Predicting Acute Kidney Injury Following Non-Emergent Cardiac Surgery: A Preoperative Scorecard

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Abstract

Objective: To determine the predictors of postoperative AKI following non-emergent cardiac surgery among patients with variable preoperative eGFR levels. Methods: Retrospective study of patients who underwent elective or in-hospital cardiac surgical procedures performed between January 2006 and November 2015. The procedures included isolated CABG, isolated AVR or combined CABG and AVR. The primary outcome AKI (any stage) following non-emergent cardiac surgery utilizing the 2012 KDIGO criteria. Patients were categorized based the following renal outcomes: mild AKI, severe AKI (KDIGO stage 2 or 3) and post-operative dialysis.. Results: A total of 6713 patients were included in our study. The mean age was 66.8 years (SD ± 10.3), with 76.2% being males. A total of 4487 patients had normal or mildly decreased eGFR (G1 or G2) preoperatively (66.8%), while 1960 patients were in the G3 category (29.1%). Only 266 patients (3.9%) had G4 or worse renal function. A total of 1489 (28.5%) patients experienced post-operative AKI. The need for postoperative dialysis occurred in 4.2% of the AKI subgroup. In-hospital mortality was higher among the AKI subgroup (7.3% vs 0.5%, $p<0.0001$). In an adjusted model, a lower pre-operative eGFR category was the strongest predictor of AKI. A practical scorecard for the preoperative estimation of severe AKI for non-emergent cardiac procedures incorporating these parameters was developed. Conclusions: Preoperative eGFR is the strongest predictor of post-operative AKI in individuals undergoing non-emergent cardiac surgery. A practical scorecard incorporating preoperative predictors of AKI may allow informed decision making and to predict AKI following non-emergent cardiac surgery

Introduction:

Perioperative acute kidney injury (AKI) is a major determinant of both short-term and long-term outcomes following cardiac surgery[1–4]. AKI has been has been shown to be an independent predictor of morbidity and mortality in the post-operative period, including adverse cardiovascular events and need for dialysis[5–7]. Depending on the definition, post-operative AKI can occur in up to 30% of patients undergoing cardiac surgery[8,9]. Approximately 5% of patients with AKI following cardiac surgery will require dialysis [3], a subgroup that suffers from dismal outcomes with mortality rates approaching 60% in some studies and a high burden on health care resources[10–13].

While the majority of patients undergo cardiac surgery electively, a significant proportion of patients undergo in-hospital surgery during index admission due to a variety of causes, including acute coronary syndrome (ACS) or exacerbation of heart failure, which can increase the risk of AKI [14,15]. Furthermore, while there is extensive literature in assessing the risk of AKI following cardiac surgery, only a few studies have aimed to address the impact of pre-operative CKD (utilizing established criteria) on post-operative AKI and predicting the need for dialysis following cardiac surgery[16–18] . In addition, rarely has the issue been examined solely in a lower-risk, non-emergent population, which may represent a significantly different population with distinctive outcomes[19].

Therefore, the objective of this current study is to identify the predictors of post-operative acute kidney injury and specifically, to determine if CKD stage is associated with an incremental increase in the risk of AKI among a cohort of Canadian, elective and non-urgent in-hospital patients undergoing cardiac surgery.

Material and Methods:

Patient Population:

The study population included patients who underwent elective or in-hospital cardiac surgical procedures performed between January 2006 and November 2015 at the Queen Elizabeth II Health Sciences Center (QEII HSC) in Halifax, Nova Scotia, Canada. The QEII HSC is the only cardiac surgical center for the Province of Nova Scotia serving a base population of 971,395. We included all patients undergoing the following cardiac surgical procedures at the QE-II-HSC: isolated coronary artery bypass grafting (CABG) surgery, isolated aortic valve replacement (AVR), or combined CABG and AVR. Patients were excluded if they underwent an emergency or urgent (defined as the need for operative intervention within 24hrs) surgery, endocarditis, mitral valve procedures and complex procedures, such thoracic aortic surgery and trauma. Cardiac surgery was performed with cardiopulmonary bypass and anticoagulation was achieved using intravenous heparin given at a dose of 400 IU/kg with a target activated clotting time (ACT) greater than 450 seconds. Antifibrinolytic agents were used routinely and consisted mainly of tranexamic acid. Intermittent cold blood cardioplegia was delivered in an antegrade or retrograde fashion based on surgeon preference. Protamine sulfate was given for reversal of heparin in all patients.

