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Pre-, Intra-, and Post-Operative Factors for Kidney Injury of Patients Underwent Cardiac Surgery: A Retrospective Cohort Study

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Background: Kidney injury is common in patients who have undergone cardiac surgery, and it has high morbidity and mortality. The objective of the study was to identify pre-, intra-, and post-operative risk factors responsible for kidney injury among patients who had undergone cardiac surgery.

Material/Methods: Patients (n=1468) who had undergone cardiac surgery were stratified into those with kidney injury (n=488) and those without kidney injury (n=980) using the KDIGO (Kidney Disease: Improving Global Outcomes) criteria. Data of pre-, intra- and post-operative variables were collected and analyzed.





Results: Acute kidney injury occurred in 33.2% of study patients. Patients with post-operative acute kidney injury had older age, comorbidities, higher preoperative serum creatinine, coronary artery bypass grafting, longer operation time, high cardiopulmonary bypass and cross-clamping time, low central venous pressure, and prolonged mechanical ventilation as compared to patients without kidney injury ($P < 0.05$ for all). Age > 65 years (OR 1.4), preoperative hypertension (OR 2.0), preoperative anemia (OR 2.3), preoperative low ejection fraction (OR 3.7), Charlson comorbidity index > 2 (OR 2.5), longer cardiopulmonary bypass time (OR 4.0), blood transfusions (OR 2.1), postoperative hypotension (OR 5.2), and low central venous pressure (OR 8.1) were responsible for kidney injury. Mortality of patients with kidney injury was significantly higher than those without acute kidney injury (52 versus 1, $P < 0.001$).

Conclusions: Appropriate and effective control of pre-, intra-, and post-operative variables can reduce the risk of kidney injury development in patients following cardiac surgeries.

MeSH Keywords: **Acute Kidney Injury • Anemia • Cardiac Surgical Procedures • Coronary Artery Bypass • Hypertension • Stroke Volume**

Abbreviations: **AKI** – acute kidney injury; **CSA-AKI** – acute kidney injury after cardiac surgery; **CPB** – cardiopulmonary bypass; **CS** – cardiac surgery; **AKIN** – Acute Kidney Injury Network, risk; **RIFLE** – injury, failure, loss of function, end-stage renal disease; **KDIGO** – kidney disease: improving global outcomes; **STROBE** – the strengthening the reporting of observational studies in epidemiology; **CABG** – coronary artery bypass grafting; **ESRD** – end-stage renal disease; **SCr** – serum creatinine; **eGFR** – glomerular filtration rate; **LVEF** – left ventricular ejection fraction; **CCI** – Charlson comorbidity index; **CPB** – cardiopulmonary bypass; **AXC** – aortic cross-clamp; **CVP** – central venous pressure; **ACEI** – angiotensin-converting enzyme inhibitor; **ARB** – angiotensin receptor blocker; **SICU** – surgical intensive care unit; **AUC** – area under the curve; **ROC** – receiver operating characteristics; **OR** – odd ratio

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Background

Acute kidney injury (AKI) in hospitalized patients causes serious complications, early and late mortality, and increases hospital expenditures [1]. AKI after cardiac surgery (CSA-AKI) commonly occurs among the adult population and is associated with high morbidity and mortality rates. CSA-AKI is the second most common type of AKI after septic AKI in intensive care units [2]. Several associated factors during cardiac surgery, including aorta cross-clamping, cardiopulmonary bypass (CPB), rate and quantity of blood transfusion, and a high dose of vasopressors that alter renal perfusion, can induce cycles of ischemia and reperfusion, increase oxidative damage, and increase renal and systemic inflammation. All these mechanisms are further implicated in the development of AKI [3]. Many pharmacological and non-pharmacological treatments have largely failed to reduce CSA-AKI in clinical trials. On the other hand, perioperative high-dose atorvastatin and remote ischemic preconditioning provided minimal evidence for the reduction of CSA-AKI [4]. Therefore, early diagnosis and risk assessment of AKI plays a pivotal role during the management of CSA-AKI.

