

Prevalence and predictors of acute kidney injury after cardiac surgery: A single-centre retrospective study in Qatar

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Abstract

Background: Despite modern advances in intensive care management, the incidence of acute kidney injury (AKI) continues to be high. This study was performed to characterise the predisposing factors impacting the development of AKI, and secondary outcomes among patients undergoing cardiac surgery.

Methods: In this single-centre retrospective study, AKI was defined according to the Acute Kidney Injury Network. Patients were divided into two groups: those without AKI (Group I, 544 patients) and those with AKI (Group II, 181 patients). Patients' admission and outcome data were analysed.

Results: The patients' mean age was 53±12 years, and 25% of the patients had AKI. The two groups were matched with regard to age, sex, body mass index (BMI), history of diabetes, and history of hypertension. Group II had a considerably higher additive EuroSCORE and lower ejection fraction than Group I. The lengths of ventilation, ICU, and hospital stay were significantly higher in Group II than I. Group II had a significantly higher incidence of postoperative atrial fibrillation and mortality rate than Group I. Interestingly, AKI was significantly more notable in Asians than in Arabs. A total of 1.9% of patients required renal replacement therapy. The independent risk factors for AKI in our population were the additive EuroSCORE, time of cardiopulmonary bypass, low postoperative haemoglobin level, postoperative white cell count, and total amount of blood loss.

Conclusion: Cardiac surgery-induced AKI is highly prevalent and prognostically fundamental. Management options targeting treating preoperative anaemia, shortening cardiopulmonary bypass time, and reducing red blood cell transfusion may help to prevent this complication.

Background

Acute kidney injury (AKI) is one of the most prevalent complications following cardiac surgery, especially in patients undergoing cardiopulmonary bypass (CPB).^[1] AKI prolongs the postoperative stay, in turn causing increased use of hospital resources. Despite recent evolution of perioperative care in cardiac surgery patients, AKI remains a common complication.^[2] The reported incidence of AKI after cardiac surgery varies from 5% to 31%.^[3-10] The demand for renal replacement therapy (RRT) in this population ranges from 1% to 5% of patients and is associated with increased postoperative morbidity and mortality.^[11] Patients who develop AKI are prone to an increased hospital stay, higher mortality rates, and greater use of resources, all of which are more pronounced in patients requiring RRT.^[12]

Patient-related risk factors for the evolution of AKI after cardiac surgery include cardiogenic shock requiring treatment with an intra-aortic balloon pump (IABP), total circulatory arrest, left main disease, peripheral vascular disease, diabetes mellitus, chronic obstructive pulmonary disease, deteriorated left ventricular function, the need for emergency surgery, and renal insufficiency.^[13] The known procedure-related risk factors after cardiac surgery include the aortic cross-clamp (ACC) time, CPB time, haemolysis, and haemodilution.^[14]

Multifactorial mechanisms of the development of AKI after cardiac surgery have been proposed, including renal autoregulation impairment secondary to a low intraoperative mean arterial blood pressure below the limits of autoregulation and generation of free haemoglobin and iron from the haemolysis that occurs during CPB, which predisposes patients to ischaemic kidney injury.^[13] Rhabdomyolysis has also been described as a possible cause of AKI after cardiac surgery.^[15]

Other possible causes of AKI include a systemic inflammatory response secondary to contact of blood ingredients with the synthetic surface of the CPB circuit, ischaemia-reperfusion injury, and Gram-negative endotoxaemia.^[13,16]

Aim of this work

The prevalence and predictors of AKI after cardiac surgery have been infrequently evaluated in the Gulf area. Therefore, this study was performed to identify the prevalence and predictors of postoperative AKI in adults undergoing cardiac surgery using CPB in the state of Qatar.

Methods

Study design and assessments

This single-centre retrospective study was conducted during a 3-year period (October 2011 to October 2014) in a 12-bed cardiothoracic intensive care unit (ICU) of a tertiary hospital in Qatar. The ethics committee at Hamad Medical Corporation approved this study (reference number 15094/15), and informed consent was waived for all patients enrolled in this study. However, all study data were maintained anonymously. The exclusion criteria included patients who require RRT, either dialysis or transplantation, which defines pre-existing end-stage renal disease,^[17] age of <18 years, aortic dissection repair surgery, off-pump cardiac surgery, and death within 24 hours postoperatively. We evaluated 836 patients who underwent cardiac surgery during the study duration; of these, 725 patients were eligible for enrolment in the study.