Data Source:

Data was obtained using the using the Maritime Heart Center (MHC) Cardiac Surgery Registry. The MHC registry is a detailed prospectively collected clinical database containing perioperative data on all cardiac surgery cases at the Queen Elizabeth Health Sciences Centre (QEII HSC) and commenced in 1995 [20].

Primary Outcome, determination of Preoperative eGFR and post-operative AKI:

The primary outcome was the development of AKI (any stage) following cardiac surgery utilizing the 2012 KDIGO criteria (Table 1)[21]. Severe AKI was defined as patients fulfilling stage 2 or stage 3 AKI, while post-operative dialysis was defined as patients requiring dialysis regardless of stage. Additional outcomes of clinical significance included mortality and the need for post-operative dialysis. Preoperative eGFR was calculated based on the Kidney Disease-Improving Outcomes 2012 Guidelines [22] (Table 2). The following formula was used to calculate eGFR as per the CKD-EPI equation: GFR = 141 * min(Scr/ϰ,1)α * max(Scr/ϰ, 1)-1.209 * 0.993Age * 1.018 [if female]. For analytical purposes, G1 and G2 patients were assessed together while all other eGFR categories were analyzed separately.

Variable Selection and analysis:

Other preoperative clinical characteristics of interest included age, sex, chronic obstructive pulmonary disease (COPD), peripheral and/or cerebral vascular disease, New York Heart Association (NYHA) functional class, diabetes, redo surgery, clamp time, cardioplegia type and completeness of revascularization. Variable selection was based on multiple models predicting postoperative AKI in cardiac surgery that have been both internally and externally validated [23]. Individual procedure types were categorized as follows: isolated CABG, isolated AVR and combined AVR/CABG.

Statistical Analysis

Continuous variables were compared using a 2-tailed t test or Wilcoxon rank sum test, and categorical variables were analyzed using a chi-square or Fisher's exact test, as appropriate.

Adjusted logistic regression models were generated to examine the association of AKI with pre-operative eGFR and pre-operative surgical status. Variables to be included in the model included sex, age, diabetes, chronic obstructive pulmonary disease, COPD, left ventricular ejection fraction (LVEF), Peripheral vascular disease, cerebrovascular disease, glomerular filtration rate (eGFR), type of surgery and previous cardiac surgery. A bedside post-operative scorecard for predicting AKI was then generated then utilizing the results of the logistic regression. This was developed by determining the potential strength of individual relationships between the previously identified variables based on the method described by Sullivan et al [24]. Scores for each factor were assigned relative weights of each coefficient in the multivariable regression model. Initial scores were assigned an integer value based on the B -coefficient of the OR, and the scores were subsequently adjusted up or down by increments of 0.5 to ensure that the sum of the risk scores corresponded to the category of predicted risk.

All statistical analyses were performed using SAS software version 9.4 (The SAS Institute, Cary, NC).

Ethics

This study was conducted with the full approval of the institutional (Nova Scotia Health Authority) Research Ethics Board.

Results:

Study population

A total of 6713 patients were included in our study. Table 3 demonstrates the baseline characteristics of the cohort. The mean age was 66.8 years (SD ± 10.3) and men accounted for the majority of the study population (76.2%). A total of 4487 patients had normal or mildly decreased eGFR (G1 or G2) preoperatively (66.8%), while 1960 patients were in the G3 category (29.1%). Only 266 patients (3.9%) had G4 or worse renal function. A total of 2852 (42.5%) of patients had NYHA class III or IV. The spectrum of surgical interventions performed included the following: isolated CABG (n=4766, 71%), isolated AVR (n=1251, 18.6%), combined AVR and CABG (n=696, 10.4%). Among these, 3192 (47.5%) were elective, and 3521 (52.2%) were determined to be urgent. A total of 1489 (28.5%) patients experienced post-operative AKI. Patients who developed postoperative AKI were more likely to have reduced preoperative eGFR. Those with G3 or higher CKD were at a significantly higher risk of post-operative AKI. In addition, patients with AKI tended to be older (mean age 69.6, ± 10), and had higher rates of comorbidities, including diabetes (50% vs 35.2%, p<0.0001) and COPD (19.3% vs 11.6%, p<0.0001). In contrast, the risk of AKI was no different comparing elective versus in-house cardiac surgery. The AKI subgroup had a higher rate of combined procedures (16.7% vs 8.6%, p<0.0001).