Recently, 2 meta-analyses demonstrated an incidence rate for CSA-AKI of 22%, with the majority of patients having mild AKI [5,6]. Patients with CSA-AKI also portend higher short-term and long-term mortality rates as compared to those undergoing cardiac surgery without AKI. After adjustments for other covariates that might explain mortality, there is a proportionally increased risk for mortality based on the severity stage of AKI [7]. In addition to increased morbidity and mortality, CSA-AKI is associated with increased costs and use of resources as indicated by longer hospital stays, which further proportionates with the severity of AKI [8]. Understanding individual risk factors might help in preventing AKI, which could be further translated into reduced morbidity, mortality, and cost of care. This is particularly helpful in the hospital setting, where a patient's susceptibility can be assessed before surgery or administration of potentially nephrotoxic agents [9]. Accurate prediction of AKI provides the opportunity for clinicians to optimize management of high-risk patients, increase monitoring, enroll patients in clinical trials, and initiate preventative and therapeutic treatments [10]. Although many studies have identified risk factors of CSA-AKI [5,11–16], data on clinical risk factors are still limited [10], particularly in the Chinese population. There are very few studies evaluating risk factors of CSA-AKI in the Chinese population [5,13–16]. Moreover, most of the previously conducted studies stratified AKI by using the AKNI (Acute Kidney Injury Network) classification system and the RIFLE (Risk, Injury, Failure, Loss of Function, End-Stage Renal Disease) classification system. While few studies have used the validated KDIGO (Kidney Disease: Improving Global Outcomes) criteria [17,18] in the cardiac surgery setting.

Within the aforementioned context, our study analysis aimed to evaluate the pre-, intra-, and post-operative risk factors of AKI among a Chinese population undergoing cardiac surgery by using the KDIGO criteria.

Material and Methods

Ethical consideration and consent to participate

The protocol (CB/CR/ERBA/CHS-15/45781, dated January 1, 2014) of the study was approved by the ethical review board of Central Hospital of Shanghai Jiading District. The study adhered to the law of China, the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) statement, and the Declarations of Helsinki. As this study was a retrospective review of medical records, the requirement for informed consent and registration in the Chinese clinical trial registry were waived. All the study procedures were performed according to institutional guidelines, and the identity of study participants was anonymized before analysis.

Inclusion criteria

Medical records of patients who underwent any type of cardiac surgical procedure were reviewed. The types of the cardiac surgical procedure were defined as coronary artery bypass grafting (CABG), valve surgery, combined CABG and valve procedures, congenital heart disease repair, and aorta aneurysm.

Exclusion criteria

Exclusion criteria included: patients age younger than 18 years and older than 90 years, patients receiving dialysis before surgery, patients with end-stage renal disease (ESRD), and patients with missing clinical data in the medical records of the institute.

Definition of AKI

The KDIGO classification was used to stratify AKI among cardiac surgery patients, where AKI was defined as: serum creatinine (SCr) ≥ 0.3 mg/dL (≥ 26.5 μ M/L) within 48 hours or an increase in SCr ≥ 1.5 times from the baseline value, known or presumed to have occurred within the prior 7 days [19]. The KDIGO also recommended a staging system for AKI: stage 1 was SCr ≥ 0.3 mg/dL (≥ 26.5 μ M/L) within 48 hours or an increase in SCr ≥ 1.5 times from the baseline value, stage 2 was an increase in SCr ≥ 2.0 – 2.9 times from the baseline value, and stage 3 was an increase in SCr ≥ 3 times from the baseline value [17]. Urine criterion was not used in the present analysis. The latest value of SCr during admission and before surgery was referred to as the baseline SCr. The baseline values of SCr were aggressively adjudicated under the

expert opinion of nephrologists (minimum 3-years of experience) of our institute.

