Original Article

Applicability of the Cleveland clinic scoring system for the risk prediction of acute kidney injury after cardiac surgery in a South Asian cohort

Shobhana Nayak Rao[a,*], Pradeep Shenoy M[b], Mundayat Gopalakrishnan[b], Amith Kiran B[a]

[a] Deptartment of Nephrology, K.S.Hegde Medical Academy, Derlakatte, Mangalore, Karnataka, India
[b] Department of Cardiothoracic Surgery, K.S.Hegde Medical Academy, Derlakatte, Mangalore, Karnataka, India

A B S T R A C T

Background: Acute kidney injury (AKI) after cardiac surgery is a frequent post-operative complication associated with an increased risk of mortality, morbidity and hospital costs. Preoperative risk scores such as the Cleveland Clinic Scoring Tool (CCST) have been validated in Western population group to identify patients at higher risk of AKI and may facilitate preventive strategies. However, the scoring tool has not been validated systematically in a South Asian cohort. We aimed to evaluate the applicability of the CCST in prediction of AKI after open cardiac surgery in a South–Indian tertiary care center.

Materials and methods: A retrospective study of all patients who underwent elective open cardiac surgery over a 4 year period from Jan 2012 to Dec 2015 at a single centre were included and relevant details extracted from a comprehensive chart review. The primary outcome was AKI as defined by the Kidney Disease Improving Global Outcomes (KDIGO) criteria. Patients were risk stratified as per the CCST to assess for prediction of AKI into low risk (0–2), intermediate risk (3–5) and high risk (>6) groups.

Results: A total of 276 patients underwent open cardiac surgery with mean age of 51.5 ± 13.06 yrs. This included 177 (64.1%) males and 99 females (35.8%). Overall incidence of AKI was 6.88%. Mean age, gender, BMI, preoperative serum creatinine, diabetes mellitus, chronic obstructive pulmonary disease, cardiopulmonary bypass time was similar in patients who developed AKI vs those who did not have AKI postoperatively. The mean CCST scores were 1.6 in those without AKI, 1.5 in stage 1, 3.0 in stage 2 and 3.4 in stage 3 AKI. Higher risk scores predicted greater risk of AKI. A total of 106 patients (38.4%) were on ACE/ARB, 119 patients (43.1%) received beta-blockers, 110 (39.8%) received diuretics while 144 (52.1%) had received preoperative statins. Comparison of drug use between the two groups revealed that preoperative use of ACEI/ARB was associated with highest risk of AKI (p = 0.006). Mortality rate was also high at 15.7% in those with AKI compared to 3.1% in non-AKI group (p = 0.04).

Conclusion: The modified CCST was valid in risk identification of patients with severe stage of AKI but did not have strong discrimination for early AKI stages. Preoperative statin use did not protect against AKI in our study, however preoperative ARB/ACEI use was significantly associated with occurrence of postoperative AKI.

1. Background

Acute kidney injury (AKI) after cardiac surgery is a serious complication. Depending on the definition used, upto 30% of cardiac surgery patients develop some form of AKI post surgery[1–3] and 1–5% develop severe kidney injury necessitating dialysis AKI-D.[2,4–5] The mortality following AKI-D has been reported to be very high in the range of 50–80%.[6,7] Even milder forms of AKI can have an impact on short term and long term morbidity and mortality. AKI associated with cardiac surgery increases infectious risk, extends the length of stay in the intensive care unit thereby increasing the utilization of health care resources and independently predicts death.[8] Recent advancements have led to less invasive surgical techniques and off–pump coronary artery bypass procedures have reduced mortality, however the incidence of renal dysfunction has more or less remained the same.[9] The accurate prediction of patients who are likely to develop AKI, application of measures to prevent AKI and the early recognition and the

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treatment of AKI are goals for nephrologists involved in the care of these patients.