Postoperative Outcomes:

Unadjusted postoperative outcomes are shown in Table 4. The majority of patients with AKI were classified as stage 1 AKI (94.6%). The need for postoperative dialysis occurred in 4.2% of the AKI subgroup. In-hospital mortality was higher among the AKI subgroup (7.3% vs 0.5%, p<0.0001). The incidence of low cardiac output syndrome reintubation, tamponade, prolonged ventilation was also markedly higher among the AKI subgroup.

Independent Predictors of Renal Outcomes:

Predictors of AKI, severe AKI and post-operative AKI, along with odds ratios (OR) and confidence limits (CI) are shown in Figure 1. In an adjusted model, a lower pre-operative eGFR category was the strongest predictor of AKI. For the G3 category, there was a significant association with any AKI (OR 2.11, 95% CI 1.84 – 2.41), but not with severe AKI or post-operative dialysis. In contrast, the G4 category predicted any AKI (OR 4.29, 95% CI 3.22 – 5.71), severe AKI (OR 23.97, 95% CI 11.5 – 49.95) and post-operative dialysis (OR 14.83, 95% CI 6.8 – 32.33). G5 CKD had the strongest association with all renal outcomes (any AKI; OR 69.65, 95% CI 16.61 - 292.08, severe AKI; OR 385.4, 95% CI 150.5 – 986.66 and postoperative dialysis; OR 124.1, 95% CI 49.4 – 311.73).

Other independent predictors of the need for post-operative dialysis included COPD (OR 2.24, 95% CI 1.2 - 4.12), diabetes (OR 2.45, 95% CI 1.38 - 4.54) and LVEF <30% (OR 2.64, 95% CI 0.86 - 3.08). In contrast, age, male sex, redo sternotomy and complexity of procedure were not predictive of severe AKI or DIALYSIS in our cohort.

Scorecard for Preoperative Estimation of Severe AKI Risk for Non-emergent Cardiac Procedures

A practical scorecard for the preoperative estimation of severe AKI for non-emergent cardiac procedures is noted in Table 5. As shown in Table 5b, using these scores, risk estimates for severe AKI ranged from 1% (for scores of 0-3.5) to >90% (for scores [?]13.5).

Discussion:

In this study, we analyzed post-operative AKI among a large cohort of patients undergoing non-emergent cardiac surgery. As expected, patients with AKI were more likely to have predisposing risk factors that have been reported in the literature including advanced age, CKD, diabetes, chronic lung disease and peripheral vascular disease. Following adjustment for clinical differences, we found that a lower pre-operative eGFR was the strongest predictor of any AKI, severe AKI and need for post-operative dialysis among patients undergoing elective and in-hospital cardiac surgery. While age, female sex, redo sternotomy and complexity of procedure were not independently predictive of severe AKI or need for dialysis in our cohort (in contrast to other models[2,12,23,25–28]), Importantly, we were able to combine these predictors (along with low eGFR) into a pragmatic risk prediction tool that may have practical implications for the care of patients requiring non-emergent cardiac surgery.

Our study expands on the existing literature around risk prediction for AKI following cardiac surgery. Predicting major adverse outcomes post-operatively is a vital aspect of patient-centered care with shared decision making. This is even more crucial given the demographics of patients who require cardiac surgery; the increase in the proportion of frail and multi-comorbid patients that require cardiac surgery further emphasizes the need for better risk prediction.[29]. Unlike prior studies, we opted to focus solely on a low-risk, non-emergent population. Acknowledging that emergency surgery is an established risk factor for AKI and that decisions around emergency surgery may not provide the same time frame for patient discussion, our risk prediction model is more focussed on clinical scenarios where the discussion of risks may have a greater impact on patient choice.[30].