Data collection

All pre-, intra- and post-operative data were collected in a pre-defined form. Preoperative variables included anthropometric and social characteristics, the presence of comorbidities, level of protein in the urine, SCr level, estimated glomerular filtration rate (eGFR), left ventricular ejection fraction (LVEF), Charlson comorbidity index (CCI), and the emergence of surgery. Intraoperative variables were the type of surgical procedure, duration of surgery, cardiopulmonary bypass (CPB) time, aortic cross-clamp (AXC) time, and requirement of blood transfusion. Postoperative variables were blood pressure, central venous pressure (CVP), the volume of urine, re-exploration, need and time of artificial ventilation, use of angiotensin-converting enzyme inhibitor (ACEI)/angiotensin receptor blocker (ARB), and renal replacement therapy.

Patients who underwent cardiac surgery were stratified into 2 groups: patients with AKI and those without AKI. All the aforementioned variables were compared in order to determine the significant risk factors for AKI. GFR was calculated using the Chronic Kidney Disease Epidemiology Creatinine equation [20]. The length of hospital stay and SICU (surgical intensive care unit) stay were noted. The level of protein greater than 15 mg/dL in spot urine specimens was considered as proteinuria. The level of serum uric acid more than 6.6 mg/dL in females and more than 7.0 mg/dL in males was considered as hyperuricemia. Postoperative systolic blood pressure less than 90 mm Hg before the diagnosis of AKI was considered as hypotension. If the total duration of ventilator-assisted respiration was 48 hours or more in the SICU than it was considered as prolonged mechanical ventilation. If the patient had undergone more than 1 surgical procedure, in such a condition, the data of the first surgical technique was considered in the analysis. Urine output less than 400 mL/day was considered as oliguria.

Statistical analysis

All the data were analyzed by SPSS version 20.0. Continuous variables were presented as mean with standard deviation or median with 25–75% percentiles, while categorical variables were expressed as frequency (n) and proportion (%). The Mann Whitney U-test was used to compare continuous variables, while categorical variables were compared with the Fischer's exact test. Variables that were statistically associated with AKI or biological plausible with the development of AKI regardless of statistical significance were subjected to logistic regression. Variables in univariate analysis with *P* values <0.25 were included in the multivariate analysis where variables with *P* values <0.05 in the multivariate analysis were

considered independent risk factors of AKI [21,22]. The predictive accuracy of the final model of CSA-AKI was evaluated by the area under the curve (AUC) of receiver operating characteristics (ROC) analysis.

Results

Medical history

A total of 1761 patients underwent cardiac surgery from January 5, 2014 to December 31, 2016 at Central Hospital of Shanghai, China. Of these, 214 patients had missing clinical data, 24 patients were younger than 18 years of age, 46 patients were older than 90 years of age, and 9 patients had ESRD. Therefore, these patients were excluded from the final analysis. Data of 1468 patients were included in the final analysis. According to the KDIGO definition, the population of the study was stratified into 2 cohorts. Patients who had AKI were included in the AKI cohort (n=448) and patients who had not reported AKI were included in the non-AKI cohort (n=980).

The mean age of study participants was 57.8±14.3 years with a male preponderance (62.1%). About 32% of patients were hypertensive and 23.5% of patients had anemia. The most frequent type of surgery was CABG (39.9%) and the second most frequent surgical procedure was valve surgery (38.4%). The mean operation time was 3.4±1.7 hours while CPB time was 116.2±6.8 minutes. The incidence of AKI was 33.2% with stage 1 in 348 patients (23.7%), stage 2 in 95 patients (6.5%) and stage 3 in 45 patients (3.1%). Out of 585 CABG procedures, CSA-AKI occurred in 42.9% while it occurred in 26.1% of all valve surgeries. Significantly higher numbers of aged (*P*<0.001), male (*P*=0.041), and obese (*P*=0.01) patients were reported in AKI cohort than non-AKI cohort.

Clinical-laboratory characteristics

The preoperative variables which differed between AKI and non-AKI cohorts were SCr (*P*<0.001), eGFR (*P*<0.001), hypertension (*P*<0.001), diabetes mellitus (*P*=0.002), anemia (*P*<0.001), LVEF <45% (*P*=0.002), proteinuria (*P*=0.047), hyperuricemia (*P*=0.011), and CCI (*P*<0.001). The other preoperative clinical-laboratory characteristics of the enrolled patients were the same between both cohorts (Table 1).

