Cardiovascular Topics

Factors associated with acute kidney injury and mortality during cardiac surgery

Gontse Leballo, Hlamatsi Jacob Moutlana, Michel Kasongo Muteba, Palesa Motshabi Chakane

Abstract

Background: Cardiac surgery with cardiopulmonary bypass (CPB) is known to contribute towards the incidence of acute kidney injury (AKI) and peri-operative morbidity and mortality. There are several patient, anaesthetic and surgical factors that contribute to its occurrence. It is imperative to know the profile of a patient who is likely to develop this complication to mitigate for modifiable risks. This study aimed at describing a profile of AKI in an adult patient (over the age of 18 years) following cardiac surgery on CPB. Factors associated with the development of cardiac surgery-associated acute kidney injury (CSA-AKI) are described, as well as the relationship between CSA-AKI and in-hospital mortality.

Methods: This was a contextual, descriptive and retrospective single-centre study with data of 476 adult patients admitted post cardiac surgery between January 2016 and December 2017. Data were collected from Charlotte Maxeke Johannesburg Academic Hospital (CMJAH) in South Africa. All adult patients who presented for elective cardiac surgery (coronary artery bypass graft), valvular, aortic and other cardiac surgery on CPB were included. Peri-operative factors such as patient demographics, baseline renal function, co-morbid factors, length of CPB and aortic cross-clamp time, degree of hypothermia, use of assist devices, and post-operative serum creatinine (SCr) levels were collected. Incomplete essential peri-operative data and data for patients who presented on renal replacement therapy (RRT) already were excluded. AKI was defined by Kidney Disease Improving Global Outcomes (KDIGO) criteria.

Results: One hundred and thirty-five (28%) patients developed CSA-AKI and 20, 5 and 3% were in KDIGO 1, 2 and 3, respectively. Older age ($p = 0.024$), female gender ($p = 0.015$), higher serum creatinine level ($p = 0.025$), and lower estimated glomerular filtration rate (eGFR) ($p = 0.025$) were associated with the development of CSA-AKI, while a history of hypertension was predictive. Forty-six of the 476 patients died. Mortality rates were significantly higher in those with AKI compared to those without [28 (21%) vs 18 (5%), respectively ($p = 0.001$)]. The incidence was significantly worse in those with severe kidney injury, as evidenced by mortality rates of 44 versus 5% between KDIGO 3 and KDIGO 1 ($p < 0.001$). Pre-operative eGFR and CSA-AKI requiring RRT were significantly associated with mortality, while pre-operative eGFR was an independent predictor of mortality (hazard ratio 0.99, 95% confidence interval: 0.97–0.99, $p = 0.019$).

Conclusion: A history of hypertension was predictive of the development of CSA-AKI, and pre-operative eGFR was an independent predictor of mortality in this cohort. Both factors are modifiable.

Keywords: cardiac surgery-related acute kidney injury, cardiopulmonary bypass, adults, kidney disease improving global outcomes, renal replacement therapy

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Cardiac surgery-associated acute kidney injury (CSA-AKI) is a peri-operative complication that carries increased mortality rates,[1] as high as 50% in patients who require renal replacement therapy (RRT) following surgery.[1,2] The incidence of AKI is reported in up to 30% of patients who present for cardiac surgery, with risk factors in the peri-operative period.[3] An increase in pre-operative serum creatinine (SCr) level is significantly prognostic of morbidity and mortality following cardiac surgery.[4]

There are nearly two million cardiac surgeries performed globally per year.[5] There is a paucity of statistical data with regard to the incidence and mortality rate of CSA-AKI in sub-Saharan Africa. Studies that have reported on AKI in this region have been in non-surgical patients.[6,7] These reported on mortality rates of up to 43.5% from AKI. Insufficient resources such as RRT and renal transplant services in developing countries should encourage clinicians and scientists in developing approaches aimed at early recognition, diagnosis and the timeous management of AKI.

Peri-operative risk factors of CSA-AKI have been investigated and reported on extensively.[3,8,9] These are classified as modifiable and non-modifiable risk factors.[9] They include illnesses such as renal insufficiency, diabetes mellitus, peripheral vascular disease, chronic obstructive pulmonary disease, congestive cardiac failure, left main coronary artery disease and a left ventricular ejection fraction of less than 30%.[10] Procedure-related modifiable risk factors include surgical urgency, the length of cardiopulmonary

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bypass (CPB) time, aortic cross-clamping time, off-pump surgery, non-pulsatile flow, haemolysis, haemodilution,[10] and the rewarming process following hypothermic arrest.[11] Knowledge of the risk factors allows for optimisation in the peri-operative period.

Charlotte Maxeke Johannesburg Academic Hospital (CMJAH), a hospital affiliated to the University of the Witwatersrand in Johannesburg, South Africa, performs over 200 adult cardiac surgeries annually. The incidence of CSA-AKI and factors associated with it in this population are not known. This knowledge would allow for modifiable risk factors to be mitigated in the peri-operative period.

