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Original Article

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Risk Factors and Outcomes of Acute Kidney Injury After Cardiac Surgery: A Retrospective Observational Single-Center Study

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Abstract

Background: Acute kidney injury (AKI) following cardiac surgery is a well-described phenomenon, usually associated with hemodynamic changes ultimately leading to ischemic injury to the kidneys. In this study, we assessed the occurrence of AKI in a cohort of patients undergoing elective cardiac surgery at a single center.

Methods: Patients undergoing elective cardiac surgery (coronary artery bypass grafting (CABG) and/or valve repair) between the years 2016 and 2022 were retrospectively included in the study.

Results: During the study, 167 patients underwent CABG, valve replacement, or both procedures. The majority were male (85.0%). Post-operative AKI was observed in 27.5% of patients, with 2.4% requiring continuous renal replacement therapy (CRRT)/dialysis. The majority of AKI cases were staged as Kidney Disease: Improving Global Outcomes (KDIGO) stage 1. Among patients needing CRRT/dialysis, 1.8% recovered renal function within 3 months, with 0.6% experiencing 30-day mortality. In univariate analysis, factors associated with AKI included older age (P = 0.003), severe anemia (P < 0.0001), pre-operative creatinine elevation (P < 0.0001), complex surgeries (P < 0.0001), blood product transfusion (P < 0.0001), longer cross-clamp (XC) and cardiopulmonary bypass (CPB) times (P < 0.0001), and inotropes usage (P < 0.0001). Classical risk factors like diabetes mellitus (DM) and hypertension did not show significant differences. The majority of these factors (severe anemia, age, pre-operative creatinine, post-operative inotrope usage, and cross-clamp times) were consistently significant (P < 0.05) in logistic regression analysis.

Conclusion: Post-operative AKI following cardiac surgery is frequent, with significant associations seen especially with pre-operative anemia. Future investigations focusing on the specific causes of anemia linked to AKI development are essential, considering the high prevalence of hemoglobinopathy traits in our population.

Keywords: Acute kidney injury; Cardiac surgery; CABG; Valve replacement; KDIGO

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Introduction

Acute kidney injury (AKI) is the rapid decline of the glomerular filtration rate (GFR), leading to significant impairment of renal function [1]. It has a serious medical, social, and financial impact on patients' lives [2]. There are numerous non-modifiable risk factors for AKI such as hypertension, advanced age, hyperlipidemia, and peripheral vascular disease. Uniquely among surgical procedures, cardiac surgery has some properties that increase the risk of AKI such as cardiopulmonary bypass (CPB), cross-clamping (XC) time, and volumes of exogenous blood product transfusion and alongside high doses of vasopressors [1, 3].

The aforementioned makes AKI a common complication of cardiothoracic surgery with significant short- and long-term survival implications, even for those who do not progress to renal failure [4, 5]. Studies indicate that up to 30% of cardiac surgery patients experience AKI, with around 3% requiring dialysis [3]. There is some evidence suggesting that the risk factors for AKI occurrence after cardiac surgery include elevated pre-operative serum creatinine (SCr) alongside prolonged CPB [6].

The risk, injury, failure, loss of kidney function, and end-stage renal failure (RIFLE) classification indicates AKI severity based on changes in SCr relative to the baseline condition,

Table 1. KDIGO Severity Staging for AKI

Stage	eGFR/serum creatinine criteria	Urine output criteria
Stage 1	1.5 - 1.9 times baseline OR ≥ 26.5 µmol/L increase within 48 h	≤ 0.5 mL/kg/h for 6 - 12 h
Stage 2	2 - 2.9 times baseline	≤ 0.5 mL/kg/h ≥ 12 h
Stage 3	Three times baseline OR Increase in serum creatinine ≥ 354 µmol/L OR Initiation of renal replacement therapy (e.g., dialysis)	≤ 0.3 mL/kg/h ≥ 24 h OR Anuria for ≥ 12 h

eGFR: estimated glomerular filtration rate; KDIGO: Kidney Disease: Improving Global Outcomes.

and its association with short-term mortality after cardiac surgery has been validated previously. Recently, a modification of this classification by staging the acute need for renal replacement therapy (RRT) in the failure stage F - entailing SCr × 3 baseline or GFR decrease > 75% - improved predictive accuracy for AKI in patients undergoing cardiac surgery, being superior to Acute Kidney Injury Network (AKIN) criteria if there is no correction of SCr for fluid balance, which leads to over-diagnosis of AKI [4]. Current standards established by the Acute Dialysis Quality Initiative (ADQI), AKIN, and KDIGO groups underscore the importance of diagnosing AKI based on abnormal SCr levels and urine volume alterations [3].