More patients underwent CABG (*P*<0.001) and aortic (*P*=0.029) surgeries in the AKI cohort than the non-AKI cohort. The patients with AKI had significantly longer operation time (*P*<0.001), CPB time (*P*<0.001), and AXC time (*P*<0.001) as compared to those without AKI. Also, the amount and frequency of blood transfusion (*P*=0.003) were higher among AKI cohort patients than non-AKI cohort patients (Table 2).

Table 1. Anthropometric, social parameters, and preoperative clinical-laboratory characteristics of the enrolled patients.

Variables	Total	Cohort		Comparison between cohorts	
		AKI	Non-AKI		
Numbers patients evaluated	1,468	488	980	p-Values	
Age (years)	57.8±14.3	59.6±11.6*	55.1±17.8	<0.001	
Gender	Male	911 (62)	321 (66)*	590 (60)	0.041
	Female	557 (38)	167 (34)	390 (40)	
Body mass index (kg/m ²)	24.1±3.2	25.1±4.5*	23.8±2.6	0.010	
Area of residence	Rural	701 (48)	224 (46)	405 (41)	0.105
	Urban	768 (52)	264 (54)	575 (59)	
Serum creatinine (uM/L)	79.4±7.5	81.7±5.7*	75.5±8.2	<0.001	
Estimated glomerular filtration rate (mL/min)	81.4±4.1	80.2±3.8	90.1±6.2**	<0.001	
Comorbidities	Hypertension [#]	466 (32)	211 (43)*	255 (26)	<0.001
	Diabetes mellitus ^{##}	232 (16)	104 (23)*	128 (13)	0.002
	Chronic obstructive pulmonary disorder	19 (1)	6 (1)	13 (1)	0.168
	Acute myocardial infarction	61 (4)	21 (4)	40 (4)	0.672
	Chronic kidney disease	11 (1)	5 (1)	6 (1)	0.190
	Cerebrovascular disease	78 (5)	30 (6)	48 (5)	0.078
	Anemia ^{###}	345 (24)	170 (35)*	175 (18)	<0.001
Coronary angiography	401 (27)	141 (29)	260 (27)	0.389	
Urgent surgery	21 (1)	10 (2)	11 (1)	0.159	
Statins administration	376 (26)	132 (27)	244 (25)	0.063	
Left ventricular ejection fraction <45%	167 (11)	120 (25)*	47 (5)	0.002	
Proteinuria ^{&}	289 (20)	110 (23)*	179 (18)	0.047	
Hyperuricemia ^{&&}	311 (21)	122 (25)*	189 (19)	0.011	
Contrast media	154 (11)	54 (11)	100 (10)	0.142	
Charlson Comorbidity index >2	167 (11)	98 (20)*	69 (7)	<0.001	

[#] Blood pressure >90/130 mmHg; ^{##} random blood glucose >140 mg/dL; ^{###} hemoglobin <13.5 g/dL for men and <12 g/dL for women; [&] protein >15 mg/dL in spot urine specimens; ^{&&} serum uric acid >6.6 mg/dL in women and >7.0 mg/dL in men. Continuous data are presented as mean ±SD while quantitative data are expressed as the frequency with proportion n (%). Mann Whitney U-test for continuous data and the Fischer exact test for quantitative data were used statistical analysis. A p<0.05 was considered significant. * Significant higher for patients who had acute kidney injury than who had no acute kidney injury. ** Significant higher for patients who had not acute kidney injury than who had acute kidney injury.

Postoperative hypotension (P<0.001), CVP <6 cmH₂O (P<0.001), oliguria (P<0.001), prolonged mechanical ventilation (P<0.001), and use of ACEIs/ARBs (P=0.003) were significantly more common among patients who developed AKI as compared to those who did not. The patients with AKI also reported poor

outcomes in terms of increased hospital stay (P<0.001), SICU stay (P=0.003), and need for dialysis (P<0.001). The case fatality rate was higher among patients with AKI than without AKI. Patients meeting the definition of AKI who died during hospital stay were 104 times higher than patients without

Table 2. Intraoperative clinical-laboratory characteristics of the enrolled patients.