This research study aimed to describe a profile of AKI in adult patients post cardiac surgery on CPB. The primary objective was to identify the profile of a patient who is likely to develop AKI following cardiac surgery. The secondary objectives were to define factors associated with the development of CSA-AKI using logistic regression analysis to describe the relationship between CSA-AKI and in-hospital mortality using a Kaplan–Meier survival curve, and to determine factors associated with mortality with a Cox regression analysis.

Methods

This was a descriptive, retrospective cohort study. Data were collected from a single centre. The study population consisted of adult patients over the age of 18 years at CMJAH between January 2016 and December 2017 following cardiac surgery on CPB. Patient information was obtained from anaesthetic, intensive care unit (ICU) and perfusionist charts.

A total of 482 peri-operative patient data were retrospectively analysed during the study period. Six patients were excluded from the study due to incomplete essential data, which included SCr levels during the study period, age, gender and race/ethnicity. Patients on RRT pre-operatively were also excluded from the study. Fig. 1 represents a flow diagram of the study data.

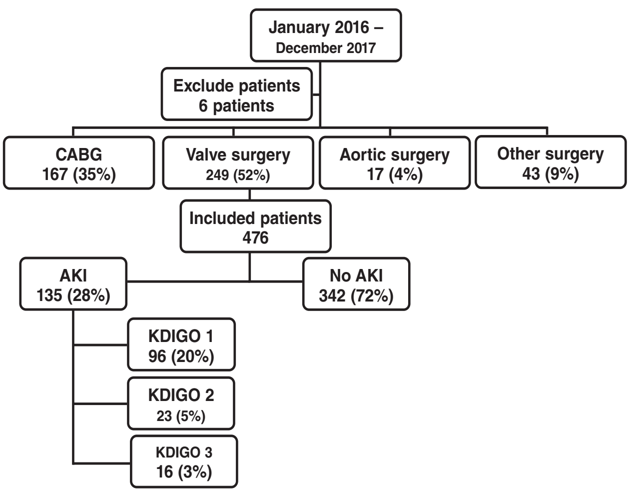

Fig. 1. A flow chart showing the derivation of the study cohort. CABG, coronary artery bypass graft; CSA-AKI,cardiac surgery-associated acute kidney injury; KDIGO, Kidney Disease Improving Global Outcomes.

Table 1. Definitions of diagnostic criteria[5,13,14]

Variables	*Definition*
AKI	An increase in SCr of > 0.3 mg/dl within 48 hours OR an increase in SCr of > 1.5 times baseline known or presumed to have occurred within the prior 7 days OR urine output < 0.5 ml/kg/h for 6 hours
eGFR	Normal: > 90 ml/min/1.73 m^2 Mild: 60–89 ml/min/1.73 m^2 Moderate to severe: < 60 ml/min/1.73 m^2 Renal failure: < 15 ml/min/1.73 m^2
KDIGO criteria	
Class 1	Increased SCr 1.5–1.9 times from the baseline OR urine output < 0.5 ml/kg/h for 6–12 hours
Class 2	Increased SCr 2.0–2.9 times from baseline OR urine output < 0.5ml/kg/h for ≥ 12 hours
Class 3	Increased absolute SCr to > 4.0 mg/dl OR initiation of RRT OR increased SCr 3.0 times from baseline OR 0.3 ml/kg/h for 24 hours OR anuria for 12 hours

AKI, acute kidney injury; SCr, serum creatinine; eGFR, estimated glomerular filtration rate; KDIGO, Kidney Disease Improving Global Outcomes.

The current consensus for diagnosing and classifying AKI uses the Kidney Disease Improving Global Outcomes (KDIGO) criteria (Table 1).[4,8,12] In this study, the worst renal functional state within seven days post cardiac surgery was used to diagnose AKI and to grade into KDIGO classes. SCr levels were measured by the National Health Laboratory Service (NHLS), a national government laboratory. A rise of 0.3 mg/dl and higher was used to diagnose AKI. Baseline renal function was determined by calculating pre-operative estimated glomerular filtration rate (eGFR) levels using the Modification of Diet in Renal Disease (MDRD) equation. Pre-operative renal function severity was classified into mild, moderate to severe, and renal failure by eGFR levels (Table 1).[13] In-hospital mortality data post surgery were collected.

Ethics approval was attained from the Human Research Ethics Committee (Medical), the Graduate Studies Committee of the University of the Witwatersrand, and the National Health Research Committee (Gauteng). This retrospective analysis of patient records did not require informed consent. Patient information was collected by the primary author (GL), and patient confidentiality was preserved by the identification and assignment of numbers to subjects in the data. The principal investigator and the supervisors had access to patient information.

