Predictors of Acute Kidney Injury in Patients Undergoing Adult Cardiac Surgery

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Abstract

Background: Acute kidney injury (AKI) after cardiac surgery (CS) is not uncommon and has serious effects on mortality and morbidity. A majority of patients suffer mild forms of AKI. There is a paucity of Indian data regarding this important complication after CS. **Aims and Objectives:** The primary objective was to study the incidence of AKI associated with CS in an Indian study population. Secondary objectives were to describe the risk factors associated with AKI-CS in our population and to generate outcome data in patients who suffer this complication. **Methods:** Serial patients (n = 400) presenting for adult CS (emergency/elective) at a tertiary referral care hospital in South India from August 2016 to November 2017 were included as the study individuals. The incidence of AKI-CS AKI network (AKIN criteria), risk factors associated with this condition and the outcomes following AKI-CS are described. **Results:** Out of 400, 37 (9.25%) patients developed AKI after CS. AKI associated with CS was associated with a mortality of 13.5% (no AKI group mortality 2.8%, P = 0.001 [$P < 0.05$]). When AKI was severe enough to need renal replacement therapy, the mortality increased to 75%. Patients with AKI had a mean hospital stay 16.92 ± 12.75 days which was comparatively longer than patients without AKI (14 ± 7.98 days). Recent acute coronary syndrome, postoperative atrial fibrillation, and systemic hypertension significantly predicted the onset of AKI-CS in our population. **Conclusions:** The overall incidence of AKI-CS was 9.25%. The incidence of AKI-CS requiring dialysis (Stage 3 AKIN) AKI-CS was lower (2%). However, mortality risks were disproportionately high in patients with AKIN Stage 3 AKI-CS (75%). There is a need for quality improvement in the care of patients with AKI-CS in its most severe forms since mortality risks posed by the development of Stage 3 AKIN AKI is higher than reported in other index populations from high resource settings.

Keywords: *Acute kidney injury, acute kidney injury network criteria, cardiac surgery, mortality, renal failure requiring dialysis, risk stratification*

Introduction

Acute kidney injury (AKI) after cardiac surgery (CS) is fairly common with some reports citing a figure close to 30% although the exact incidence varies with definition and based on the numerous scoring systems available. About 1%–2% of patients develop severe renal injury requiring dialysis.[1] AKI after CS is associated with a substantial increase in morbidity and mortality which can exceed 60% among patients requiring dialysis. Even when there is a modest increase in serum creatinine values from baseline values, it is associated with longer hospital stay and increased costs besides adverse prognostication in outcomes.[2] A majority of patients suffer mild forms of AKI; even as knowledge and ability to detect subclinical disease using specific biomarkers evolves for this condition, it is likely that both the estimates of incidence and prognostication will evolve.

AKI-CS is occurs due to combination of preoperative, intra- and post-operative factors. There is no specific pharmacologic strategy to treat AKI. However, it might still be helpful to identify patients at risk of this complication; this could help in triage to focus on amelioration of modifiable risk factors before CS.

The incidence of community-acquired AKI reported in India was 4.14 per 1000 admissions in 1996–2008 with a mortality of 10.98%.[2] There are at present only limited descriptions of the epidemiology of postoperative renal injury after CS.[1] There is also a significant lacuna in our care continuum that there

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are no national or region-specific databases on the outcomes of treatment of cardiovascular disease, unlike our Western counterparts. As the population in our part of the subcontinent suffers significant cardiovascular disease burden and, as it progressively ages these descriptions will likely be important. This study was therefore planned to describe the risk factors for suffering AKI-CS from a tertiary referral hospital in South India. It additionally attempts to detail the consequences of suffering this complication. It strives to extend the literature on perioperative outcomes in general, and that of CS in the Indian subcontinent.

