperative approaches.[2] Data on the incidence of cardiac surgery varies between countries due to differences in health care facilities and developments in technology and procedures.[3] A study shows that global heart surgery data in 2020 was 123.2/100,000 population per year (with a range of 27.3/100,000 population in South Korea - 271.5/100,000 population in the United States), where CABG procedures were 36.7/100,000, valve surgery was 30.8/100,000, and congenital heart disease surgery was 7.9/100,000.[4]

**Author for Correspondence: Yonarti*

Undergoing cardiac surgery can result in several postoperative complications, with the most common being postoperative bleeding, acute kidney injury (AKI), mesenteric ischemia, atrial fibrillation, cardiogenic shock, and respiratory distress. The incidence of AKI following cardiac surgery varies from 5% to 45%, with about 1–2% of cases necessitating renal replacement therapy.[5] Acute kidney injury following cardiac surgery is characterized by a rapid decline in kidney function after the procedure, indicated by increased serum creatinine levels or decreased urine output. As per the 2012 Kidney Disease Improving Global Outcomes (KDIGO) guidelines, Acute Kidney Injury (AKI) is defined as a quick reduction in kidney function occurring within hours to days. It is identified by an increase in the absolute serum creatinine level of ≥ 0.3 mg/dL (≥ 26.5 µmol/L) within 48 hours, or an increase of ≥ 1.5 times the baseline value within 7 days, and/or urine output of < 0.5 mL/kg per hour lasting more than 6 hours.[6] Previous research has shown that the incidence of acute kidney injury requiring dialysis after isolated CABG procedures is approximately 1.4%. This rate significantly increases in patients who undergo both CABG and valve surgery. Mortality rates for cardiac surgery without AKI range from 1% to 8%; however, when AKI occurs, the mortality rate increases more than fourfold. The need for renal replacement therapy is associated with a mortality rate of up to 63%.[7]

The onset of acute kidney injury linked to cardiac surgery (CSA-AKI) is complex and influenced by various factors, such as diminished renal blood flow, damage from ischemia and reperfusion, inflammation, oxidative stress, hemolysis, and processes associated with cardiopulmonary bypass.[8] Identification of risk factors and early diagnosis of AKI remains a challenge. Most of the knowledge regarding risk factors for AKI following cardiac surgery is derived from retrospective observational research. These risk factors are categorized into preoperative, intraoperative, and postoperative stages.[9] Numerous factors have been recognized as contributing to the risk of renal dysfunction before surgery. Chertow et al.[8] indicated that the independent risk factors for developing dialysis-dependent renal failure include the type of valve surgery performed, existing chronic kidney disease (CKD), previous cardiac surgeries, congestive heart failure, a left ventricular ejection fraction (LVEF) below 35%, chronic obstructive pulmonary disease (COPD), high blood pressure, the use of an intra-aortic balloon pump (IABP), and peripheral vascular disease. The underlying mechanisms of cardiac surgery–associated acute kidney injury (CSA-AKI) are not fully understood and are believed to be complex, involving factors such as decreased blood flow to the kidneys, renal microembolization, ischemia–reperfusion injury, hemolysis, systemic inflammation, oxidative stress, and mechanisms related to cardiopulmonary bypass (CPB).[10]

Additional risk factors include valve surgery, the use of an intra-aortic balloon pump (IABP), peripheral vascular disease, a left ventricular ejection fraction (LVEF) below 35%, pulmonary rales, chronic obstructive pulmonary disease (COPD), and systolic blood pressure either below 120 mmHg or above 160 mmHg. Recent research has identified several more risk factors that occur preoperatively, intraoperatively, and postoperatively. Previous studies have identified several intraoperative factors that can predict acute kidney injury associated with cardiac surgery (CSA-AKI). These factors encompass prolonged durations of cardiopulmonary bypass (CPB), extended aortic cross-clamp times, increased operative durations, and the necessity for blood transfusions during surgery. In addition, postoperative complications such as sepsis and other infectious events are strongly associated with AKI development.[11] Our research sought to identify and analyze the risk factors linked to AKI in cardiac surgery, based on our experiences at Wahidin Sudirohusodo Hospital. This included factors present before, during, and after the surgery. By identifying these risk factors, it is hoped that preventive measures can be taken to prevent AKI after cardiac surgery.