The following data were recorded for all patients: age, sex, weight, height, body mass index, history of diabetes or hypertension, type of surgery, length of anaesthesia, CPB time, ACC time, utilisation of vasopressors and inotropes, EuroSCORE, preoperative anaemia (defined as a haemoglobin level of <12 g/dl and <13 g/dl for women and men, respectively, according to the World Health Organisation),^[18] time interval between coronary angiography and surgery, time interval between recent myocardial infarction (MI) and surgery, preoperative ejection fraction, preoperative glycosylated haemoglobin, preoperative blood urea nitrogen (BUN) concentration, preoperative serum creatinine concentration, preoperative international normalised ratio (INR), preoperative platelet count, cardiogenic shock and use of IABP, postoperative serum creatinine concentration, postoperative BUN concentration, peaked postoperative white blood cell (WBC) count within first 60 hours, total blood loss, total blood transfusion, rates of re-exploration and readmission to the cardiothoracic ICU, and rate of AKI development.

The outcome variables included the length of mechanical ventilation (LOV), length of stay in the ICU (LOS_{ICU}), length of stay in the hospital (LOS_{hosp}), postoperative atrial fibrillation, and the patients' need for RRT. Dendrite Clinical Systems (London, UK) were used to retrieve these data.

Outcome definitions

The primary outcome was the diagnosis of AKI in the entire patient population. With reference to the Acute Kidney Injury Network definition, AKI was defined as an acute (≤ 48 hours) deterioration in the renal functions, with an absolute increase in the serum creatinine concentration of ≥ 0.3 mg/dl (26.4 μ mol/l) or an increase of $\geq 50\%$ (1.5-fold from baseline).^[19] The secondary outcome measures were the LOV, LOS_{ICU}, and LOS_{hosp}. Based on the presence of AKI, patients were divided into two groups: those with and without AKI.

Statistical analysis

Normally distributed continuous variables are presented as mean \pm standard deviation, and skewed variables are presented as median (interquartile range). The patients were divided into two groups based on the presence of AKI. The groups were compared using parametric tests, nonparametric tests, or the chi-square test as appropriate. A p value of ≤ 0.05 was considered to indicate statistical significance. Correlations of log AKI were first examined by single-variable linear or logistic regression and presented as the non-adjusted coefficient and 95% confidence interval. Factors with a p value of ≤ 0.05 by single-variable regression analyses were included in a multivariable linear regression model, presented as the adjusted coefficient with 95% confidence interval. Multivariable logistic regression modelling was carried out to validate the adjusted combinations of the measured perioperative variables with the AKI threshold. Statistical analysis was performed using SPSS software (version 22; IBM Corp., Armonk, NY, USA).

Results

During the study period (October 2011 to October 2014), 836 patients underwent cardiac surgery. After patient selection according to the preset exclusion criteria, 725 patients were enrolled in the study (*figure 1*). A total of 181 (25%) patients had AKI. Fourteen patients (1.9%) received postoperative RRT in the hospital. The patients' mean age was 53 ± 12 years, and the patients were predominantly male ($n=649$, 89.5%) (*table 1*). Both study groups were matched with regard to age, BMI, preoperative hypertension, diabetes, preoperative use of angiotensin-converting enzyme inhibitors, and angiotensin receptor blockers (*table 2*).

The following preoperative risk factors were significantly different between the two groups according to univariate analysis: the additive EuroSCORE, preoperative WBC count, preoperative BUN concentration, and ejection fraction (*table 2*). In conjunction with previous risk factors, we found the following preoperative factors to be significantly different between the two groups: atrial fibrillation, anaemia, and IABP (*table 2*).