Statistical analysis

Data were collected on a Microsoft® Excel spreadsheet. Stata® 14 (StataCorp.2015, Stata Statistical Software: Release 14. College Station, TX: StataCorp LP) was utilised for data processing and evaluation. Variables are presented as panel data analytics using absolute numbers, percentages, mean (SD), median (IQR) and categories. The occurrence of CSA-AKI on CPB was estimated with an overall 95% confidence interval and *p*-values less than 0.05 were statistically significant. Logistic regression analysis was used to determine factors associated with CSA-AKI, the relationship between CSA-AKI and mortality was assessed using a Kaplan–Meier survival curve, and factors associated with mortality with a Cox regression analysis.

Results

Demographic and pre-operative data for 476 patients are presented in Table 2. The total median (IQR) age was 53

(39–62) years. Patients were predominantly male 255 (53%), and the majority were of the African race [245 (52%)]. A total of 135 (28%) patients developed CSA-AKI within seven days following cardiac surgery on CPB (Table 3). These patients were older and predominantly female. Although they presented with significantly lower eGFR and higher SCr levels pre-operatively as a group compared to those without CSA-AKI, 32 (24%) had presented with normal renal function (eGFR levels) on admission.

Prolonged CPB time, peri-operative use of extracorporeal membrane oxygenator (ECMO), and intra-aortic balloon pump (IABP) were associated with the development of CSA-AKI (p < 0.05) (Table 3). History of hypertension was predictive of development of CSA-AKI (p < 0.05) in an adjusted model (Table 3). Ninety-six (71%) patients were classified as KDIGO 1, 23 (17%) KDIGO 2, and 16 (12%) KDIGO 3 (Table 4).

The mortality rate was 9.6% (46 out of 476 patients). Mortality rates were significantly higher in those with AKI compared to those without [28 (21%) vs 18(5%), respectively] (p = 0.001) (Table 5). The incidence was significantly worse in those with more severe kidney injury, as evidenced by mortality rates of 44 versus 5% between KDIGO 3 and KDIGO 1 (p < 0.001) (Table 4).

Causes of mortality for 21 patients were unclear and unspecific in the reports, while four were reported to be from septic shock with multi-organ failure, one from renal failure, one from left ventricular rupture, and one death on the table following relook surgery. The pre-operative eGFR status of the 28 patients who had developed AKI and died are as follows: five had normal renal function, 13 mild renal dysfunction, eight moderate-to-severe renal dysfunction and two had renal failure.

The Kaplan–Meier survival analysis (Fig. 2) showed the cumulative probability of dying on the first day to be higher for patients without AKI (15.8%, 95% CI: 5–41%) compared to patients with AKI (3.7%; 95% CI: 1–23.5%). The median (IQR) failure time (time to mortality) was 13 (1–40) days for patients without CSA-AKI and only 6 (3–16) days for patients with CSA-AKI. The difference was not statistically significant. Although mortality for patients with CSA-AKI seemed higher (Fig. 2) after the first week, with a shorter median (IQR) time to mortality, the overall in-hospital mortality rate was not statistically different (UHR = 1.51, 95% CI: 0.76–2.99, p = 0.240) between groups.

Table 2. Demographic and pre-operative data of patients who presented for cardiac surgery on CPB

Pre-operative variables	*All patients* (n = *476*) *[median (IQR)/*n *(%)/mean (SD)]*
Age (years)	53 (39–62)
Male gender	255 (53)
Weight (kg)	70 (59.5– 83)
Height (m)	1.66 (1.6–1.73)
BMI (kg/m²)	2 4 (21.5–29.8)
African race	245 (52)
Diabetes mellitus	67 (14)
Hypertension	126 (26)
Hypercholesterolaemia	77 (16)
Smoking	84 (18)
Pre-operative SCr (mg/dl)	1.03 (0.89–1.24)
Type of cardiac surgery	
CABG	172 (36)
Valve surgery	253 (36)
Aortic surgery	18 (4)
Other	43 (9)
eGFR (ml/min/1.73 m²)	
< 15	4 (1)
15–60	97 (20)
60–90	(48)
> 90	148 (31)
KDIGO class	
0	342 (72)
1	96 (20)
2	23 (5)
3	16 (3)

BMI, body mass index; SCr, serum creatinine; CABG, coronary artery bypass graft; eGFR, estimated glomerular filtration rate; KDIGO, Kidney Disease Improving Global Outcomes.