Materials and Methods

This was an observational prospective study conducted in a tertiary referral hospital in South India (Amrita Institute of Medical Sciences and Research Centre, Kochi, India, from August 2016 to November 2017. Serial adult patients (n = 400) presenting for cardiac surgical procedures (elective and emergency) were recruited into the study after due obtainment of clearance from the Institute Ethics Committee. Informed written consent was also obtained from study individuals or their delegated consent providers when applicable. Patient data were acquired and processed with due respect to confidentiality and in accordance with the information technology policies applicable at the hospital. Data were acquired both prospectively from the physical and electronic medical records of the individuals as also mined from the hospital information system by the study investigators for missing data/accuracy of data acquired from the physical medical record.

AKI was defined by the AKI network (AKIN) criteria [Table 1].

Sample size

The sample size was based on an observed incidence of 30% of AKI-CS in a similar publication (AKI after CS – Focus on Modifiable risk factors – Circulation – 2009; 119: 495–502). The minimum sample size was 225 with 95% confidence limit and 20% allowable error. Recruiting 400 patients was shown to provide a study with an estimated 15% allowable error.

Table 1: AKIN criteria

Stage	Creatinine	Urinary volume
STAGE 1	Increase in serum creatinine ≥0.3 mg/dl (or) increase ≥150%-200%	<0.5 ml/kg/hour for >6 h
STAGE 2	Increase in serum creatinine >200%-300% (>2-3 fold) from baseline	<0.5 ml/kg/hour for >12 h
STAGE 3	Increase in serum creatinine >300% (>3 fold from baseline (or) >4 mg/dl (or) requirement of RRT)	<0.3 ml/kg/hour for 24 h or anuria for 12 h

RRT: Renal replacement therapy, AKIN: Acute Kidney Injury Network

Inclusion criteria

All adult presents presenting for cardiac surgical procedures whether performed on or off cardiopulmonary bypass. An indicative list includes coronary artery bypass grafting, valve replacement/repair, thoracoabdominal aneurysm repair, aortic dissection, septal myectomy for hypertrophic cardiomyopathy, closure of atrial septal defects in adulthood and combined procedures such as valve and coronary bypass together.

Exclusion criteria

- Patients with preoperative renal failure requiring hemodialysis
- Missing pre-/post-operative creatinine values
- Patients who undergo more than one chronologically distinct cardiac surgical procedure during a hospital stay
- Baseline serum creatinine >1.5 mg/dl
- Patients on extracorporeal membrane oxygenation before surgery
- Patients who died in the OR (operation room) or within 24 h after surgical procedure or in whom the surgical procedure was aborted for any reasons.

Variable definitions

- Demographic characteristics – age, sex, weight, height, body mass index
- Comorbidities – diabetes mellitus, systemic hypertension, dyslipidemia, chronic obstructive pulmonary disease, pulmonary veno-occlusive disease
- Euro SCORE II
- Recent acute coronary syndrome (ACS)
- Baseline serum creatinine – serum creatinine before surgery
- Postoperative serum creatinine – highest value in the postoperative period during intensive care unit stay
- History of stroke/transient ischemic attack defined by the presence of neurological deficit before surgery
- Timing of coronary angiogram (hours) – time from coronary angiogram to the time of surgery
- Involvement of the left main coronary artery disease
- Cardiac surgical procedure-type, emergency/elective, redo surgery
- Preoperative ejection fraction based on echocardiographic reports
- The requirement of cardiopulmonary bypass
- Need for total circulatory arrest (min)
- Need for intra-aortic balloon counterpulsation (intra-aortic balloon pump [IABP]) and duration of IABP (min)
- The requirement of blood transfusion (packed red blood cell, platelets, fresh frozen plasma, and cryoprecipitate)

- Requirement of inotropes, maximum dose of inotrope postoperatively, total duration of inotropes in minutes
- Atrial fibrillation in postoperative period
- Hourly urine output.