The duration between the onset of MI and cardiac surgery was significantly different between the two groups. We found

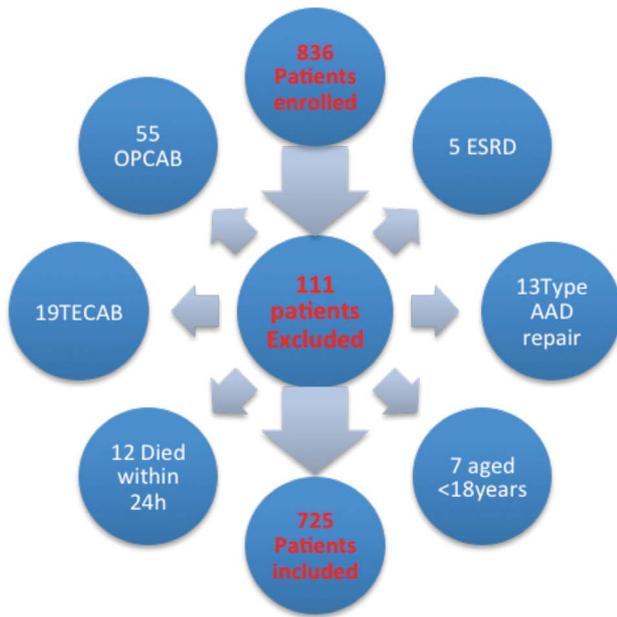


Figure 1. Number of patients enrolled at current study with exclusion

ESRD = end-stage renal disease; AAD = type A aortic dissection; TECAB = total endoscopic coronary artery bypass; OPCAB = off pump coronary artery bypass

that patients who developed a recent MI within the first 30 days were more liable to develop AKI. Urgency and ethnicity were significantly different between the two groups. Among intraoperative risk factors, the CPB time, ACC time, lowest haematocrit on CPB, and anaesthesia time were significantly different between the groups. The transfusion variables were also significantly different (table 3).

The LOV, LOS_{ICU}, and LOS_{hosp} were significantly higher in the AKI group, with a higher incidence of postoperative atrial fibrillation (table 3). Multivariate logistic regression analysis demonstrated that the additive EuroSCORE, preoperative BUN concentration, recent MI, CPB time, lowest haematocrit on CPB, lowest postoperative haematocrit, and total blood loss were independent predictors of AKI (table 4).

Discussion

The key findings of this study are as follows. First, many variables may precede AKI. Second, AKI is a common cause of morbidity and mortality after cardiac surgery and occurred in 25% of the present cohort; additionally, 1.9% of the study population required RRT. Third, a high WBC count was associated with AKI development.

Results in the context of previous studies

Among the clinical predictors of AKI, we found several independent risk factors including the additive EuroSCORE, preoperative BUN concentration, recent MI, CPB time, lowest haematocrit on CPB, lowest postoperative haematocrit, and total blood loss during the first 48 hours. All of these were also identified in previous studies.^[20-24]

Table 1. Description of the studied group

Variable	Number	Minimum	Maximum	Mean±SD
Age	725	19	85	53±12
BMI (kg/m ²)	725	14.5	51.9	27±5
Creatinine (µmol/l)	725	32	152	97.1±60.1
Ejection fraction, %	720	20	70	49.6±10.2
Additive EuroSCORE	717	0	22	4.1±2.9
Preoperative BUN (mmol/l)	725	1.8	19.7	5.8±2.8
Preoperative serum creatinine (µmol/l)	725	32.0	286.0	91.6±60.8
CPB time (min)	725	29	364	120.2±48.3
ACC time (min)	675	0	251	76.4±37.2
Lowest HCT on CPB (%)	725	16.2	35.7	25.9±3
Total blood loss in first 48 hours	725	50.0	11,400.0	1027±918
Total PRBCs transfusion (units)	725	0.00	49.00	2.5±4.2
Total FFP transfusion (units)	725	0.00	16.00	0.6±1.7
Peaked 36-60 h postoperative WBCs (10 ³)	725	3.90	35.00	13.2±5.2
Lowest postoperative HCT (%)	725	18.60	42.00	25±2.7
LOV (hours)	725	2	449	14±38
LOS _{hosp} (days)	725	5	151	35.1±30.6
LOS _{ICU} (days)	725	1	72	2.6±3.8