Table 3. Comparison of peri-operative/baseline parameters

Parameter	*CSA-AKI* (n = *135*) *[mean (SD)/median (IQR)/*n *(%)]*	*No CSA-AKI* (n = *342*) *[mean (SD)/median (IQR)/*n *(%)]*	p-*value*
Age (years)	56 (42–63)	52 (37.5–61)	0.024
Male gender	51 (37)	171 (50)	0.015
Weight (kg)	73 (60–85)	70 (59–83)	0.146
Height (m)	1.69 (1.64–1.74)	1.65 (1.59–1.72)	0.996
BMI (kg/m²)	26 (21.6–30.3)	2 2 (21.5–29.8)	0.603
African race	76 (56)	157 (45)	0.441
Diabetes mellitus	24 (18)	42 (12)	0.120
Hypertension	34 (25)	91 (27)	0.724
Smoking	25 (19)	58 (17)	0.696
Cholesterol	20 (15)	56 (74)	0.666
Pre-operative eGFR (ml/min/1.73 m²)	76.5 (58.3–89.9)	80.4 (61–98.35)	0.024
eGFR			
< 15	2 (2)	2 (0.5)	0.099
15–60	34 (25)	63 (18.5)	
60–90	66 (49)	160 (47)	
> 90	32 (24)	115 (34)	
Baseline SCr (mg/dl)	1.09 (0.92–1.3)	1.01 (0.87–1.21)	0.005
Type of cardiac surgery			0.319
CABG	56 (41)	111 (33)	0.319
Valves	56 (41)	186 (55)	
Aorta	5 (4)	12 (3)	
Other	11 (8)	32 (9)	
CPB time (min)	157 (121–203)	144 (113.5–179)	0.040
IABP	13 (10)	6 (2)	< 0.001
Cross-clamp time (min)	100 (81–133)	95 (71–120)	0.053
Lowest temperature on pump	30 (30–32)	32 (30–32)	0.200
ECMO	13 (10)	8 (2)	0.001
VAD	0	2 (0.6)	0.372
SCr difference from baseline (mg/dl)			
Day 1	0.10 (–0.05–0.27)	–0.09 (–0.19–0.01)	< 0.001
Day 2	0.35 (0.18–0.61)	–0.06 (–0.19– –0.19)	< 0.001
Day 3	0.38 (0.08–0.74)	–0.14 (–0.27– –0.02)	< 0.001
Day 4	0.25 (–0.02–0.67)	–0.18 (–0.36– –0.06)	< 0.001
Day 5	0.08 (–0.11–0.62)	–0.21 (–0.42– –0.09)	< 0.001
Day 6	0.09 (–0.20–0.57)	–0.25 (–0.61– –0.10)	< 0.001
Day 7	0.05 (–0.24–1.26)	–0.20 (–0.50– –0.05)	< 0.001
Mortality	28 (21)	18 (5)	< 0.001

BMI, body mass index; eGFR, estimated glomerular function; SCr, serum creatinine; CABG, coronary artery bypass graft; IABP, intra-aortic balloon pump; ECMO, extracorporeal membrane oxygenator; VAD, ventricular assist device.

Table 4. Demographic data of patients who underwent cardiac surgery on CPB, classified using KDIGO criteria

Parameter	*KDIGO 0 (*n *= 342) [mean (SD)/median (IQR)/*n *(%)]*	*KDIGO 1 (*n *= 96) [mean (SD)/median (IQR)/*n *(%)]*	*KDIGO 2 (*n *= 23) [mean (SD)/median (IQR)/*n *(%)]*	*KDIGO 3 (*n *= 16) [mean (SD)/median (IQR)/*n *(%)]*	p-*value*
Age (years)	52 (38–61)	57 (42.5–63.5)	60 (50–63)	49 (30.5–39.5)	0.0299
BMI (kg/m²)	2 2 (21.5–29.8)	26 (21–30)	26.7 (21.5–32.7)	26.2 (22.8–31.2)	0.840
Male gender	172 (50)	35 (36)	9 (39)	7 (44)	0.094
Diabetes mellitus	42 (12)	19 (18)	4 (17)	1 (6)	0.206
Hypertension	91 (27)	26 (27)	4 (17)	4 (25)	0.798
Mortality	18 (5)	13 (14)	8 (35)	7 (44)	< 0.001
Hypercholesterolaemia	56 (16)	16 (17)	3 (13)	1 (6)	0.717
Smoking	58 (17)	16 (17)	5 (22)	4 (25)	0.795
Pre-operative eGFR (ml/min/1.73 m²)	80.5 (6 1–98.1)	76.7 (57.3–89.9)	74.1 (48.8–89.9)	80.3 (66.6–92.6)	0.1278
eGFR					
< 15	2 (0.6)	2 (0.2)	Nil	Nil	0.0734
15–60	63 (18)	25 (27)	7 (30)	2 (12.5)	
60–90	160 (47)	45 (47)	11 (48)	10 (63)	
> 90	116 (34)	23 (24)	5 (22)	4 (25)	
Pre-operative SCr (mg/dl)	1 (0.87–1.2)	1.1 (0.95–1.29)	1 (0.87–1.32)	0.98 (0.89–1.26)	0.0338
Cross-clamp time (min)	95 (71–120)	100 (78–128)	119 (84–171)	95 (90–124)	0.1414
CPB time (min)	144 (114–178)	153 (121–192)	174 (124–239)	158.5 (118–250)	0.1554
IABP	6 (2)	10 (10)	2 (9)	1 (6)	0.001
VAD	2 (0.6)	Nil	Nil	Nil	0.851
ECMO	8 (2)	6 (6)	2 (9)	5 (31)	< 0.001
Lowest temperaure	32 (30–32)	30 (30–32)	32 (30–32)	31 (30–32)	0.6142
SCr change from baseline					
Day 1	0.94 (0.78–1.1)	1.2 (0.98–1.39)	1.24 (1–1.59)	1.4 (1.2–2.0)	0.0001
Day 2	0.97 (0.76–1.15)	1.4 (1.18–1.74)	1.69 (1.39–2.17)	1.76 (1.4–2.6)	0.0001
Day 3	0.87 (0.71–1.06)	1.4 (1–1.67)	1.79 (1.58–2.4)	2.6 (1.86–3.72)	0.0001
Day 4	0.81 (0.63–0.98)	1.2 (0.95–1.64)	1.5 (1.2–2.39)	3.0 (2.5–4.2)	0.0001
Day 5	0.78 (0.59–0.96)	1 (0.89–1.48)	1.6 (1–2.64)	3.0 (2.38–3.4)	0.0001
Day 6	0.78 (0.55–0.96)	1 (0.79–1.44)	1.6 (0.88–2.5)	2.8 (2–3.98)	0.0001
Day 7	0.8 (0.6–1)	1 (0.78–1.4)	1.3 (0.98–2)	2.8 (1.67–4.4)	0.0001
Type of cardiac surgery					
CABG	111 (66)	40 (24)	8 (5)	8 (5)	0.155
Valve	187 (75)	48 (19)	10 (4)	5 (2)	
Aortic	12 (70)	4 (24)	Nil	1 (6)	
Other	32 (74)	4 (9)	5 (12)	2 (5)	
RRT	Nil	3 (3)	Nil	Nil	0.007