Variables	Total	Cohort		Comparison between cohorts
		AKI	Non-AKI	
Data of patients evaluated	1,468	488	980	p-Values
Coronary artery bypass grafting	585 (40)	251 (51)*	334 (34)	<0.001
Valve	563 (38)	147 (30)	416 (42)**	0.041
Type of cardiac surgery				
Coronary artery bypass grafting + valve	151 (10)	71 (15)*	80 (8)	0.001
Coronary heart disease	138 (9)	17 (4)	121 (12)**	0.002
Aortic	31 (4)	17 (4)*	14 (1)	0.029
Operation time (h)	3.4±1.7	4.8±1.3*	3.2±1.1	<0.001
Cardiopulmonary bypass time (min)	116.2±6.8	125.5±5.3*	107.4±4.1	<0.001
Aortic cross-clamp time (min)	66.3±2.9	74.3±1.3*	60.6±2.5	<0.001
Blood transfusion (>400 mL)	298 (20)	134 (28)*	164 (17)	0.003
Red blood cells transfused	502 (34)	212 (43)*	290 (30)	0.002

Continuous data are presented as mean ±SD while quantitative data are expressed as the frequency with proportion n (%). Mann-Whitney *U*-test for continuous data and Fischer exact test for quantitative data were used for statistical analysis. A *p*<0.05 was considered significant. * Significant higher for patients who had acute kidney injury than who had no acute kidney injury. ** Significant higher for patients who had not acute kidney injury than who had acute kidney injury.

AKI (Table 3). Comparatively higher numbers of patients died who had stage 3 AKI (30 patients) than stage 2 AKI (17 patients), and stage 1 AKI (5 patients) during the follow-up period (Figure 1). Also, the hospital stays were increased with respect to progression of AKI.

Risk factor evaluation

The pre-, intra- and post-operative factors for clinical relevance with AKI were subjected to logistic regression analysis. The independent risk factors of CSA-AKI were evaluated through a series of logistic regression. A total of 11 significant determinants of CSA-AKI were identified in the current study including old age, preoperative hypertension, preoperative anemia, LVEF <45%, CCI >2, CPB time ≥110 minutes, RBCs transfused, postoperative hypotension, CVP <6 cmH₂O, mechanical ventilation ≥9 hours, and use of ACEIs/ARBs. Postoperative CVP <6 cmH₂O and hypotension were the strongest predictors of CSA-AKI.

The ROC curve analysis of the final predictive model yielded the AUC of 0.911 with standard error 0.013 and *P*-value <0.001. Also, subgroup analysis revealed that CABG [OR=3.2 (2.2–4.8), *P*<0.001] and mixed surgery [OR=1.8 (1.3–5.8), *P*=0.037] were associated with the development of AKI in patients following cardiac surgery (Table 4).

Discussion

In the analysis of 1468 patients who underwent cardiac surgery, postoperative AKI occurred in 33.2% of cases where the majority of patients had stage 1 according to KDIGO criteria. The incidence of AKI in the analysis was in concordance with the findings of other studies conducted on Asian populations [15,23]. However, the incidence reported in the current finding was higher than reported in the other studies conducted using the AKIN criteria [24] and the RIFLE criteria [25]. The difference in the incidence reported might be attributed to several reasons, including varying definitions used to classify AKI, the timing of AKI evaluation, urine output versus SCr criteria, and population characteristics. Using several criteria to stratify AKI leads to a greater disparity in incidence as well as the epidemiology of AKI [21]. Moreover, in the present analysis, most of the participants belong to an older age cohort accompanied by compromised renal function. However, the incidence of AKI in the present study was closely related to previous studies conducted in the Chinese population [15,23]. Nonetheless, the most important aspect of the current finding was a substantial number of patients who experienced AKI following different types of cardiac surgery. Uniform and consented definitions should be utilized to generalize and compare the findings across published literature.