In this study, we assessed the incidence, various risk factors, and outcomes of renal impairment associated with cardiac surgery in a single-center setting.

Materials and Methods

All consecutive patients who underwent elective CABG, valve replacement, or a combination of both at Prince Mohammed bin Naser Hospital (PMNH) in Jazan, Saudi Arabia, were included in the study, from November 2016 to October 2022. Patients aged < 18 years old, patients on dialysis pre-operatively, and patients operated emergently were excluded from the study for a more homogenous patient cohort. The data were collected retrospectively through chart review for pre-, intra-, and post-operative data alongside mortality data alternatively when last known alive. Ethical approval was granted through the Jazan Health Ethics Committee, Ministry of Health, Saudi Arabia (approval number: 22105). All patients were put on CPB as per institutional protocol. This study was conducted following the Declaration of Helsinki.

The baseline labs with which the comparisons were made were drawn, as per protocol, 1 day before surgical intervention. Therefore, the pre-operative creatinine level was considered baseline for all comparisons. The presence of post-operative AKI was defined as per the KDIGO criteria presented in Table 1. This involves SCr elevation ≥ 26.5 µmol/L within 48 h or SCr increase by ≥ 1.5 times baseline within 7 days or urine volume < 0.5 mL/kg/h for 6 h. Three severity stages are present within the criteria, and these are detailed in Table 1.

Normal distribution was not assumed when performing the statistical analysis. Median values for the continuous data were analyzed alongside the interquartile range (IQR), while absolute numbers with percentages were presented for categorical data. Mann-Whitney U tests were used to compare continuous variables, while cross-tabular analysis involving Chi-square tests (χ^2) was used with Fisher's exact test reported for categorical variable comparisons. Where appropriate, logistic regression with odds ratio (OR) was reported. P-value below 0.05 was considered significant. Analyses were performed using SPSS software version 25 (IBM Corp, Armonk, New York).

Results

During the study period, a total of 167 patients (majority male, 142 (85.0%)) underwent only CABG (114 (68.3%)), valve replacement (43 (25.7%)) or procedure involving both (10 (6.0%)). Pre-operatively, creatinine was 81 (68 - 102) µmol/L, urea was 5.5 (4.3 - 7.4) and hemoglobin was 11.7 (10.0 - 13.2) g/dL. Detailed pre-operative patient characteristics are presented in Table 2, while detailed intra- and post-operative data are presented in Table 3.

Table 2. Pre-Operative Patient Characteristics

Patient characteristics	Data (% or IQR)
Gender (male)	142 (85.0)
Age (years)	57 (44 - 64)
BMI	26.3 (23.5 - 30.2)
Diabetes	88 (52.7)
Hypertension	94 (56.3)
Ischemic heart disease	119 (71.3)
Smoking (active or ex-smoker)	54 (32.3)
Previous CVI	11 (6.6)
Congestive heart failure	8 (4.8)
Creatinine (µmol/L)	81 (68 - 102)
Urea (mmol/L)	5.5 (4.3 - 7.4)
Hemoglobin (g/dL)	11.7 (10.0 - 13.2)

BMI: body mass index; CVI: cerebrovascular insult; IQR: interquartile range.

Table 3. Intra- and Post-Operative Patient Characteristics

Patient characteristics	Data (% or IQR)
Type of surgery	
CABG	114 (68.3)
Valve replacement	43 (25.7)
Both	10 (6.0)
Cardiopulmonary bypass duration (min.)	80 (67 - 105)
Cross-clamping time (min.)	55 (42 - 69)
Blood products transfused?	69 (41.3)
AKI post-operatively	46 (27.5)
CRRT/dialysis	4 (2.4)
ICU or CCU stay?	128 (76.6)
Duration (days)	5 (3 - 8)
Post-operative inotropic support	72 (43.1)
Death	5 (3.0)
30-day mortality	4 (2.4)

AKI: acute kidney injury; CABG: coronary artery bypass grafting; CCU: cardiac care unit; CRRT: continuous renal replacement therapy; ICU: intensive care unit; IQR: interquartile range.

As per the KDIGO criteria, post-operative AKI developed in 46 (27.5%) patients, of which four (2.4%) required continuous renal replacement therapy (CRRT)/dialysis. Per the KDIGO staging, the majority (27 (16.2%)) of the patients with AKI were defined as stage 1, while 12 (7.2 %) and seven (4.2%) were defined as stage 2 and 3, respectively. Of those requiring CRRT/dialysis, three (1.8%) recovered with regards to renal function, returning to baseline creatinine within 3 months, while one (0.6%) suffered 30-day mortality. No patient required long-term (> 3 months) dialysis post-operatively.