BMI, body mass index; IABP, intra-aortic balloon pump; VAD, ventricular assist device; ECMO, extracorporeal membrane oxygenator; eGFR, estimated glomerular filtration rate; SCr, serum creatinine; CABG, coronary artery bypass graft; RRT, renal replacement therapy.

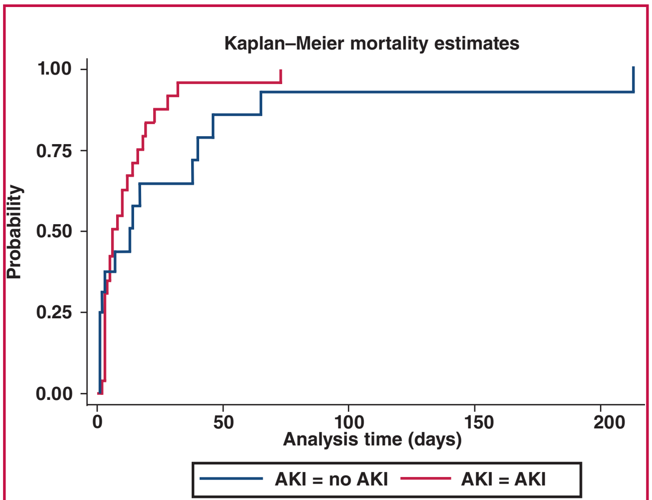

Fig. 2. Post-operative in-hospital survival probability curve in cardiac patients with and without cardiac surgery-associated acute kidney injury (CSA-AKI).

A univariable Cox regression analysis (Table 6) showed a significant relationship between in-hospital mortality and a history of smoking, coronary artery bypass graft (CABG)

Table 5. Logistic regression analysis of factors associated with CSA-AKI

Predictors of CSA-AKI (n = 135)	*Unadjusted logistic regression analysis*		*Adjusted logistic regression analysis*	
	UOR (95% CI)	p-*value*	*AOR (95% CI)*	p-*value*
Age	1.02 (1.00–1.03)	0.024	1.02 (0.99–1.03)	0.052
Female gender	0.60 (0.40–0.91)	0.017	0.58 (0.36–0.93)	0.025
African race	1.51 (1.01– 2.25)	0.044	1.12 (0.66–1.88)	0.676
ECMO	4.42 (1.79–10.93)	0.001	3.05 (1.11–8.39)	0.030
IABP	93 (2.21–1 95)	< 0.001	3.78 (1.29–11.03)	0.015
CPB time (min)	1.00 (1.00–1.01)	0.036	1.00 (0.99–1.04)	0.363
Baseline SCr	1.01 (0.89–1.15)	0.853	0.95 (0.77–1.19)	0.675
Pre-operative eGFR	0.99 (0.98–0.99)	0.010	0.99 (0.98–1.01)	0.253
Hypertension	0.92 (0.58–1.45)	0.724	0.53 (0.29–0.97)	0.041
Diabetes mellitus	1.54 (0.89–2.66)	0.122	1.69 (0.86–3.33)	0.126
Smoking	1.11 (0.66–1.86)	0.696	0.79 (0.43–1.45)	0.448

UOR, unadjusted odds ratio; AOR, adjusted odds ratio; SCr, serum creatinine; CI, confidence interval; ECMO, extracorporeal membrane oxygenator; IABP, intra-aortic balloon pump.