Figures are numbers or mean ± standard deviation. BMI = body mass index; BUN = blood urea nitrogen; CPB = cardiopulmonary bypass; ACC = aortic cross clamp; HCT = haematocrit; PRBCs = packed red blood cells; FFP = fresh frozen plasma; WBCs = white blood cells; LOV = length of mechanical ventilation; LOS_{hosp} = length of stay in hospital; LOS_{ICU} = length of stay in intensive care unit

Some authors found a significant increment in the incidence of AKI when the time from coronary angiography to surgery was ≤5 days, and they recommended postponing cardiac surgery for at least 5 days after coronary angiography.^[25,26] Similarly, using univariate analysis we found a high incidence of AKI within 5 days after coronary angiography. This was not in agreement with the study conducted by Moulton et al.,^[27] who did not find an association between coronary angiography and deterioration of postoperative renal function.

Preoperative or intraoperative use of an IABP was considered to be a risk factor for AKI in the present study, which is in agreement with previous studies.^[20-22] Furthermore, we found that the relationship among preoperative anaemia, red blood cell transfusion, and AKI was statistically significant, which is in accordance with the results obtained by Karkouti et al.^[20] in 2009. They found that association of anaemia preoperatively and red blood cell transfusions perioperatively were strongly associated with AKI.

Karkouti et al.^[20] found that surgical re-exploration after cardiac surgery was considered to be a risk factor for the development of AKI, which is consistent with our retrospective data. In 2014, Kandler et al.^[24] found that AKI was independently associated with increased mortality after cardiac surgery, which is also in agreement with the results obtained in the current study.

We found that neither diabetes mellitus nor hypertension showed any predictive value for the development of AKI. Our

Table 2. Preoperative risk factors univariate analyses

Variable (Total number =725)	No AKI 544(75%)	AKI 181 (25%)	P value
Age	52.43±10.6	54.09±10.5	0.13
Gender			
Male	490 (90.1)	159 (87.8)	0.40
Female	54 (9.9)	22 (12.2)	
BMI	27±5	27±6	0.11
Additive EuroSCORE	4±2	6±4	0.00
Ethnicity			
Asian	337 (61.9%)	92 (50.8)	
Arab	169 (31.1)	77 (42.5)	
African	32 (5.9)	9 (5)	0.04
Western	6 (1.1)	3 (1.7)	
Preoperative MI			
No MI	255 (46.9)	82 (45.3)	
MI 1-30 days	121 (22.2)	61 (33.7)	
MI 31-90 days	87 (16)	14 (7.7)	0.03
MI >90 days	81 (14.9)	24 (13.3)	
Cardiogenic shock	5 (0.9)	12 (6.6)	0.000
IABP	9 (1.7)	15 (8.3)	0.000
Ejection fraction <40	63 (11.7)	36 (19.9)	0.008
DCAS ≤5 days	49 (9.7)	40 (26.7)	0.001
Preoperative AF	23 (4.2)	25 (13.8)	0.000
PVD	16 (2.9)	4 (2.2)	0.795
COPD	8 (1.5)	6 (3.3)	0.126
Hypertension	342 (63.1)	110 (60.8)	0.596
Diabetes type I	49 (9)	21 (11.6)	0.502
Diabetes type II	164 (30.1)	57 (31.5)	
Preoperative anaemia	148 (27.2)	72 (39.8)	0.002
Preoperative BUN ≥ 6 (mmol/L)	157 (28.9)	92 (50.8)	0.001
Preoperative serum creatinine ≥120 (micromole/L)	32 (5.9)	26 (14.4)	0.001
HbA1c >8 (%)	132 (28)	42 (26.8)	0.837
ACE-ARB	311 (57.2)	110 (60.8)	0.434
Urgency			0.001
Elective	372 (68.2)	92 (50.8)	
Urgent	157 (28.9)	67 (37)	
Emergency	15 (2.8)	22 (12.2)	