There are few externally valid tools for risk stratification for AKI-D such as the Cleveland Clinic scoring tool (CCST), Mehta score etc.[3] The CCST tested a large cohort of patients (n = 15,838) to identify patients at risk of developing AKI after open heart surgery.[10] Multiple comparison studies have found that the Cleveland Clinic Score has the highest discriminative power in a Western population,[11] however, as the authors themselves have stated the model needed to be tested prospectively at multiple centers and heterogenous population to substantiate its broad applicability.[12] A key limitation of this risk score is also that it does not predict milder forms of AKI, which may have significant and long term effects. The purported reasons for AKI following cardiac surgery include renal ischemia-reperfusion injury, inflammation and atheroembolism, neurohormonal activation and oxidative stress.[13,14] The role of statins to reduce inflammation and oxidative stress and thereby lowering the risk of renal dysfunction after cardiac surgery has been investigated and some studies have found lower incidence of AKI in patients in whom statins were started or continued into the early post-operative period[15,16] though this is not equivocal. Most of this data again has been from the Western literature in a predominantly white, Caucasian population with essentially no available data in a South Asian patient population who may exhibit different clinical outcomes. The Indian population is probably the best suited to test the applicability of the scoring tool given that India has one of the highest rates of diabetes and cardiovascular disease in the developing world. The purpose of our study was to assess the applicability of the CCST in prediction of AKI in a South Indian patient population and to assess the effect of preoperative statin use on the risk of AKI following open cardiac surgery.

2. Methods

Data collection and Study Cohort: We conducted a retrospective chart review of all adult patients (≥18 yrs) who underwent elective open cardiac surgery from Jan 2012 to Dec 2015 at our institute. All study data including intra-operative and post-operative details were abstracted after a thorough in-patient chart review. Predictors of AKI in the CCST: gender, co-morbidities including diabetes mellitus, chronic obstructive pulmonary disease (COPD), congestive cardiac failure, type of cardiac surgery and preoperative and postoperative serum creatinine (mg/dl) were included. We were not able to sub classify diabetics into type 1/2 and hence included all patients with diabetes as a parameter. Since our study included only patients undergoing elective surgery, emergency surgery as a parameter was not included in the score. Information about the exact numerical value of the left ventricular ejection fraction (LVEF) was not accurately available from records and hence it was included as a dichotomous variable as either LVEF<35 or >35% in the scoring system.

Types of surgery included coronary artery bypass graft (CABG), aortic valve replacement or repair (AVR), mitral valve repair or replacement (MVR), tricuspid valve repair or replacement (TVR) and combinations of CABG and AVR, MVR or TVR as well as other cardiac surgery such as atrial septal defect closure (ASD), ventricular septal defect closure (VSD), ventricular aneurysm repair, pericardiectomy etc. In addition, we collected data on other preoperative variables such as age, body mass index (BMI), preoperative diagnosis of chronic kidney disease (CKD), presence of significant proteinuria (>300 mg/day), pre-operative use of drugs including statins, ACEI/ARB, beta–blockers and diuretics. The class of statins used included simvastatin, rosuvastatin, atorvastatin or others. Dosage used and continuation/stoppage of drug during the peri and post-operative period was recorded. Perioperative variables include the length of cardiopulmonary bypass

Table 1
Pre and periop risk variables associated with AKI.