Table 6. Cox regression analysis of predictors of in-hospital mortality

Predictors of mortality (n = 46)	Univariable regression analysis UHR (95% CI)	p-value	Multivariable regression analysis HR (95% CI)	p-value
Age	1.02 (0.99–1.04)	0.115		
Male gender	0.86 (0.44–1.69)	0.667		
African race	1.34 (0.71–2.55)	0.368		
Valve surgery	0.54 (0.27–0.06)	0.073	0.60 (0.22–1.61)	0.309
CABG	2.02 (1.02–3.99)	0.043	1.16 (0.41–3.31)	0.775
Aortic surgery	22.56 (6.96–73.09)	< 0.001	0.54 (0.06–4.69)	0.575
Hypertension	0.89 (0.44–1.78)	0.742		
Cholesterol	0.97 (0.34–2.84)	0.962		
Diabetes mellitus	1.53 (0.77–3.02)	0.222		
Smoker	2.89 (1.21–6.91)	0.017	0.45 (0.17–1.23)	0.121
ECMO	1.20 (0.67–2.15)	0.540		
IABP	1.46 (0.74–2.89)	0.273		
Pre-operative eGFR	0.983 (0.97–0.99)	0.006	0.99 (0.97–0.99)	0.019
AKI	1.52 (0.72–3.23)	0.269		
RRT	0.64 (0.43–0.97)	0.034	2.64 (0.13–1.61)	0.223

UHR, unadjusted hazards ratio; HR, hazard ratio; CI, confidence interval; CABG, coronary artery bypass graft; ECMO, extracorporeal membrane oxygenator; IABP, intra-aortic balloon pump; eGFR, estimated glomerular filtration rate; AKI, acute kidney injury; RRT, renal replacement therapy.

surgery, aortic surgery, pre-operative eGFR and CSA-AKI requiring RRT ($p < 0.05$). Inclusion of those factors from the univariable Cox regression with $p \leq 0.1$ in a multivariable Cox regression model showed pre-operative eGFR to be the sole predictor of in-hospital mortality (HR 0.99, 95% CI: 0.97–0.99, p = 0.019).

Discussion

AKI is an important factor affecting outcomes following cardiac surgery. Its importance is emphasised in the Enhanced Recovery After Cardiac Surgery (ERACS) recommendations.[15] It is highlighted that 'early detection of kidney stress and interventions to avoid acute kidney injury after surgery' are necessary.[15]

This single-centre study was a retrospective records review of adult patients who presented for cardiac surgery. The cases included CABG, cardiac valve repair surgery, aortic surgery, and other cardiac-related surgeries on CPB. The prevalence of CSA-AKI, defined using the KDIGO criteria, at 28% in our study, is similar to that reported in previous reports that show the frequency of CSA-AKI to be up to 30%.[3,16] Thirty-two (24%) of these patients had presented with a normal pre-operative eGFR. This suggests a peri-operative and possibly modifiable factor in the development of their AKI. The majority had early kidney stress (KDIGO 1), which could have been improved with early detection and intervention.

The study highlights several modifiable factors that can be mitigated for better post-operative outcomes. Pre-operative eGFR and SCr levels, and long CPB times were three such factors associated with CSA-AKI. An elevated pre-operative SCr level was found to be an independent risk factor for the development of CSA-AKI and to contribute to mortality in one study.[4] Identifying patients with low eGFR and planning for renal rescue in the peri-operative period could lead to better outcomes, including in-hospital mortality rate.

Although a previous study[17] found no relationship between low cardiac output and need for IABP, duration of CPB and cross-clamping, we postulate that these factors were reflective of the peri-operative course and complications. Early identification of patients with these factors and planning for renal rescue in the peri-operative period could lead to better outcomes, including in-hospital mortality rate.[4]

Patients who developed AKI displayed a steady increase in SCr levels from baseline, notable on day one, the peak occurring on day three. The changes in SCr ranged from 1 (0.78–1.4) to 1.4 (1.18–1.74) over seven days. Patients in the non-AKI group, on the contrary, displayed a decline in SCr levels from day one, which continued over seven days. Although these changes seemed minor, Lassnigg *et al.*[18] in their study stated that 'even minor degrees of post-operative AKI, as manifest by only a 0.2 to 0.3 mg/dl rise in serum creatinine from baseline, predicted a significant increase in short-term mortality'. As part of a management strategy for CSA-AKI, the following recommendations have been made: prevention, optimisation pre-operatively, modification of risk factors, and peri-operative management using the KDIGO care bundle.[19]