Outcome variables are defined as follows:

- Need for hemodialysis/continuous veno-venous hemofiltration during entire postoperative hospital stay or within 30 days' postoperatively
- Operative mortality – defined as in-hospital mortality (or) 30 days' mortality
- Length of hospital stay is defined from the day of admission until the day of discharge.

Statistical analysis

Statistical analysis was compiled using SPSS 20.0 (SPSS Inc., Chicago, IL, USA). Continuous variables were presented as mean (± standard deviation). Univariate analysis for continuous variables was done by independent samples *t*-test for normally distributed continuous variables, for nonparametric variables the Mann–Whitney U test was used. Univariate statistical analysis of categorical variables was performed by Chi-square test/Fisher's exact test as appropriate. When sample distributions were small for a risk variable, the population was bootstrapped before determining significance to be entered into the stepwise regression. IABP use was not considered as none of the patients in whom IABP use was reported suffered AKI. The variables which were significant in Univariate analysis were considered for Multivariate logistic regression. Binary stepwise multivariate logistic regression to assess independent correlates of AKI associated with CS and requirement for renal replacement therapy (RRT), AKI associated with hospital stay and mortality. $P < 0.19$ was considered to be statistically significant. The regression model was evaluated by Hosmer– Lemeshow test-goodness of fit. Odds ratio (OR) for mortality in patients with and without AKI was also calculated.

Results

In our study, 37 (9.25%) patients developed AKI after CS. There were no gross differences between the groups with and without AKI in terms of age [Table 1]. Male individuals suffered a higher risk of developing AKI-CS (10.9% of the males patients suffered AKI-CS while only 4.2% of the opposite sex had this complication ($P < 0.049$)), [Figure 1].

Overall within the cohort that suffered some or the other form of AKI 13.5% of this group died; in stark comparison, in the non-AKI group the overall mortality was only 2.5% showing how even mild forms of the complication have ominous consequences (OR 5.52 95% confidence interval 1.8–17.1) [Figure 2]. Even more dramatically, when AKI-CS was severe enough to warrant RRTs 75% of such patients died [Figure 3]. This result, however, should be tempered by the overall low incidence of this complication since only 9 patients needed RRT, but 6 of these 9 individuals died.

The results of the univariate regression analysis are reported in Tables 2-4. Variables shown to independently predict AKI-CS with AKI are recent ACS, atrial fibrillation and systemic hypertension on stepwise multivariate binary logistic regression. The independent risks of these individual factors are depicted in Table 5.

Discussion

We successively recruited four hundred patients presenting to our center for elective/emergency CS during August 2016–October 2017. The overall incidence of AKI in this cohort was 9.25%. This is lower than the reported incidence in a meta-analysis of the literature which cites the overall incidence of this complication to be about 22%.[3] Most of