Table 3. Postoperative clinical-laboratory characteristics of the enrolled patients.

Variables	Total	Cohort		Comparisons between cohort
		AKI	Non-AKI	
Numbers of patients' data analyzed	1,468	488	980	p-Values
Hypotension [#]	167 (11)	121 (25)*	46 (5)	<0.001
Central venous pressure <6 cmH ₂ O	272 (19)	232 (48)*	40 (4)	<0.001
Oliguria (urine output <400 mL/day)	98 (7)	87 (18)*	11 (1)	<0.001
Prolonged mechanical ventilation ^{##}	148 (10)	121 (25)*	27 (3)	<0.001
Use of ACEIs/ARBs	302 (21)	132 (27)*	170 (17)	0.003
Use of non-steroidal anti-inflammatory drugs	511 (35)	174 (36)	337 (34)	0.811
Hospital stay (≥9 days)	250 (17)	176 (36)*	100 (10)	<0.001
Surgical intensive care unit stay (≥1 days)	44 (3)	20 (4)*	24 (2)	0.003
Dialysis	66 (5)	66 (14)*	0 (0)	<0.001
Mortality	53 (4)	52 (11)*	1 (0.1)	<0.001
Bone pain	42 (3)	34 (7)*	8 (1)	<0.001
Unusual pain	22 (1)	19 (2)*	3 (0.3)	<0.001
Numbness or tingling	47 (3)	40 (4)*	7 (1)	<0.001
Decreased mental sharpness	31 (2)	30 (18)*	1 (0.1)	<0.001
Feeling unwell	62 (4)	42 (4)*	20 (2)	<0.001
Estimated glomerular filtration rate (mL/min)	80.48±3.12	70.21±4.78	89.12±5.92**	<0.001

[#] Systolic blood pressure <90 mmHg. ^{##} Total duration of ventilator-assisted respiration ≥48 h. Continuous data are presented as mean ±SD while quantitative data are expressed as the frequency with proportion n (%). Mann Whitney U-test for continuous data and Fischer exact test for quantitative data were used for statistical analysis. ACEI – angiotensin-converting enzyme inhibitor; ARB – angiotensin receptor blocker. A p<0.05 was considered significant. * Significant higher for patients who had acute kidney injury than who had no acute kidney injury. ** Significant higher for patients who had not acute kidney injury than who had acute kidney injury.

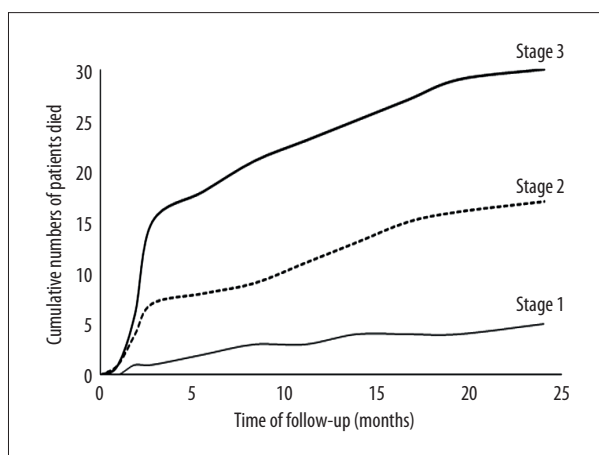


Figure 1. Mortality of patients according to the stage of acute kidney injury during follow-up time.

The most common surgeries in the present study were CABG and valve procedures, but the prevalence of AKI was higher in patients who underwent CABG as compared to those who underwent valve and other surgeries. These findings were consistent with the results of retrospective analyses [7,14,26,27] but in contrast with the results of a study where the prevalence of CSA-AKI was significantly higher in valve surgery [5], but this was a meta-analysis and had indirect evidence. In the present analysis, the patients who underwent CABG were older, had more renal compromised functions and comorbidities as compared to those who underwent valve and other surgeries. This might be a possible reason that the prevalence of AKI was higher in CABG as compared to other surgeries. AKI in valve surgery patients is different from that in CABG surgery patients.