In an attempt to detect early 'kidney stress', newer modalities of detection have been described and include the use of biomarkers such as neutrophil gelatinase-associated lipocalin (NGAL), interleukin-18 (IL-18), cystatin C, insulin-like growth factor binding protein 7 (IGFBP-7) and tissue inhibitor of metalloproteinases-2 (TIMP-2).[20] These biomarkers have been investigated in line with the principles of the KDIGO care bundle.[21] Early biomarker-based prediction of imminent AKI followed by implementation of the KDIGO care bundle reduced AKI severity, post-operative creatinine increase, and length of ICU and hospital stay in patients after major non-cardiac surgery. Use of renal vascular ultrasound is one other modality being investigated.[22,23]

The mortality rate was 9.6% (46 out of 476 patients). Mortality rates were significantly higher in those with AKI compared to those without [28 (61%) vs 18 (39%), respectively] (p = 0.001). The incidence was significantly worse in those with more severe kidney injury. Similarly, a previous study has shown an association of increased 30-day mortality[24] with a higher KDIGO class. In a meta-analysis of 91 observational studies with 320 086 patients, Hu *et al.*[25] found pooled short- and long-term mortality rates of 10.7 and 30%, respectively, with increases along with the severity of stages.

The current study found pre-operative eGFR to be the sole predictor of in-hospital mortality. A Japanese study also found pre-operative eGFR to be predictive of all-cause mortality, cardiac mortality, and an increased risk of major adverse events (MACE) (HR 0.983, p = 0.026; HR 0.963, p = 0.006; HR 0.983, p = 0.002), respectively, in patients following cardiac surgery.[26] Due to the association with increased mortality rate and length of hospital stay, with mortality rates varying from 22 to 36%, and rates of 50 to 80% in severe AKI requiring renal replacement therapy, early detection of CSA-AKI is necessary to mitigate risk.[20] This is also emphasised in the ERACS recommendations.[15]

Limitations

Retrospective cohort studies rely on accurate record keeping, as errors related to bias and confounding factors are high, affecting the level of the evidence. Large sample sizes are required, as some statistical analysis cannot be measured. Data were obtained from a single centre, therefore, results are contextual and may not be extrapolated to other population groups. The probable presence of unknown confounding factors affects the interpretation of the results. A multicentre study would be beneficial to permit larger sample sizes.

The mortality rate was low, making the regression models likely to be over-fitted. It also narrowed the scope of variables that could be included in the multivariable regression models. This may have confounded the results. Relationships were, however, apparent and echoed in other studies. This rapidly growing field with the novel use of biomarkers and ultrasound allows for further exploration. Pre-operative echocardiography information, together with data on the use of inotropes, diuretics, fluids and blood products intra-operatively, leaves the researchers with an opportunity to investigate such variables in a future prospective study.

Conclusion

Numerous modifiable factors including pre-operative renal dysfunction were found to be associated with the development of CSA-AKI and mortality. Identification of patients at risk of CSA-AKI, relying on serial SCr and/or urine output measurements may not be time sensitive and may delay timeous interventions. The use of novel biomarkers and renal vascular ultrasound promises the possibility of early diagnosis of renal injury. Kidney injury should be considered an important factor in post-operative outcomes in cardiac surgery. Those at risk of kidney injury should be identified and risk-modification strategies employed. Renal function is crucial for enhanced recovery after cardiac surgery, as evidenced by studies that show its association with adverse outcomes.