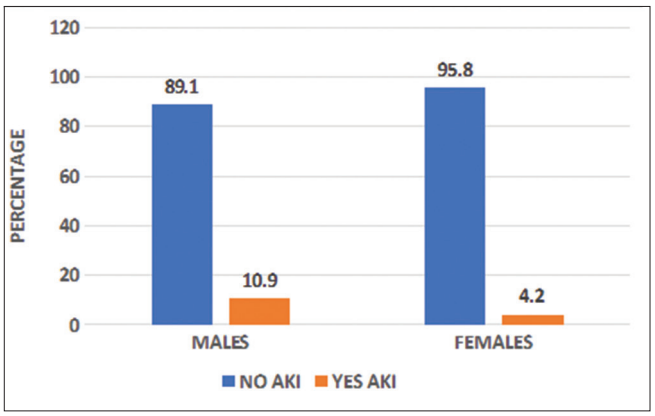

Figure 1: Gender distribution in patient population

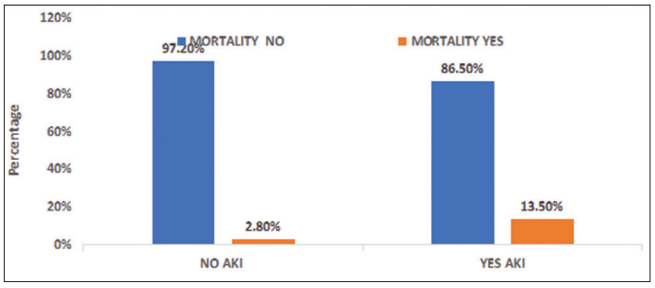

Figure 2: Mortality risk due to acute kidney injury cardiac surgery (10/353 patients without acute kidney injury cardiac surgery died whereas 5/32 patients with acute kidney injury cardiac surgery died, *P* < 0.001)

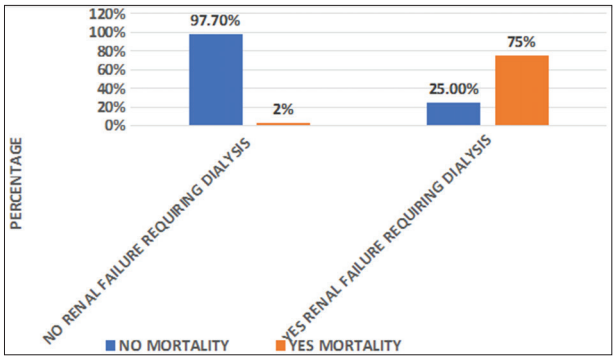

Figure 3: Renal failure requiring dialysis and mortality

Table 2: Comparison between continuous variables and acute kidney injury

Variable	AKI						*t*	*P*
	No (*n*=363)			Yes (*n*=37)				
	n	Mean/median	SD/IQR	*n*	Mean/median	SD/IQR		
Age	363	59.60	11.68	37	62.14	9.49	1.275	0.203^
Body surface area	363	1.68	0.17	37	1.72	0.14	1.011	0.313^
Time of CAG in hours	298	120	48-336	34	168	24-366	0.067	0.947$
Euro SCORE II (%)	363	1.69	1.09-2.82	37	2.31	1.43-4.23	2.628	0.009$,*
Hospital stay	363	11	9-15	37	12	8.50-20.50	0.557	0.578$

**P*<0.19 significant. Independent samples *t*-test; $Mann–Whitney U-test *P* value; ^*P*<0.19 considered significant for univariate analysis. SD: Standard deviation, IQR: Interquartile range

Table 3: Ionotrope requirement and aortic occlusion time in patient population

Variable	AKI						*t*	*P*
	No			Yes				
	n	Mean/median	SD/IQR	*n*	Mean/median	SD/IQR		
Noradrenaline (mcg/kg/min)	267	0.04	0.02-0.06	34	0.04	0.02-0.065	0.109	0.913$
Adrenaline (mcg/kg/min)	116	0.03	0.02-0.06	20	0.035	0.02-0.05	0.060	0.952$
Dobutamine (mcg/kg/min)	78	4.38	2.5-5.0	1	10	10-10	1.723	0.085$,*
Milrinone (mcg/kg/min)	49	0.3	0.23-0.4	8	0.27	0.23-0.3	0.231	0.817$
Levosimendan (mcg/kg/min)	16	0.10	0.06-0.1	5	0.10	0.05-0.2	0.667	0.505$
Vasopressin (units/kg/min)	16	0.0003	0.0002-0.0004	6	0.00045	0.0002-0.0007	1.161	0.246$
DOPA (mcg/kg/mins)	6	2.50	2.0-4.0	2	5.60	2.5-8.7	1.031	0.302$
Ionotrope usage (mins)	300	2130	1320-3131.3	35	2410	1005-4882	0.581	0.561$
Aortic occlusion time (mins)	126	104.01	39.72	13	119.62	54.34	1.300	0.196^