METHODS

Study Design and Population

This study, employing a retrospective cohort design, was conducted at Wahidin Sudirohusodo Hospital in Makassar, Indonesia. Initiated in October 2025, the research focused on adult patients who underwent open-heart surgery between January and December 2025, identified through a retrospective review of medical records. A total of 89 patients were selected using a consecutive sampling method. Eligible participants were those aged 18 years or older who had cardiac surgery with CPB and had complete preoperative and postoperative renal function data documented in their medical records. Individuals with end-stage kidney disease, a history of renal replacement therapy before surgery, or incomplete serum creatinine data were excluded from the study.

In this study, cardiac surgery encompassed open-heart operations that necessitated CPB, such as CABG, valve surgeries, procedures for congenital heart defects, and other significant cardiac interventions. The minimum sample size required was calculated using a standard formula, resulting in a determination of 89 participants.

Data Collection and Variable Definitions

Hospital medical records were used to retrospectively gather clinical and perioperative information. The data collected encompassed demographic details, existing health conditions, factors during surgery, and outcomes after surgery. The study examined independent variables such as age, gender, hypertension, diabetes mellitus, CKD, the duration of cardiopulmonary bypass, the use of an intra-aortic balloon pump (IABP), and the type of cardiac surgery performed. The primary focus was on the occurrence of postoperative AKI.

Postoperative acute kidney injury (AKI) was determined according to the KDIGO 2012 guidelines. This involves a serum creatinine increase of at least 0.3 mg/dL within 48 hours, a rise in serum creatinine to 1.5 times the baseline level within 7 days, or a urine output of less than 0.5 mL/kg/hour for at least 6 hours post-surgery. Patients were classified as having postoperative AKI if these criteria were met within 7 days following cardiac surgery.

Hypertension was defined as a systolic blood pressure of 140 mmHg or higher and/or a diastolic blood pressure of 90 mmHg or more, as documented in medical records or through a previous diagnosis of hypertension. Diabetes mellitus was identified by a prior diagnosis, the use of antidiabetic medications, or an HbA1c level of 6.5% or higher. CKD was characterized by persistent abnormalities in kidney structure or function lasting at least three months, including an estimated glomerular filtration rate (eGFR) below 60 mL/min/1.73 m^2 or indicators of kidney damage such as albuminuria or structural irregularities observed in imaging studies.

Cardiac surgeries were divided into two categories: CABG and non-CABG procedures. The CABG category encompassed surgeries involving only coronary artery bypass grafting or CABG in conjunction with other operations. In contrast, non-CABG surgeries comprised valve surgeries, operations for congenital heart defects, aortic surgeries, and other open-heart procedures that did not involve coronary artery bypass grafting. CPB duration was defined as the total duration of cardiopulmonary bypass in minutes, measured from initiation until termination of CPB support. IABP use was defined as documented preoperative or perioperative insertion of an intra-aortic balloon pump for circulatory support.

Statistical Analysis

Data analysis was performed using SPSS version 25. Categorical variables were presented as counts and percentages, while continuous variables were displayed as either mean ± standard deviation or median with interquartile range, depending on their distribution. The Chi-square test was applied to explore relationships between categorical variables. For continuous variables, the independent t-test was used for data with a normal distribution, and the Mann–Whitney U test was employed for data that were not normally distributed. Odds ratios (ORs) with 95% confidence intervals (CIs) were calculated to evaluate the strength of associations between risk factors and postoperative AKI.