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References

1. Bastin AJ, Ostermann M, Slack AJ, Diller GP, Finney SJ, Evans TW. Acute kidney injury after cardiac surgery according to Risk/Injury/Failure/Loss/End-stage, Acute Kidney Injury Network, and Kidney Disease: Improving Global Outcomes classifications. *J Crit Care* 2013; **28**: 389–396.
2. Freeland K, Hamidian Jahromi A, Duvall LM, Mancini MC. Post-operative blood transfusion is an independent predictor of acute kidney injury in cardiac surgery patients. *J Nephropathol* 2015; **4**: 121–126.
3. O'Neal JB, Shaw AD, Billings FT. Acute kidney injury following cardiac surgery: current understanding and future directions. *Crit Care* 2016; **20**: 187.
4. Machado MN, Nakazone MA, Maia LN. Acute kidney injury based on KDIGO (Kidney Disease Improving Global Outcomes) criteria in patients with elevated baseline serum creatinine undergoing cardiac surgery. *Rev Bras Cir Cardiovasc* 2014; **29**: 299–307.
5. Fuhrman DY, Kellum JA. Epidemiology and pathophysiology of cardiac surgery-associated acute kidney injury. *Curr Opin Anaesthesiol* 2017; **30**: 60–65.
6. Adu D, Okyere P, Boima V, Matekole M, Osafo C. Community-acquired acute kidney injury in adults in Africa. *Clin Nephrol* 2016; **86**: 48–52.
7. Olowu WA, Niang A, Osafo C, Ashuntantang G, Arogundade FA, Porter J, *et al.* Outcomes of acute kidney injury in children and adults in sub-Saharan Africa: a systematic review. *Lancet Glob Health* 2016; **4**: e242-250.
8. Bhadade R, De'Souza R, Harde MJ, Mehta KS, Bhargava P. A prospective study of acute kidney injury according to KDIGO definition and its mortality predictors. *J Assoc Physicians India* 2016; **64**: 22–28.
9. Chakravarthy M. Modifying risks to improve outcome in cardiac surgery: An anesthesiologist's perspective. *Ann Card Anaesth* 2017; **20**: 226–233.
10. Rosner MH, Okusa MD. Acute kidney injury associated with cardiac surgery. *Clin J Am Soc Nephrol* 2006; **1**: 19–32.
11. Boodhwani M, Rubens FD, Wozny D, Nathan HJ. Effects of mild hypothermia and rewarming on renal function after coronary artery bypass grafting. *Ann Thorac Surg* 2009; **87**: 489–495.
12. James M, Bouchard J, Ho J, Klarenbach S, LaFrance JP, Rigatto C, *et al*. Canadian Society of Nephrology commentary on the 2012 KDIGO clinical practice guideline for acute kidney injury. *Am J Kidney Dis* 2013; **61**: 673–685.
13. Fiseha T, Mengesha T, Girma R, Kebede E, Gebreweld A. Estimation of renal function in adult outpatients with normal serum creatinine. *BMC Res Notes* 2019; **12**: 462.
14. Khwaja A. KDIGO clinical practice guidelines for acute kidney injury. *Nephron Clin Pract* 2012; **120**: 179–184.
15. Gregory AJ, Grant MC, Manning MW, Cheung AT, Ender J, Sander M, *et al.* Enhanced Recovery After Cardiac Surgery (ERAS Cardiac) recommendations: an important first step-but there is much work to be done. *J Cardiothorac Vasc Anesth* 2020; **34**: 39–47.
16. Weir MR, Aronson S, Avery EG, Pollack CV, Jr. Acute kidney injury following cardiac surgery: role of peri-operative blood pressure control. *Am J Nephrol* 2011; **33**: 438–452.
17. Vellinga S, Verbrugghe W, De Paep R, Verpooten GA, Janssen van Doorn K. Identification of modifiable risk factors for acute kidney injury after cardiac surgery. *Neth J Med* 2012; **70**: 450–454
18. Lassnigg A, Schmidlin D, Mouhieddine M, Bachmann LM, Druml W, Bauer P, *et al*. Minimal changes of serum creatinine predict prognosis in patients after cardiothoracic surgery: a prospective cohort study. *J Am Soc Nephrol* 2004; **15**: 1597–1605.
19. Nadim MK, Forni LG, Bihorac A, Hobson C, Koyner JL, Shaw A, *et al.* Cardiac and vascular surgery-associated acute kidney injury: the 20th International Consensus Conference of the ADQI (Acute Disease Quality Initiative) Group. *J Am Heart Assoc* 2018; **7**.
20. Leballo G, Chakane PM. Cardiac surgery-associated acute kidney injury: pathophysiology and diagnostic modalities and management. *Cardiovasc J Afr* 2020; **31**: 1–8.
21. Göcze I, Jauch D, Götz M, Kennedy P, Jung B, Zeman F, *et al.* Biomarker-guided intervention to prevent acute kidney injury after major surgery: the Prospective Randomized BigpAK Study. *Ann Surg* 2018; **267**: 1013–1020.
22. Beaubien-Souligny W, Benkreira A, Robillard P, Bouabdallaoui N, Chasse M, Desjardins G, *et al*. Alterations in Portal Vein Flow and Intrarenal Venous Flow Are Associated With Acute Kidney Injury After Cardiac Surgery: A Prospective Observational Cohort Study. *J Am Heart Assoc.* 2018; **7**: e009961.
23. Pettey G, Motshabi P. Novel modalities for the diagnosis of cardiac surgery associated acute kidney injury: a narrative review of the literature. *Sthn Afr J Anaesth Analg* 2020; **26**: 65–72.
24. Machado MN, Nakazone MA, Maia LN. Prognostic value of acute kidney injury after cardiac surgery according to kidney disease: improving global outcomes definition and staging (KDIGO) criteria. *PLoS One* 2014; **9**: e98028.

25. Hu J, Chen R, Liu S, Yu X, Zou J, Ding X. Global incidence and outcomes of adult patients with acute kidney injury after cardiac surgery: a systematic review and meta-analysis. *J Cardiothorac Vasc Anesth* 2016; **30**: 82–89.

26. Domoto S, Tagusari O, Nakamura Y, Takai H, Seike Y, Ito Y, *et al.* Pre-operative estimated glomerular filtration rate as a significant predictor of long-term outcomes after coronary artery bypass grafting in Japanese patients. *Gen Thorac Cardiovasc Surg* 2014; **62**: 95–102.