**P*<0.19 significant. Independent samples *t*-test; $Mann–Whitney U-test *P* value; ^*P*<0.19 considered significant for univariate analysis. Dobutamine, Milrinone, Levosimendan, Vasopressin, and DOPA are presented with bootstrap median due to insufficient sample size. SD: Standard deviation, IQR: Interquartile range, AKI: Acute kidney injury, DOPA: Dopamine

the AKI reported, however, was deemed mild and therefore of less consequence. However, it should be pointed out that a majority of our patients underwent coronary artery revascularization (270/400); it is usual to perform this in centers such as ours without the use of cardiopulmonary bypass. The overall incidence of this complication is, therefore, closer to that reported in this population.[4] It should, however, be pointed out that the complication rate can, however, be as high as 14%–15% in this limited population as well.[5,6] It is, also a matter of current debate, a matter of current debate whether or not off-pump coronary artery bypass (OPCAB) revascularization is inferior to on-pump coronary artery bypass (ONCAB) in the mid/long term as opposed to short-term outcomes.[7] In the coronary trial which was a randomized controlled trial of ONCAB versus OPCAB with a study population across 16 countries, OPCAB was clearly beneficial in preventing AKIN Stage I AKI-CS with a strong trend toward preventing AKIN Stages 2/3 at 30 days.[8] However, there was no protection from renal failure requiring dialysis either in the short or intermediate term.[8] Further, in all prevalence studies of AKI-CS, there is divergence on account of patient enrolment and definitions of the condition, the nature and types of surgery which the individuals underwent. It is also questionable as to what should be the real outcome of interest considering that AKIN Stage I AKI-CS is less devastating, reversible, and therefore, probably of less clinical import than other more advanced forms of renal injury at least in the intermediate term.[9]

It is widely regarded that inotrope use or a compromised hemodynamic state is an important substrate in the causation of AKI-CS.[10] In our cohort, dobutamine use was associated with AKI in initial univariate analysis, but this risk was found to be insignificant on multivariate regression. On further univariate analysis, it was also determined that recent acute coronary events and emergent surgery were significantly more common in the adverse event group; these index risks advert to perturbations in hemodynamics not adequately captured in the enumerated data and to that extent, undermine the conclusions of the study. It should, however, be moot to point out, that, in any case, observational studies do not and should not attempt to hint at or prove causation.

Lower ejection fractions, the presence of long-standing diabetes and hypertension expectedly were markedly more prevalent in the group suffering AKI-CS. However, the time interval between angiography and procedure was not significant in risk for AKI-CS, and there is an ongoing debate about the attributable risk owing to radiocontrast agents outside the domain of CS.[11] The use of blood products has increasingly been a point of focus

Table 4: Association between acute kidney injury and demographic and clinical variables