Most of the cases of AKI in the present analysis were mild (stage 1), however, the study found cases of mortality in the

Table 4. Assessments of independent risk factors for acute kidney injury by logistic regression analysis.

Variables	Univariate analysis			Multivariate analysis		
	OR	95% CI	p Values	OR	95% CI	p Values
Age >65 years*	1.9	1.2–3.2	<0.001	1.4	1.1–2.8	0.031
Male	1.5	1.1–2.8	0.033	1.8	0.09–2.1	0.510
Preoperative hypertension*	2.7	1.8–4.6	<0.001	2.0	1.5–3.7	0.002
Diabetes mellitus	1.4	0.98–2.7	0.051	1.7	0.81–2.6	0.641
Anemia*	3.7	3.0–6.2	<0.001	2.3	1.9–4.7	0.001
Left ventricular ejection fraction <45%*	5.2	3.8–8.4	<0.001	3.7	2.8–5.5	<0.001
Charlson comorbidity index >2*	3.7	2.9–6.0	<0.001	2.5	1.9–4.8	0.003
Operation time >4 h	1.9	0.81–4.6	0.311	–	–	–
Coronary pulmonary bypass time ≥110 min*	4.3	2.1–6.7	<0.001	4.0	2.9–5.8	<0.001
Aortic cross-clamping time >60 min	1.7	1.02–2.8	0.031	1.1	0.72–2.2	0.712
Red blood cells transfused*	2.1	1.4–3.6	0.002	1.5	1.4–4.1	0.003
Postoperative Hypotension*	7.8	3.6–9.1	<0.001	5.2	4.9–8.7	<0.001
Central venous pressure <6 cmH ₂ O*	8.4	4.3–12.5	<0.001	8.1	6.4–12.5	<0.001
Mechanical ventilation ≥9 h*	2.5	1.8–4.8	<0.001	1.8	1.4–3.9	0.016
Use of ACEIs/ARBs*	3.1	2.2–6.4	<0.001	1.9	1.1–2.8	0.005

Operation time was not included in multivariate analysis due to *p* value >0.25 (*p*=0.311). ACEI – angiotensin-converting enzyme inhibitors; ARB – angiotensin receptor blockers; OR – odd ratio; CI – confidence interval. Variables in univariate analysis with *p* values <0.25 were included in the multivariate analysis where variables with *p* values <0.05 in the multivariate analysis were considered independent risk factors. * Significant parameter for acute kidney injury.

stage 1 AKI group. Also, our study results demonstrated that mild AKI also caused poor outcomes and mortality as compared to non-AKI cases. KDIGO criteria of AKI includes mild cases with a transient increase in SCr [19]. Therefore, it is a primary necessity to identify and treat even mild AKI to reduce post-operative mortality in patients undergoing cardiac surgery.

Patients with AKI had a significantly higher mortality rate as compared to those without AKI. The mortality rate in our current study (4%) was in agreement with the findings of retrospective analysis, where the overall in-hospital mortality rate was 4.1% [14]. Moreover, patients with CSA-AKI requiring dialysis showed higher mortality rates; similar findings were presented by a retrospective study [23]. In addition, in our study, patients with AKI had significantly longer hospital and ICU stays than patients who did not meet AKI criteria. These findings were consistent with the results of other studies conducted in a Chinese population [12,15,23]. Taken together, the present study found that post-operative AKI was a common complication following cardiac surgery and was accompanied by poor outcomes and high mortality.

Our study found that a higher number of patients who died had AKI stage 3, followed by stage AKI 2, and then AKI stage 1. The results of our study were in line with retrospective studies [14,17,23,28]. The KDIGO classification yields more accurate reflections on the mortality rate, and improves the sensitivity of the AKI diagnosis [29]. Our study results supported the recommendation to assess the risk factors for AKI development prior to cardiac surgeries.