Risk factors (n = 276)	Total N = 276		No AKI N = 257		AKI N = 19		
Preop Continuous	Mean	SD	Mean	SD	Mean	SD	P value
Age	51.5	13.06	50.8	12.9	62.93	8.66	0.35
BMI	21.62	4.02	21.64	4.09	21.3	2.72	0.63
Preop creatinine	0.93	0.24	0.92	0.23	1.06	0.29	0.98
Preop categorical	N	%	N	%	N	%	P value
Male	177	64.10	164	63.8	12	63.1	0.69
Female	99	35.80	94	36.5	5	26.3	
Diabetes mellitus							
Absent	196		186		10		0.58
Present	80		71		9		
Chronic obstructive pulmonary disease							
No	258		247		16		0.2
Yes	18		10		3		
Types of surgery							
CABG only	173	62.6	163	63.40	10	52.60	NS
Valve only	63	22.8	56	21.70	7	36.80	NS
CABG + valve	8	2.9	6	2.33	2	10.50	NS
Other cardiac surgery	32	11.5	32	12.40	0	0.0	NS
Medication	Mean	SD	Mean	SD	Mean	SD	P value
Cardiopulmonary bypass time in mins	125.1	39.40	124.6	39.4	133	42.5	0.99
Statin (n = 144)			124	48.20	10	52.6	0.419
ACEI/ARB (n = 106)			**90**	**35.0**	**16**	**84.20**	**0.006**
β Blockers (n = 119)			111	43.10	8	42.10	0.39
Diuretics (n = 110)			102	39.60	8	42.10	0.58

(in minutes). Renal replacement therapy (RRT) if required was recorded. We did not include parameters such as hematocrit and number of blood transfusion in the final analysis since this is not part of the CCST, though this was recorded.

2.1. Outcomes

Our primary outcome was AKI as defined by the KDIGO (Kidney Diseases Improving Global Outcomes) criteria; stage 1, stage 2 or stage 3. Stage 1 was defined as an increase in serum creatinine 1.5–1.9 times the baseline within 5 days, stage 2 was an increase in creatinine 2.0–2.9 times the baseline within 5 days and stage 3 was a documented increase of more than 3.0 times the baseline or requirement or initiation of RRT during hospital stay. We did not use urine output as a measure due to limitations in data availability and the postoperative use of diuretics which may have an impact on urinary output.

2.2. Cleveland Clinic Score

To evaluate the use of the scoring tool, we calculated a score for each patient based on the general method described previously by Thakar et al.[10] As noted earlier, we were limited to use presence of diabetes mellitus as a parameter instead of insulin–requiring diabetes that has been used in the risk scoring. We were also unable to include emergency surgery in the scoring tool also as mentioned earlier. Thereby, the minimum score in our data set was 0 and the maximum score was 15. Patients were risk stratified as per the score into Low risk (score 0–2), Intermediate risk (3–5), and high risk (≥6) groups as described in the original study.

2.3. Statistical analyses

Descriptive statistics for categorical variables were reported as frequency (percentage) while continuous variables were reported as means (standard deviation). Categorical variables were compared between patients who developed AKI and those that did not develop AKI using Chi-square or Fischer's exact test when applicable. Continuous variables were compared using one way ANOVA. Logistic regression models and receiver–operating analyses were used to calculate the area under the curve (AUC) for the prediction of stage 1,2,3 AKI using the Cleveland Clinic Score. All statistical tests were two-sided with alpha level set at 0.05 for statistical significance. Statistical analyses was performed using STATA version 11.0 SE (Statacorp LP, College Station, Tex). The Institutional Ethical board approved of the study and the study was performed in accordance with the Declaration of Helsinki.

3. Results

A total of 276 patients who underwent open cardiac surgery were included. Table 1 summarises the patient details and demographics. Mean age was 51.5 ± 13.06 yrs. There were 177 (64.1%) males and 99 females (35.8%) in the study. The overall incidence of AKI in our study was 6.88%. of which Kidney Disease Outcomes Quality Initiative (KDOQI) stage 1 accounted for 63.1%, stage 2, 10.5% and stage 3, 26.3%. All patients with stage 3 required renal replacement therapy. Mean age, gender, BMI, preoperative serum creatinine, diabetes mellitus, chronic obstructive pulmonary disease, cardiopulmonary bypass time was similar in patients who developed AKI vs those who did not have AKI postoperatively. A total of 173 (62.6%) underwent CABG alone, 63 patients (22.8%) underwent valve surgery alone, 8 patients (2.9%) underwent CABG + valve surgery while 32 (11.5%) had undergone other cardiac surgery which included repair of atrial, ventricular septal defects, left ventricular aneurysm surgery, coarctation of aorta repair and