Variable	AKI		Chi-square value test	*P*
	No, *n* (%)	Yes, *n* (%)		
LMCA category				
No	296 (92.5)	24 (7.5)	5.837	0.016*
Yes	67 (83.8)	13 (16.2)		
Gender				
Male	271 (89.1)	33 (10.9)	3.888	0.049*
Female	92 (95.8)	4 (4.2)		
Diabetes mellitus				
No	169 (94.4)	10 (5.6)	5.180	0.023*
Yes	194 (87.8)	27 (12.2)		
Systemic hypertension				
No	114 (97.4)	3 (2.6)	8.806	0.003*
Yes	249 (88)	34 (12)		
Dyslipidemia				
No	171 (95.5)	8 (4.5)	8.821	0.003*
Yes	192 (86.9)	29 (13.1)		
Recent ACS				
No	216 (95.2)	11 (4.8)	12.128	0.0001*
Yes	147 (85)	26 (15)		
Ejection fraction (%)				
<50	111 (85.4)	19 (14.6)	6.605	0.010*
>50	252 (93.3)	18 (6.7)		
NYHA Class				
NYHA Class I and II	264 (90.1)	29 (9.9)	0.548	0.828[a]
NYHA Class III and IV	99 (92.52)	8 (7.47)		
Redo				
No	345 (90.8)	35 (9.2)	0.014	0.706[a]
Yes	18 (90.0)	2 (10.0)		
Emergency				
No	354 (91.5)	35 (9.2)	7.412	0.024[a,*]
Yes	9 (69.2)	4 (30.8)		
CABG				
No	121 (92.4)	10 (7.6)	0.606	0.436
Yes	242 (90)	27 (10)		
CABG + valve				
No	343 (91.2)	33 (8.8)	1.673	0.262[a]
Yes	20 (83.3)	4 (16.7)		
Valve replacement/repair				
No	271 (89.1)	33 (10.9)	3.888	0.049*
Yes	92 (95.8)	4 (4.2)		
Others				
No	352 (91)	35 (9)	0.602	0.342[a,*]
Yes	11 (84.6)	2 (15.4)		
Reintubation				
No	338 (91.8)	30 (8.2)	6.604	0.020[a]*
Yes	25 (78)	7 (21.9)		
Stroke				
No	345 (91.5)	32 (8.5)	4.534	0.050[a,*]
Yes	18 (78.3)	5 (21.7)		
IABP				
No	359 (90.7)	37 (9.3)	0.412	1.000[a]
Yes	4 (100.0)	0		
CPB				
No	235 (90.7)	24 (9.3)	0.0001	0.988
Yes	128 (90.8)	13 (9.2)		
History of prior PTCA				
No	313 (89.9)	35 (10.1)	0.007	1.000[a]
Yes	50 (96.2)	2 (3.8)		
Atrial fibrillation				
No	299 (93.4)	21 (6.6)	13.767	0.0001*
Yes	64 (80)	16 (20)		
Re exploration				
No	355 (90.8)	36 (9.2)	0.038	0.586[a]
Yes	8 (88.9)	1 (11.1)		
PRBC				
No	187 (89)	23 (11)	1.526	0.217
Yes	176 (92.6)	14 (7.4)		
FFP				
No	342 (90.2)	37 (9.8)	2.259	0.241[a]
Yes	21 (100.0)	0		
Platelet				
No	342 (90.5)	36 (9.5)	0.614	0.708[a]
Yes	21 (95.5)	1 (4.5)		
Cryoprecipitate				
No	352 (90.7)	36 (9.3)	0.012	1.000[a]
Yes	11 (91.7)	1 (8.3)		

[a]Fisher's exact test value. *$P<0.19$ significant. LMCA: Left main coronary artery, ACS: Acute coronary syndrome, AKI: acute kidney injury, FFP: Fresh frozen plasma, PRBC: Packed red blood cell, PTCA: Percutaneous transluminal coronary angioplasty, IABP: Intra aortic balloon counter pulsation, CPB: Cardiopulmonary bypass, CABG: Coronary artery bypass, NYHA: New York Heart Association

in perioperative care (Farmer *et al*. 2017)[12] with a proven reduction in both costs and complications. There have however been contrarian thoughts from the specialty of CS highlighting the role of anemia in aggravating renal injury[13] and transfusion in improving more global outcome,[14] our study could not demonstrate any association between blood component use and AKI-CS.

On multivariate regression analysis of the univariate predictors of AKI-CS only the following three predictors were found significant: systemic hypertension, recent ACS, and postoperative atrial fibrillation. We surmise that this is on account of a coalescence of the extremely deleterious risks that atrial fibrillation has on systemic hemodynamics in the presence of diastolic dysfunction.