Moreover, a Classification and Regression Tree (CART) model was employed to identify the primary predictors of postoperative AKI and to classify patients according to their risk profiles. The model's performance was evaluated using metrics such as accuracy, sensitivity, specificity, Cohen’s kappa coefficient, and the area under the receiver operating characteristic curve (AUC). Throughout the analysis, a p-value of less than 0.05 was considered statistically significant.

RESULTS

Characteristics of Research Subjects

In this research, 55 male and 34 female participants were included. Among them, 50.6% were under the age of 50, while 49.4% were over 50. Hypertension was present in 41.6% of the participants, and 24.7% had diabetes. Most participants did not have CKD (93.3%) and did not use IABP (66.3%). The most common CPB duration exceeded 100 minutes (59.6%), with non-bypass surgeries being the most prevalent (76.4%). Additionally, 30.3% of the participants experienced AKI. (Table 1)

Analysis of the Risk Factors of AKI in Cardiac Surgery

The analysis of risk factors associated with postoperative AKI is presented in Table 2. Individuals over 50 years old had a 2.76 times greater likelihood of developing AKI compared to those under 50, with this association being statistically significant ($p = 0.02$). Male patients were 1.71 times more likely to develop AKI than female patients, although this difference was not statistically significant ($p = 0.19$). Those with hypertension faced a 1.47 times increased risk of AKI compared to those without hypertension, but this was not statistically significant ($p = 0.27$). Similarly, patients with diabetes had a 1.44 times higher risk of AKI than those without diabetes, yet this finding was not statistically significant ($p = 0.32$). Patients with a history of CKD were 13.86 times more likely to develop AKI compared to those without CKD, and this association was statistically significant ($p = 0.01$). The use of an IABP and CPB duration were not significantly associated with AKI. Patients undergoing CABG surgery were 2.72 times more likely to develop AKI compared to those undergoing non-CABG procedures ($p = 0.04$) (Table 2).

Analysis of the Risk Factors of AKI in Cardiac Surgery – Classification and Regression Tree (CART) Model

The Classification and Regression Tree (CART) model illustrating the hierarchy of risk factors for postoperative AKI is shown in Figure 1. Overall, the model demonstrated good performance, with an accuracy score of 86.52% and an AUC of 86.47% (Figure 1). However, sensitivity was lower than specificity (62.96% vs. 96.77%), indicating that the model was more effective in identifying patients without AKI than detecting all patients with AKI. A Kappa score of 65.19% indicated a fairly strong classification agreement.

Among patients with CKD, there seemed to be an elevated risk of developing AKI. When individuals with CKD underwent CABG surgery, every patient in this category was identified as having AKI. Conversely, for CKD patients who had non-CABG surgeries, those with hypertension were more likely to experience AKI, whereas those without hypertension generally fell into the non-AKI category. This indicates that the combination of CKD with either CABG or hypertension is closely linked to a heightened risk of AKI.

In patients without CKD, the next most important factor is age. In the age group ≥50 years, further stratification is determined by gender. Female patients ≥50 years old without CKD tend to be classified as non-AKI. On the other hand, for male patients aged 50 and above, factors such as the type of surgery, the duration of CPB, hypertension, and the use of IABP further affect the risk of AKI. In men aged 50 and older who undergo surgeries other than CABG, the likelihood of developing AKI seems to rise when CPB lasts less than 100 minutes in the presence of hypertension, and when CPB exceeds 100 minutes without hypertension. In CABG surgery, the risk of AKI increases especially when CPB duration is >100 minutes and without IABP. Conversely, when CPB is <100 minutes or IABP is present, patients are more likely to be classified as non-AKI.

In patients without CKD and aged <50 years, the type of surgery again plays a significant role. The non-CABG group at this age group is predominantly non-AKI, thus appearing to be the lowest-risk group. In the CABG group, subsequent risk was influenced by diabetes mellitus (DM) and IABP. CABG patients aged <50 years who did not have diabetes and did not use IABP tended to be in the AKI group, while patients with diabetes or with IABP were more likely to be in the non-AKI group.