Figures are numbers (%) or mean ± standard deviation. AKI = acute kidney injury; BMI = body mass index; MI = myocardial infarction; IABP = intra-aortic balloon pump; DCAS = difference between coronary angiography and surgery; AF = atrial fibrillation; PVD = peripheral vascular disease; COPD = chronic obstructive pulmonary disease; BUN = blood urea nitrogen; Hb = haemoglobin; ACE-ARB = angiotensin-converting inhibitors - angiotensin receptor blockers

data were close to those from the study by Lopez-Delgado et al. where diabetics comprised only 10% of the patients who suffered or were at risk of AKI; however, the same group found that 67.5% of the AKI study population had hypertension. We tend to operate at a younger age where hypertension may not be fully established; the mean age in our study was 53±12 years, in comparison with Lopez-Delgado's cohort which had a mean age of 67.7 ± 9.8.^[28]

Table 3. Intraoperative risk factors and postoperative outcome (univariate analyses)

Variable (Total number =725)	No AKI 544(75%)	AKI 181 (25%)	P value
Procedure description			
CABG	412 (75.7)	105 (58.0)	
Single valve	78 (14.3)	29 (16)	
CABG + valve	53 (9.7)	20 (11)	
DVR	0 (0)	12 (6.6)	0.001
VSD	1 (0.2)	2 (1.1)	
Anaesthesia time(Hours)	5.7±1.3	6.5±1.5	
CPB (min)	110±40	150±58	0.000
ACC (min)	70±31	96±45	0.000
Lowest HCT on CPB	26±3	24±3	0.000
Intraoperative urine output	905±400	891±413	0.697
Inotropic support			
Dopamine	48 (8.9)	24 (13.3)	0.86
Adrenaline	76 (14)	35 (19.3)	0.095
Noradrenaline	63 (11.7)	36 (19.9)	0.008
Dobutamine	8 (1.5)	6 (3.3)	0.126
IABP	19 (3.5)	29 (16)	0.000
Intraoperative PRBCs (units)	1.5±2	5.2±6.9	0.001
ICU PRBCs (units)*	1 (0-18)	2 (0-49)	0.001
FFP (units)*	0.00 (0-8)	0.0 (0-16)	0.001
Cryoprecipitate (units)*	1 (0.2)	1 (0.6)	0.52
Highest serum creatinine (mmol/L) micromole/L	90±26	151±85	0.000
Peaked 36-60 h postoperative WBCs	12.5±5	15.2±5.3	0.000
Total blood loss (ml)	884±613	1445±1410	0.001
Lowest postoperative HCT (%)	25.4±2.7	23.4±2.1	0.001
Postoperative arrhythmia			
AF	57 (10.5)	54 (29.8)	
CHB	3 (0.6)	6 (3.3)	0.001
SVT	3 (0.6)	2 (1.7)	
VT	1 (0.2)	3 (1.7)	
LOS _{ICU} (days)*	2 (1-72)	3 (1-40)	0.001
LOV (hours)*	6 (2-449)	10.5 (2.5-406)	0.001
LOS _{hosp} (days)*	6 (5-74)	8.5 (5-151)	0.001
Reoperation within 24h	25 (4.6)	43 (23.8)	0.001
Readmission To ICU	9 (1.7)	13 (7.2)	0.001
VAP	5 (0.97)	2 (1.1)	0.8
In hospital mortality	3 (0.6)	8 (4.4)	0.001

Figures are numbers (%), median (maximum-minimum)*or mean ± standard deviation. AKI = acute kidney injury; CABG = coronary artery bypass graft; DVR = double valve replacement; VSD = ventricular septal defect; CPB = cardiopulmonary bypass; ACC = aortic cross clamp; HCT = haematocrit; IABP = intra-aortic balloon pump; PRBCs = packed red blood cells; FFP = fresh frozen plasma; WBCs = white blood cells; AF = atrial fibrillation; CHB = complete heart block; SVT = supraventricular tachycardia; VT = ventricular tachycardia; LOS_{ICU} = length of stay in intensive care unit; ; LOV length of mechanical ventilation; LOS_{hosp} = length of stay in hospital ;VAP = ventilator associated pneumonia

In another review article by Shin et al., the authors identified the potential risk factors for cardiac surgery-induced AKI to include anaemia, ischaemic reperfusion, CPB, and use of aprotinin but