Comparing the patients fulfilling AKI definition versus those who did not, AKI patients were, as a group, older (P = 0.003), more severely anemic (P < 0.0001), had higher pre-operative creatinine elevation (P < 0.0001), and had undergone more complex surgery (19.6% vs. 0.8% underwent combined procedures; P < 0.0001). AKI patients also had a higher proportion of blood products transfused (P < 0.0001), longer XC times (P < 0.0001), longer CPB times (P < 0.0001), and a higher proportion of inotropes usage post-operatively (P < 0.0001). Classical risk factors for AKI such as diabetes and hypertension did not differ between both groups (P > 0.05). These comparisons are detailed in Table 4. Performing logistic regression, the significant correlation persisted (P < 0.05) for pre-operative hemoglobin, age, pre-operative creatinine, post-operative inotrope usage and XC times, as presented in Table 5.

Thirty-day mortality occurred in four (2.4%) patients, of which all fulfilled the AKI criteria. Three patients (1.8%) were staged as stage 2 AKI and one (0.6%) as stage 3 per the KDIGO criteria.

Discussion

In this study, we analyzed the incidence of post-operative AKI after common cardiothoracic procedures, alongside risk factors for its development and its association with post-operative mortality. There are certain details that need to be highlighted and appreciated.

In comparison to multiple previous studies [7-9] exploring AKI post-cardiac surgery, roughly a quarter of the patients in our cohort had pre-operative anemia near the transfusion limit - if considered as per the most liberal transfusion cut-offs [10] - of 10 g/dL, while over 50% were diabetics and our patient cohort was relatively “young” with roughly 25% of our patients

Table 4. Univariate Comparison Between AKI Versus Non-AKI Patients

Factor predisposing for AKI	AKI (N = 46)	Non-AKI (N = 121)	P-value
Hemoglobin (g/dL)	9.9 (8.9 - 11.9)	12.0 (10.8 - 13.9)	< 0.0001
Age (years)	65 (40 - 72)	56 (44 - 62)	0.003
Diabetes	21 (45.7)	67 (55.4)	0.300
Hypertension	24 (52.2)	70 (57.9)	0.601
Pre-operative creatinine (µmol/L)	97.5 (77.2 - 127)	77.0 (67.0 - 93.5)	< 0.0001
Pre-operative urea (mmol/L)	7.2 (5.4 - 9.4)	5.2 (4.2 - 6.3)	< 0.0001
Type of surgery			< 0.0001
CABG	25 (54.3)	89 (73.6)	
Valve	12 (26.1)	31 (25.6)	
Both	9 (19.6)	1 (0.8)	
Post-operative inotropes	43 (93.5)	29 (24.0)	< 0.0001
Intra-operative blood products transfused?	32 (69.9)	37 (30.6)	< 0.0001
Cross-clamp time (min)	68.5 (57.3 - 98.0)	47.0 (38.0 - 61.0)	< 0.0001
Cardiopulmonary bypass time (min)	100.5 (80.5 - 119.5)	72.5 (63.0 - 90.0)	< 0.0001

AKI: acute kidney injury.

Table 5. Logistic Regression Analysis for the Development of Post-Operative AKI Based on Significant Results Obtained in Univariate Analysis Detailed in Table 4

Factor predisposing for AKI	OR (95% confidence interval)	P-value
Hemoglobin (g/dL)*	0.480 (0.279 - 0.826)	0.008
Age (years)*	1.101 (1.021 - 1.186)	0.012
Pre-operative creatinine (µmol/L)*	1.037 (1.000 - 1.076)	0.048
Pre-operative urea (mmol/L)*	0.986 (0.752 - 1.293)	0.921
Type of surgery[a]	4.387 (0.797 - 24.149)	0.089
Post-operative inotropes[b]	0.022 (0.002 - 0.242)	0.002
Intra-operative blood products transfused?	0.459 (0.069 - 3.047)	0.420
Cross-clamp time (min)*	1.099 (1.009 - 1.197)	0.030
Cardiopulmonary bypass time (min)*	1.039 (0.987 - 1.094)	0.142

[a]Type of surgery: CABG, valve repair or both in increasing level of complexity. [b]Post-operative inotropes: odds ratio for NO inotropic support. If YES inotropic support then OR 46.08 (4.136 - 513.3), P = 0.002. *Continuous variables in the analysis. AKI: acute kidney injury; OR: odds ratio.

being below 45 years of age. These factors, overall, suggest that our cohort has a high "pre-operative" morbidity despite the cases being elective in nature. In spite of this, the AKI rate was roughly similar to previously mentioned studies [7-9].