pericardiectomy. There was no relation between type of surgery and risk of AKI in our study population. The mean CCST scores were 1.6 in those without AKI, 1.5 in stage 1, 3.0 in stage 2 and 3.4 in stage 3 AKI. Higher risk scores predicted greater risk of AKI. A total of 106 patients (38.4%) were on ACE/ARB, 119 patients (43.1%) received beta-blockers, 110 (39.8%) received diuretics while 144 (52.1%) had received preoperative statins. Comparison of drug use between the two groups revealed by multiple logistic regression revealed that preoperative use of ACEI/ARB was associated with highest risk of AKI (p = 0.006). Statins were used in total of 52.1% of patients, 48.2% in non-AKI and 52.6% in AKI group (p = 0.4,NS). Mortality rate was also high at 15.7% in those with AKI compared to 3.1% in non-AKI group (p = 0.04). Table 2 depicts patient outcomes after surgery at the time of discharge.

4. Discussion

The incidence of AKI in our series was 6.88% and is similar to that found by Condon et al[17] as well as another study by Mahaldar et al[18] done from the Indian sub-continent in a similar patient group. The incidence of AKI-D is dependent on the type of surgery. While typical CABG has the lowest incidence of AKI-D at 1%, valvular surgery had a reported incidence of 1.7%,while the highest risk group included combined CABG with valvular surgery with an incidence of AKI-D of 3.3%.[19] The work of Thakar et al.[10] mentioned in detail in Table 3 provided the Cleveland Clinic Foundation acute renal failure scoring system that has been validated in North American patients from the USA and Canada[20] in the risk prediction of AKI after open cardiac surgery. The Canadian study by Wong et al.[20] tried to evaluate the scoring tool in the prediction of both AKI-D and less severe stages of AKI in 2316 patients from a tertiary care centre and found that it was valid in identifying patients with severe stages of AKI but had lower discriminative power for earlier stages of AKI. Englberger et al[11] and Kiers et al[21] have also used the Cleveland Clinic Score in AKI patients not requiring dialysis and found similar results. The utility of the score has also been explored by one study from India[18] mentioned earlier and its utility has been demonstrated in a different heterogenous population. However there are no firm patient data from South Asia otherwise.

While the incidence of AKI requiring dialysis was only 1.8% in our study, the scoring risk on the Cleveland risk score was higher in this group. The absence of data on whether the surgery was emergent or not and the absence of accurate LVEF data may have also reduced the predictive power of the Cleveland score in our group. The use of cardiopulmonary bypass in our series was in 36.6% of patients in our group while 63.4% of cardiac surgery was performed off pump. The incidence of AKI has been found to increase with increase in CPB and aortic cross-clamp time. A meta-analysis of 9 studies[22] reported that mean cardiopulmonary bypass time of patients who developed AKI was significantly

Table 2
Patient Outcome after cardiac surgery.

Type of dialysis				
	No AKI (n = 257)		AKI (n = 19)	
SLED	N/A		2	10.50%
In patient hemodialysis	N/A		4	21.00%
Peritoneal dialysis	N/A		0	0%
Discharge Destination				
	No AKI		AKI	
	Mean	SD	Mean	SD
Died (n = 11)	8	3.10	3	15.70
Recovered fully	249	96.8	9	47.36
Persisting/dysfunction	N/A		7	36.80

Table 3
ARF scores (adapted from Thakar et al.).