DISCUSSION

The research involved 89 adult patients who underwent cardiac surgery at Wahidin Sudirohusodo Hospital, with 55 (61.8%) being male and 34 (38.2%) female. The findings revealed that 30.3% of these patients developed AKI following their cardiac procedures. Previous studies have indicated that the occurrence of AKI post-cardiac surgery ranges from 20% to 40%, influenced by factors such as patient demographics, the specific surgical techniques employed, and the diagnostic criteria applied. Strauß, et al[12] Research indicated that 25% of individuals undergoing cardiac surgery developed acute kidney injury related to the procedure, and among these, 33% experienced a persistent form of this condition, which was linked to unfavorable outcomes. Recent research has shown that acute kidney injury associated with cardiac surgery (CSA-AKI) affects about 20–30% of individuals undergoing such procedures. This incidence varies based on patient characteristics, the complexity of the surgery, and the diagnostic criteria applied.[10,13] The AKI prevalence of 30.3% observed in this study aligns with findings from various previous studies on AKI occurrence following cardiac surgery. One possible factor affecting the AKI incidence in this study is that it was conducted at a tertiary referral hospital. Patients undergoing cardiac surgery at such facilities often present with more complex diseases and additional health conditions compared to the general population, which may elevate the risk of developing postoperative AKI.

The objective of this research was to assess the risk factors linked to AKI in adult patients who underwent cardiac surgery at Wahidin Sudirohusodo Hospital. Analysis showed that age >50 years was significantly associated with AKI (OR 2.76; p=0.02). This finding corroborates several previous studies that suggest age is a strong predictor of AKI in cardiac surgery. As people age, the kidneys undergo structural changes, such as a reduction in the number of functional nephrons, glomerular sclerosis, and diminished renal vascular autoregulation. Aging is linked to both structural and functional changes in the kidneys, including a decreased nephron reserve, compromised renal autoregulation, and heightened vulnerability to hypoperfusion and inflammatory stress during cardiac surgery. Additionally, older adults often have a higher incidence of comorbidities like atherosclerosis, hypertension, and diabetes mellitus, which further elevate renal vulnerability and the risk of AKI. In this study, men were found to be 1.71 times more likely to develop AKI following cardiac surgery compared to women, although this difference was not statistically significant (p = 0.19). Research results have varied; certain studies indicate that women might face a greater risk because of their smaller body size and heightened exposure to contrast doses or hemodilution. While other studies have found a higher risk for men due to the prevalence of comorbidities. Recent research has shown that the difference in AKI incidence between the sexes is not always consistent, and other factors such as intraoperative hemodynamic perfusion and comorbidities are often more dominant in determining the occurrence of AKI after cardiac surgery.[14]

In this study, while patients with hypertension exhibited a 1.47 times greater likelihood of experiencing AKI following cardiac surgery, the link was not statistically significant (p = 0.27). Hypertension can increase renal vulnerability through chronic endothelial dysfunction, arterial stiffness, and reduced microcirculation, which impair renal autoregulation and increase the risk of ischemia-reperfusion injury and oxidative stress during cardiopulmonary bypass procedures and intraoperative hemodynamic fluctuations. High blood pressure is linked to heightened inflammation and reduced kidney blood flow, both of which contribute to the development of AKI. However, a recent multicenter analysis showed that although hypertension may increase the risk of kidney injury, its influence as an independent predictor varies after accounting for intraoperative factors and other comorbidities.[12,15,16]

In this study, while patients with diabetes exhibited a 1.44 times greater likelihood of experiencing AKI following cardiac surgery, this link was not statistically significant (p = 0.32). Diabetes can increase the kidney's susceptibility to injury through chronic hyperglycemia, which causes endothelial dysfunction, microvascular disease, oxidative stress, and systemic inflammation, thereby impairing renal autoregulation and increasing susceptibility to ischemia-reperfusion injury during cardiopulmonary bypass procedures. These metabolic and vascular disturbances also lead to glomerular hyperfiltration and tubular hypoxia, which exacerbate injury from hemodynamic stress during surgery. While diabetes is frequently linked to an increased risk of AKI following cardiac surgery, its role as an independent predictor might diminish when other intraoperative factors and comorbidities are considered.[17–19]