One single factor that deserves special consideration is the presence of profound pre-operative anemia, especially in patients with AKI. It was surprising that such a large portion of our patients had Hgb < 10 g/dL, especially in the AKI group but even in the non-AKI group. Several factors may be implicated in this, including the high incidence of carrier state for hemoglobinopathies - specifically sickle-cell and thalassemia traits - in KSA (20% for each condition), with known potential for co-inheritance of these conditions [11, 12]. Several relevant issues exist in this specific group, such as the presence of elevated risk of hemolysis leading to increased oxidative stress [13], elevated risk for development of microthrombi alongside the risk for renal papillary necrosis, which are all factors that cause this specific patient group to be at an elevated risk for AKI [14]. These issues are further compounded in the patients who suffered AKI in our cohort, as they required longer XC times which in effect increased the oxidative stress through increased risk for hypothermia, hypoperfusion, and hemolysis [15]. Elevated free hemoglobin was associated with the increased rate of AKI post-cardiac surgery [16], which further strengthens the hypothesis that hemolysis in itself is a significant and independent risk factor for AKI development.

Previous studies have highlighted the importance of diabetes mellitus (DM) as a risk factor for AKI post-cardiac surgery [17-19]. This, however, was not reproduced by our data given the lower (albeit non-significant) DM rate in AKI patients versus those who did not have AKI. Our findings corroborate those of investigators from Greece [20] and China [21]. Such a finding may suggest that DM, although being an important risk factor for AKI, may not be the most significant risk factor for AKI's development in a population with such a high DM rate, and other risk factors, such as pre-operative anemia and complex surgery, may actually have a more significant impact on AKI development.

To further strengthen the notion of more complex procedures increasing the risk of AKI, our cohort suffering from AKI had longer procedures, longer CPB times, and a higher rate of inotropic support as compared to non-AKI cases. This was especially apparent for the XC times and the usage of post-operative inotropes, when performing the regression analysis. In addition to this, almost all patients undergoing combined procedures suffered from AKI post-operatively. These findings are in harmony with previous literature [22, 23] and are a reflection of a more profound ischemic insult suffered by all organs as a whole and specifically by the kidneys.

Several limitations need to be addressed in our study. The small number of patients included makes it difficult to draw firm conclusions albeit certain trends, such as profound pre-operative anemia, are well illustrated in our study. Related to this, the absence of the causes for anemia, including detailed hematinics such as corpuscular volume (MCV), in our cohort is another limitation, especially given the aforementioned high prevalence of hemoglobinopathy traits in our population. An added limitation is the lack of detailed data on the medications which the patients included were taking prior to surgery. This is important due to previous studies implicating medications commonly prescribed to such patients, including angiotensin converting enzyme inhibitors (ACEi) [24, 25] in the development of post-operative AKI after cardiac surgery. To supplement the previous finding, the lack of data on pre-operative iodinated contrast load and angiography timing is another limitation, given the association of angiography interval to post-operative AKI development [26]. Furthermore, the absence of long-term mortality data, given the lack of a unified mortality registry in KSA makes it difficult to ascertain mortality especially if occurring outside of the hospital.

In conclusion, AKI post-cardiac surgery is relatively common, with profound pre-operative anemia and more complex surgical procedures being associated with its occurrence. Further studies with regard to specific causes of anemia being associated with AKI development are pertinent, especially given the high population rate of hemoglobinopathy traits in our region.

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Conflict of Interest

None to declare.

Informed Consent

Not applicable.

Author Contributions

Study conception and design: Mostafa Mohrag, Mohammed Abdulrasak, Waseem Borik, Omar Oraibi, Mohammed Ali Madkhali, Atheer Alshamakhi, and Mohammed Somaili. Data collection: Atheer Alshamakhi, Nada Ageeli, Roaa Abu Allah, Maryam Al Hammadah, Somaya Saabi, Reema Moafa, Atheer Darraj, and Moath Farasani. Analysis and interpretation of results: Mostafa Mohrag, Mohammed Abdulrasak, Waseem Borik, Omar Oraibi, Mohammed Ali Madkhali, Sameer Alqassmi, and Ali Someili. Draft manuscript preparation: Mostafa Mohrag, Mohammed Abdulrasak, and Waseem Borik. All authors reviewed the results and approved the final version of the manuscript.

Data Availability

The data supporting the findings of this study are available from the corresponding author upon reasonable request.

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