Table 5: Multivariate binary logistic regression analysis with respect to acute kidney injury

Variable	OR	95% confidence limit		*P*
		Lower	Upper	
Systemic hypertension	4.002	1.177	13.603	0.026*
Recent ACS	3.340	1.553	7.184	0.002*
Atrial fibrillation	3.845	1.837	8.048	0.0001*

*P<0.05 significant, P<0.001 statistically highly significant.
OR: Odds ratio, ACS: Acute coronary syndrome

It is already well known that this combined risk of undermanaged hypertension and diastolic dysfunction has independent effects on mortality.[15] More specifically there is now further clear evidence from other investigators of the deleterious effects of heart failure with preserved ejection fraction (HFpEF) on renal outcomes, both in the community[16] and after coronary artery bypass.[3]

Our study is lacking in that specific indices of diastolic function were not systematically studied or enumerated in the risk assessment of CS-AKI. Nevertheless, we suggest that we extend the literature in our cohort and our results will also make a compelling case for both systematic study and specific measures to target HFpEF in patients presenting for CS. The risks of diabetes were however not sustained on multivariate regression. It is interesting that multivariate regression shows that dopamine was actually a risk factor for AKI-CS. Therefore, it is likely that this was rather the effect than the cause of AKI-CS and a misinformed attempt to treat this entity. Recent ACS as presentation also substantially increased the risk of AKI-CS; this likely is a surrogate for the compromised hemodynamic profile of these patients. However, other surrogates of hemodynamic compromise such as extended vasoactive drug use or use of the IABP were not shown to be independent predictors of this complication. A detailed explanation is suggested vide supra.

In the group which suffered AKI-CS of any degree hospital stay was marginally but not significantly increased. The adverse outcome group also had higher mortality overall than in the group which did not suffer AKI-CS (97% survival vs. 86.5% survival). The starkest data was from the small group of patients who suffered AKI-CS requiring dialysis; an overwhelming, 75% of the patients who suffered this degree of AKI died. This is considerably higher than the benchmark mortality rates approaching 50%–60% in the previously reported literature.[17,18] It may be evidence of how renal intensive care in low- and middle-income settings such as ours does not yet meet international benchmarks of care and that a conscious effort to improve the overall quality of evaluating and delivering RRTs in acute care after CS needs a conscious revisit.

Overall, we suggest that we extend the rather limited description of AKI-CS from limited resource healthcare. While heartening that the overall incidence of AKI-CS, we report is lower than most other reports in the literature the extraordinary risks of mortality that result from the severest forms of the condition warrant purposive and conscious quality improvement. There should be country specific registry data listing major perioperative outcomes; they will allow clinical practice guidelines based on local data. Single center, observational studies such as ours can be lamps but cannot be the beacon.

Conclusions

The overall incidence of AKI-CS was 9.25%. The incidence of AKI-CS requiring dialysis (Stage 3 AKIN) AKI-CS was lower (2%). However, mortality risks were disproportionately high in patients with AKIN Stage 3 AKI-CS (75%). Despite this study showing that the predominant severity of AKI- CS was mild mortality risks were disproportionately higher (2.8% vs 13.5%, Figure 2).

In multivariate logistic regression atrial fibrillation, systemic hypertension, recent ACS independently predict the risk of CS-AKI in our population. Systemic hypertension and occult diastolic heart failure could be linked to hemodynamic compromise secondary to onset of postoperative atrial fibrillation. Since observational studies do not prove causation, this can only be considered hypothesis generating.

There is a need for quality improvement in the care of patients with CS AKI in its most severe forms since mortality risks posed by the development of Stage 3 AKIN AKI is higher than reported in other index populations from high-resource settings.

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Conflicts of interest

There are no conflicts of interest.

References

1. Mahaldar AR, Sampathkumar K, Raghuram AR, Kumar S, Ramakrishnan M, Mahaldar DA. Risk prediction of acute kidney injury in cardiac surgery and prevention using aminophylline. Indian J Nephrol 2012;22:179-83.
2. Korula S, Balakrishnan S, Sundar S, Paul V, Balagopal A. Acute kidney injury-incidence, prognostic factors, and outcome of patients in an Intensive Care Unit in a tertiary center: A prospective observational study. Indian J Crit Care Med 2016;20:332-6.
3. 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;30:82-9.
4. Kim MY, Jang HR, Huh W, Kim YG, Kim DJ, Lee YT, *et al.* Incidence, risk factors, and prediction of acute kidney injury after off-pump coronary artery bypass grafting. Ren Fail 2011;33:316-22.
5. Kumada Y, Yoshitani K, Shimabara Y, Ohnishi Y. Perioperative risk factors for acute kidney injury after off-pump coronary artery bypass grafting: A retrospective study. JA Clin Rep 2017;3:55.