In this study, individuals with a history of CKD were found to have a 13.86 times higher likelihood of experiencing AKI following cardiac surgery, with this link being statistically significant ($p = 0.01$). The results suggest that CKD serves as a significant and standalone risk factor for AKI following cardiac surgery. From a pathophysiological perspective, individuals with CKD possess a reduced nephron reserve, experience endothelial dysfunction, uremia, oxidative stress, and impaired renal perfusion autoregulation. These conditions render the kidneys more vulnerable to hypoperfusion, ischemia-reperfusion, and the systemic inflammatory response associated with cardiopulmonary bypass. Earlier research has also indicated that AKI in CKD patients is linked to a poorer prognosis, including higher mortality rates and a swift progression to advanced renal failure.[20,21]

This research suggested that using an intra-aortic balloon pump (IABP) might provide a protective effect against acute kidney injury (AKI), with an odds ratio of 0.45, although this result was not statistically significant ($p = 0.10$). Numerous studies have reported an increased risk of AKI in patients using IABP. Previous research has indicated that employing an intra-aortic balloon pump is associated with a higher likelihood of acute kidney injury following cardiac surgery.[10] In that particular study, the use of IABP was more common among patients with severe hemodynamic issues, indicating that the increased risk of AKI likely reflects the severity of the patient's illness rather than being a direct result of the IABP itself. Previous research has shown that IABP is frequently used in patients with cardiogenic shock or low cardiac output syndrome, both of which are clinical conditions independently associated with a higher risk of acute kidney injury following cardiac surgery.[10,22] Conversely, numerous studies have indicated that IABP can physiologically benefit renal perfusion. Earlier hemodynamic research revealed that IABP assistance can enhance cardiac output and systemic perfusion, potentially improving renal blood flow and decreasing the likelihood of renal hypoperfusion in critically ill cardiac patients.[23] Improved renal perfusion could theoretically help maintain kidney function in patients with unstable hemodynamics. This mechanism may explain why IABP use appeared to have a protective effect in this study, although it was not statistically significant. However, this study focused more on hemodynamic effects and organ perfusion and did not directly evaluate AKI as the primary outcome. Therefore, variations in results between studies are likely influenced by differences in patient population characteristics, indications for IABP use, and confounding by indication, where IABP is more frequently used in patients with more severe clinical conditions. Although IABP support may improve systemic hemodynamics and renal perfusion in selected patients, current evidence remains inconclusive regarding its direct renoprotective effect following cardiac surgery.[10] Individuals undergoing coronary artery bypass grafting (CABG) face a 2.72-fold increased likelihood of developing acute kidney injury (AKI) compared to those having non-CABG surgeries, with this association being statistically significant ($p = 0.04$). Recent research has shown that patients who undergo CABG, especially when it involves complex cardiac procedures, are at a notably higher risk of experiencing postoperative AKI than those in other cardiac surgery groups.[20]