Risk Factor Points:
Female gender 1
Congestive heart failure 1
Left ventricular ejection fraction <35% 1
Preoperative use of IABP 2
COPD 1
Insulin-requiring diabetes 1
Previous cardiac surgery 1
Emergency surgery 2
Valve surgery only (reference to CABG) 1
CABG valve (reference to CABG) 2
Other cardiac surgeries 2
Preoperative creatinine 1.2 to <2.1 mg/dl (reference to 1.2) 2
Preoperative creatinine ≥2.1(reference to 1.2) 5
Minimum score, 0; maximum score, 17.

longer compared to those who did not develop AKI (23.8 mins, 95% CI 16.7–29.66, p < 0.0001). However we did not find the mean CBP time significantly different between those who developed AKI and those did not. Several factors may have contributed to the overall lower incidence of AKI in our cohort such as younger age, lesser co-morbidities and the fact that more than 30% of surgeries performed involved correction of congenital heart defects such as atrial and ventricular septal defects and/or valvular replacements. Patients undergoing these surgeries were obviously younger and with relatively better preserved cardiac function and with minimal co-morbidities lowering their preoperative risk score. The Cleveland Clinic score has also been earlier validated in a proportion of non-isolated CABG surgeries which have higher incidence of AKI compared to isolated CABG surgeries.[7] More than half of patients who developed AKI died or had persisting renal dysfunction at discharge while >95% of patients without AKI recovered fully and were discharged home. Data has shown that even early stages of AKI are associated with considerable burden on the patient and health care system, necessitating the need for preoperative risk assessment.

We also looked at the relation between preoperative statin use and risk of AKI. The use of preoperative statin use has been found in earlier studies by Brunelli et al.[16] to be consistently associated with decreased risk of acute kidney injury with adjusted odds ratio of 0.74–0.80. The protective association of statin use was however more pronounced in those undergoing vascular surgery and least among patients undergoing cardiac surgery. The use of preoperative statins however did not have any protective role in the prevention of postoperative AKI in our study. Surprisingly we did find that the preoperative use of ACEI/ARB was associated with greater risk of developing AKI post surgery (p = 0.006). This association has also been found in an earlier study by Arora et al.[23] who found that preoperative ACEI/ARB use was associated with a 27.6% higher risk of AKI. While this may be due to confounding by indication of use given that patients with pre-existing diabetes and poorer ejection fractions have been on ACE/ARB, this needs to be confirmed by larger well designed trials.

Diuretics were earlier thought to reduce the severity of AKI by preventing tubular obstruction and decreasing oxygen consumption. However a double–blind randomized controlled trial of furosemide treatment was not found to be protective, rather it doubled the incidence of AKI compared to placebo group.[24] We also did not find any difference in AKI incidence and use of diuretics.

A preoperative risk stratification tool should be ideally able to identify high-risk patients so that preventive strategies can be started earlier improving overall patient management. Although

several biomarkers such as neutrophil gelatinase–associated lipocalcin (NGAL), cystatin C, Kidney injury molecule (KIM-1) etc have shown promising results in detecting AKI at 24 h of surgery, intraoperative or immediate post-operative detection remains however unpredictable.[25] It is in this context that preoperative risk scores such as the CCST may help in identification of individuals that may have higher postoperative risk of AKI and preventive measures can be therefore be taken to prevent adverse outcomes.

5. Conclusions

We conclude based on our small study that the modified CCST was valid in risk identification of patients with severe stage of AKI but did not have strong discrimination for early AKI stages. Preoperative statin use did not protect against AKI in our study, however preoperative ARB/ACEI use was significantly associated with occurrence of postoperative AKI. Further prospective data on this is necessary from larger studies from a heterogenous population from the Indian subcontinent.

Limitations of our study

Lack of prospective validation and smaller number of AKI patients.

Research involving humans/animals

Not a randomized trial hence not applicable. The study is a retrospective review of subjects who had open cardiac surgery.

Conflict of interest

None declared.

Financial disclosures

Nil.

Ethical statement

The authors of the study do state that:

○ The manuscript has not been submitted to more than one journal for simultaneous consideration.
○ The manuscript has not been published previously (partly or in full), except in abstract form.
○ No data have been fabricated or manipulated (including images) to support the conclusions.
○ No data, text, or theories by others have been presented as if they were the author's own.

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