Table 4. Risk factors associated with acute kidney injury: a multivariate logistic regression analysis

Variable	OR	95% C.I.	P value
Additive score	1.15	1.05-1.27	0.004
Preoperative BUN ((mmol/L)	1.17	1.06-1.30	0.003
Recent MI			
1-30 day	1.77	0.97-3.20	0.06
31-90 days	0.65	0.28-1.30	0.20
More than 90 days	1.44	0.66-3.15	0.36
	1.01	1.001-1.02	0.001
	0.87	0.80-0.95	0.002
	0.39	0.27-0.58	0.001
CPB time (minutes)	1.05	1.01-1.10	0.04
Lowest HCT on CPB (gm/dl)	1.001	1.0-1.01	0.002
Postoperative lowest HCT (%)	0.39	0.27-0.58	0.001
Peaked 36-60 h postoperative WBCs ($10^3/\mu\text{L}$)	1.05	1.01-1.10	0.04
Total blood loss (ml)	725	3.90	35.00

BUN = blood urea nitrogen; CPB = cardiopulmonary bypass; HCT = haematocrit; MI = myocardial infarction; WBCs = white blood cells

they did not mention diabetes or hypertension as risk factors.^[29] In contrast, some authors^[20-22] considered diabetes mellitus and hypertension to be independent risk factors for AKI. Impaired left ventricular function was a significant risk factor for AKI after cardiac surgery in the current study, which is compatible with previous studies.^[21,23]

Chew et al.^[22] and Fernandes et al.^[30] investigated ethnic predisposition in AKI after cardiac surgery. They found that ethnicity is an independent risk factor for the development of AKI after cardiac surgery and showed that Malays and Indians have a higher risk of developing postoperative AKI than do the Chinese. They assumed that ethnicity strikes a role in the development of atherosclerosis, coronary heart disease, and associated complications, including AKI. We addressed the same concept in our study and found that AKI was more prevalent in the Asian than Arab population.

Although many predictive risk factors were recognised in the current study, most of them can be considered potentially modifiable (recent MI, time difference between coronary angiography and surgery, preoperative IABP, perioperative anaemia, total blood loss, red blood cell transfusion, and CPB duration). Therefore, if a patient recently developed MI, it may be beneficial if cardiac surgery is delayed for >30 days post-MI; for patients who recently underwent coronary angiography, it is advised to delay the surgery for more than 5 days post-angiography as long as this does not affect the patient's outcome. Patients who are at high risk and in need of prolonged surgery would benefit from less invasive surgery to reduce the CPB time, thus reducing the incidence of AKI. The total blood loss and red blood cell transfusion, when blood conservation strategies are followed, will minimise the risk of AKI and thus

the effect of perioperative anaemia. A novel, unexpected, and interesting finding of this study compared with previous studies is the significant correlation between the peaked 36-60 hour postoperative WBC count and the development of AKI after cardiac surgery in the multivariate logistic regression analysis. One pathogenetic mechanism of AKI is ischaemic kidney injury, which may develop due to the systemic inflammatory response that follows cardiac surgery.^[13] WBCs as an inflammatory marker usually peak 36 to 60 hours after CPB.^[31]

To the best of our knowledge, the relationship between the postoperative WBC count and AKI has not been studied before. Only the relationship between the postoperative WBC count and atrial fibrillation was evaluated by Lamm et al. in 2006. They found that the postoperative WBC count independently predicted the development of postoperative atrial fibrillation.^[32] We could not attribute the high WBCs to steroid administration in our study. The protective effect of steroids has been addressed in many randomised clinical trials;^[33,34] however, we do not routinely administer steroids after cardiac surgery as the evidence is not strong enough to support the possible side effects.^[35]

Conclusion

Cardiac surgery-induced AKI is highly predominant. Strategies targeting modifiable risk factors for AKI may reduce the incidence of AKI post cardiac surgery. The association of high WBCs with AKI needs to be confirmed in other cohorts.

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Disclosures

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Availability of supporting data and materials

The datasets supporting the conclusions of this article are available on request to the corresponding author Dr. Samy Hanoura (e-mail: sehanoura73@yahoo.com), after permission from the Medical Research Centre.

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