This study also implemented CART model as a way to identify patients risk factors of developing AKI. CART model is one of logistic regression models used in machine learning break the dataset into smaller and meaningful groups. This model analyzed all the variables based on the baseline characteristics and determine the significance. With the accuracy score of 86.52% and AUC of 86.47%, the model performed well. However, the lower score of sensitivity compared to the specificity (62.96% vs. 96.77%) indicates that the model was significantly better at identifying patients who did not have AKI than at detecting all patients who did have AKI. The CART model identified CKD as the leading risk factor for AKI following cardiac surgery, with additional clinical and operative factors such as older age, the type of CABG surgery, hypertension, extended CPB duration, and the use of IABP also contributing. Therefore, patients who require the closest attention are those with CKD, especially if undergoing CABG, as well as those without CKD but aged ≥50 years with a less favorable combination of operative factors. However, this interpretation also requires caution because some terminal nodes have very small sample sizes, for example, n=1, n=2, or n=3. Although these patterns continue to offer valuable clinical insights, findings in smaller branches should be viewed as preliminary and require validation through a larger sample size or additional analysis. Ryan, et al[24] used machine learning model to identify post-cardiac surgery AKI based on the onset, and found that the model has a pretty high accuracy and ROC-AUC level (86% and 95% respectively) for predicting stage 2 or above AKI in 48 hours and found the most impactful variables are static baseline parameters, hemodynamic parameters, and previous medications. With the same purpose, Omar, et al[25] compared multiple algorithms of logistic regression and found the highest accuracy and AUC being the Gradient Boosted Tree (88.66% and 94.61% respectively). There are very few studies that applied CART model to predict the risk factors of post-heart surgery AKI, so this study can serve as pilot research to show the utilization of CART model as one of the methods. This research highlights the critical need for thorough preoperative risk assessments, especially for older patients and those undergoing CABG surgery. To confirm these results, additional studies with multivariate approaches, larger participant groups, and more comprehensive intraoperative variables are necessary.

This research has a few limitations that need to be recognized. Firstly, the retrospective design conducted at a single center might restrict the applicability of the results to different populations and healthcare environments. Second, although the sample size fulfilled the minimum calculated requirement, several subgroup analyses and terminal nodes within the CART model contained relatively small sample sizes, which may reduce statistical stability and widen confidence intervals for certain variables. To minimize potential bias related to sparse data, appropriate statistical approaches, including Fisher's exact test for variables with low expected frequencies, were applied where necessary.

In addition, some potentially important perioperative variables such as detailed hemodynamic parameters, vasopressor dosage, intraoperative transfusion volume, postoperative infection severity, and serial biomarker measurements were not available due to limitations of retrospective medical record data. In this research, the CART analysis is primarily intended as a means for exploration and hypothesis generation, rather than serving as a definitive predictive tool. Nonetheless, the model demonstrated strong discriminatory power with satisfactory accuracy and AUC values, suggesting its potential value for early perioperative risk evaluation. In conclusion, since only a limited number of prior studies have assessed CART-based methods for forecasting AKI related to cardiac surgery, it is necessary to conduct external validation with larger multicenter cohorts before recommending wider clinical use.

CONCLUSION

In this study, the incidence of postoperative AKI following cardiac surgery was determined to be 30.3%. Key risk factors for developing AKI after surgery included being over 50 years old, having pre-existing chronic kidney disease (CKD), and undergoing CABG. The Classification and Regression Tree (CART) model further identified CKD as the most critical predictor of postoperative AKI, emphasizing the need for preoperative kidney evaluation and perioperative risk assessment. These findings underscore the importance of enhanced perioperative monitoring and optimization, particularly for high-risk patients undergoing CABG, to reduce the frequency and adverse outcomes of AKI associated with cardiac surgery.

DECLARATIONS

Ethics Approval and Consent to Participate

This study was approved by the Research Ethics Committee of the Faculty of Medicine, Hasanuddin University (Approval No. 952/UN4.6.4.5.31/PP36/2025). The requirement for written informed consent was waived due to the retrospective design of the study and the use of anonymized medical record data. All procedures were conducted in accordance with the Declaration of Helsinki and institutional ethical standards.

Consent for Publication

Not applicable.

Availability of Data and Materials

The dataset supporting the conclusions of this article is publicly available in the Zenodo repository: https://doi.org/10.5281/zenodo.20558558. The deposited dataset contains anonymized variables used in the present analysis. Additional materials are available from the corresponding author upon reasonable request.

Competing Interests

The authors declare that they have no competing interests.

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Authors' Contributions

Y conceived and designed the study. HR, JK, AA, SB, IM, HK, SRZR, NM, AA, KH, AF, and AAZ contributed to data collection, analysis, interpretation of data, and manuscript revision. All authors read and approved the final manuscript.

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