Logistic regression analysis determined that CVP <6 cmH₂O, postoperative hypotension, and the use of ACEIs/ARBs were important clinical factors that increased the risk of post-operative AKI. The strongest risk factor was CVP <6 cmH₂O, where patients with low CVP had 8 times the odds of developing AKI. This finding concurred with the results of previous investigations in a Chinese population and underlines the importance of post-operative fluid replacement as an effective measure to prevent AKI [15]. Hypotension, as defined by systolic blood pressure <90 mm Hg after surgery but before the development of AKI, was another strong predictor of AKI. The use of ACEIs/ARBs has been associated with the risk of decreased GFR [30]. Our study concluded that patients who were using

antihypertensive drugs would have 2 times the risk of developing AKI.

Our analysis showed that male gender had a 1.5 times higher propensity of developing AKI as compared females, but gender did not show any relationship with CSA-AKI in our multivariate analysis. The impact of gender on risk assessment of AKI is still under debate. Retrospective studies have shown that males are at high risk of developing AKI [14,20,23,26]. Other retrospective studies have found that females are at high risk of developing AKI [18,27]. Several studies have demonstrated that gender is not a predictor of CSA-AKI [1,16]. There is a need for further investigations on the impact of gender on the development of CSA-AKI.

Pre-operative anemia was identified as one of the important modifiable risk factors in the present analysis. Anemia causes a reduction in renal oxygen delivery and impairs hemostasis. CPB also induces hemostatic disturbance, which further leads to an increase in the risk of bleeding. Taken together, anemia induced platelet dysfunction causes excessive bleeding during heart surgery which requires a greater rate of blood transfusion, aggravating further risks of AKI [11]. Our study finding corroborated the results of previous literature [11,12]. Pre-operative anemia has an impact on the development of AKI.

The current analysis demonstrated that pre-operative hypertension and diabetes mellitus were significantly associated with AKI but only hypertension demonstrated an independent association with AKI in our multivariate analysis. The results of the analysis were similar to another cohort-based study [1]. Comorbidities have an impact on the development of AKI.

Other intra-operative modifiable risk parameters for the prevalence of AKI in the current analysis were an operation, CPB, and AXC time, which have been previously documented in the literature [12,14,23]. Another important intra-operative risk factor identified in the present study was a blood transfusion. Published data have shown that blood transfusion during CPB in itself can contribute to the risk of AKI by exacerbating the CPB-initiated systemic inflammatory response syndrome with a second inflammatory response, further contributing to ischemia-reperfusion injury in the kidneys [12]. Moreover, it is well documented that even a small incremental increase in SCr may cause worse short-term and long-term outcomes related to mortality and *de-novo* kidney disease [20]. The findings of the current study underscore the attention of treating

physicians towards intra-operative modifiable risk factors contributing to the development of AKI. These factors should be vigilantly monitored and if unavoidable, must be kept in mind while scheduling the follow-up of patients after cardiac surgery.

Several limitations of the current analysis should be taken into account. Since the present study was retrospective in nature, the risk of biases cannot be disregarded while interpreting the results. Moreover, the analysis did not have an accurate pre-operative estimation of GFR and it might be possible that some of the patients had pre-existing renal dysfunctions at the time of enrollment. Last but not least, the classification of AKI in the present study relied on SCr rather than urine output. However, urine output based AKI classification is less practical, due to the removal of urinary catheters 2 days after surgery. Future large population studies are needed to validate the findings of the current study and to develop modifiable risk scoring, especially among a Chinese population.

Conclusions

This observation study predicted that post-operative AKI was a frequent complication following cardiac surgery and was accompanied by high morbidity, mortality, and prolonged hospital/SICU stay. Old age, hypertension, anemia, LVEF <45%, and Charlson comorbidity index >2 were preoperative non-modifiable risk factors of cardiac surgery-associated AKI. Prolonged operation, cardiopulmonary bypass and aortic cross-clamp time, and blood transfusion were intra-operative predictors of AKI. Also, low blood pressure and central venous pressure, prolonged mechanical ventilation, and use of antihypertensive were a few of the post-operative clinical determinants of kidney injury. The analysis suggested that appropriate and effective control of these modifiable risk factors can reduce the risk of kidney injury.

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Conflict of interest

None.

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