6. Massoudy P, Wagner S, Thielmann M, Herold U, Kottenberg-Assenmacher E, Marggraf G, *et al.* Coronary artery bypass surgery and acute kidney injury – Impact of the off-pump technique. Nephrol Dial Transplant 2008;23:2853-60.
7. Filardo G, Hamman BL, da Graca B, Sass DM, Machala NJ, Ismail S, *et al.* Efficacy and effectiveness of on- versus off-pump coronary artery bypass grafting: A meta-analysis of mortality and survival. J Thorac Cardiovasc Surg 2018;155:172-9.e5.
8. Lamy A, Devereaux PJ, Prabhakaran D, Taggart DP, Hu S, Paolasso E, *et al.* Off-pump or on-pump coronary-artery bypass grafting at 30 days. N Engl J Med 2012;366:1489-97.
9. Lamy A, Devereaux PJ, Prabhakaran D, Taggart DP, Hu S, Straka Z, *et al.* Five-year outcomes after off-pump or on-pump coronary-artery bypass grafting. N Engl J Med 2016;375:2359-68.
10. Hudson C, Hudson J, Swaminathan M, Shaw A, Stafford-Smith M, Patel UD, *et al.* Emerging concepts in acute kidney injury following cardiac surgery. Semin Cardiothorac Vasc Anesth 2008;12:320-30.
11. Weisbord SD, Mor MK, Resnick AL, Hartwig KC, Palevsky PM, Fine MJ. Incidence and outcomes of contrast-induced AKI following computed tomography. Clin J Am Soc Nephrol 2008;3:1274-81.
12. Farmer SL, Towler SC, Leahy MF, Hofmann A. Drivers for change: Western australia patient blood management program (WA PBMP), world health assembly (WHA) and advisory committee on blood safety and availability (ACBSA). Best Pract Res Clin Anaesthesiol 2013;27:43-58.
13. Huybregts RA, de Vroege R, Jansen EK, van Schijndel AW, Christiaans HM, van Oeveren W, *et al.* The association of hemodilution and transfusion of red blood cells with biochemical markers of splanchnic and renal injury during cardiopulmonary bypass. Anesth Analg 2009;109:331-9.
14. Arias-Morales CE, Stoicea N, Gonzalez-Zacarias AA, Slawski D, Bhandary SP, Saranteas T, *et al.* Revisiting blood transfusion and predictors of outcome in cardiac surgery patients: A concise perspective. F1000Res 2017;6. pii: F1000.
15. Huang JT, Cheng HM, Yu WC, Lin YP, Sung SH, Wang JJ, *et al.* Value of excess pressure integral for predicting 15-year all-cause and cardiovascular mortalities in end-stage renal disease patients. J Am Heart Assoc 2017;6. pii: e006701.
16. Jain A, Scott C, Chen HH. The renal-cardiac connection in subjects with preserved ejection fraction: A population based study. ESC Heart Fail 2017;4:266-73.
17. Bove T, Calabrò MG, Landoni G, Aletti G, Marino G, Crescenzi G, *et al.* The incidence and risk of acute renal failure after cardiac surgery. J Cardiothorac Vasc Anesth 2004;18:442-5.
18. Pistolesi V, Di Napoli A, Fiaccadori E, Zeppilli L, Polistena F, Sacco MI, *et al.* Severe acute kidney injury following cardiac surgery: Short-term outcomes in patients undergoing continuous renal replacement therapy (CRRT). J Nephrol 2016;29:229-39.