Outside of the selection of a lower risk cohort, the results of our study need to be compared to other literature looking at risk prediction for AKI following cardiac surgery. Historically post-operative AKI has been defined by utilizing absolute serum creatinine, a 50% or greater increase in serum creatinine from baseline or need for dialysis (AKI-D)[7]. Various criteria to define postoperative AKI have been utilized [31,32]. However, a consensus has been established to utilize the KDIGO criteria in order to achieve more consistent and reproducible results when assessing postoperative AKI. Among stable, elective patients, eGFR represents a more accurate reflection of kidney function and is less susceptible to other confounders, such as sex, age and weight [33]. The prevalence of patients with moderate renal dysfunction (G3 and worse) among our cohort was 33.1%, which approximates the larger Society of Thoracic Surgery (STS) database (prevalence of 27.1%) accounting for the differences in the urgency of surgery and the use of the MDRD formula to calculate eGFR [3]. The inclusion of CKD in our model is significant, as it has been established as most important predictor in prior models that included preoperative eGFR[19,27,33]. As expected in our cohort, preoperative CKD was the highest predictor of poor renal outcomes, with category G4 being threshold for independent prediction of severe AKI and the need for dialysis following cardiac surgery.

With regards to postoperative outcomes, the incidence of post-operative AKI within our population followed the expected published frequency (5-28%), accounting for variability in definitions of AKI[8,9]. However, the rate of postoperative dialysis among our study cohort was lower as compared to the rates reported in other centers [19,34–36]. Multiple explanations underpin this finding, including the exclusion of more complicated procedures and the lower overall clamp time among the non-AKI group.

Our scorecard for predicting severe AKI is has several clinical implications. To our knowledge, it was derived from the largest known cohort of exclusively elective cardiac surgery procedures, improving generalizability. Furthermore, the scorecard integrates exclusively pre-operative variables, emphasizing its value as a bedside tool to identify patients at risk for AKI in advance of surgery to allow the provision of perioperative clinical strategies to mitigate the risk of renal injury.

To our knowledge, only a few existing studies have utilized scorecards in predicting AKI among non-emergent cardiac surgery patients. Callejas et al enrolled 942 electively undergoing cardiac surgery among a multicentre Spanish cohort [26]. This scorecard was externally validated against the Thakar model, despite the inclusion of emergency cases. Interestingly, preoperative creatinine determination and eGFR displayed no statistical significance in predicting post-operative AKI. Palomba et al showed that in a prospective cohort of 603 patients undergoing elective cardiac surgery, the incidence of AKI was 11% (n=66), with 18% of those patients requiring dialysis (n=11).[37]. However, the inclusion of intraoperative and postoperative variables in this study precludes the use of their derived scoring tool (the Acute Kidney Injury following Cardiac Surgery score) prior to determining the need for surgery.

Our study has several strengths. In addition to being a large cohort of non-emergent cardiac patients, this is one of few studies that have formally utilized the KDIGO criteria (an established AKI stratification tool) following elective cardiac surgery to predict postoperative AKI[26,38]. In addition, our derived scorecard is truly "bedside" where all the required variables to provide a risk-estimate are pre-operative.

There are limitations to this study that warrant further discussion. Due to the retrospective design, there is an inherent risk of bias and residual confounding. We acknowledge that a points-based risk-scoring derived from B -coefficient models may be limited due to competing risks, namely, mortality [39]. Furthermore, our risk prediction model and scorecard require external validation prior to widespread use. We relied solely on serum creatinine to classify AKI as per the KDIGO criteria, (rather than urine output), and this may have led to an underestimate of the outcome of AKI. However, urine output is poorly documented in the reported literature of post-operative patients[40]. In addition, we acknowledge that race was not used in the calculation of eGFR, due to a lack of data. However, given the known demographics of the Nova Scotia population, this is unlikely to have led to a large error in the observed association. Although race was not able to be included in the eGFR calculation (as it is not routinely captured in the MHC), only a paucity of individuals in Nova Scotia are African descendants based on 2016 census data, (21,910 individuals (2.4%) out of 908,340 Nova Scotians) [41]. Nonetheless, the results of this study may not be generalizable to populations with a larger proportion of African descendants. Finally, this study was derived from a single centre, rather than a multicenter study, which may limit external validity.

Conclusion:

In this study we identified that preoperative eGFR remains the biggest predictor of all stages of post-operative AKI in individuals undergoing non-emergent cardiac surgery. A practical scorecard incorporating preoperative predictors of AKI and the need for dialysis may allow informed decision making and provision of strategies to prevent AKI following non-emergent cardiac surgery.

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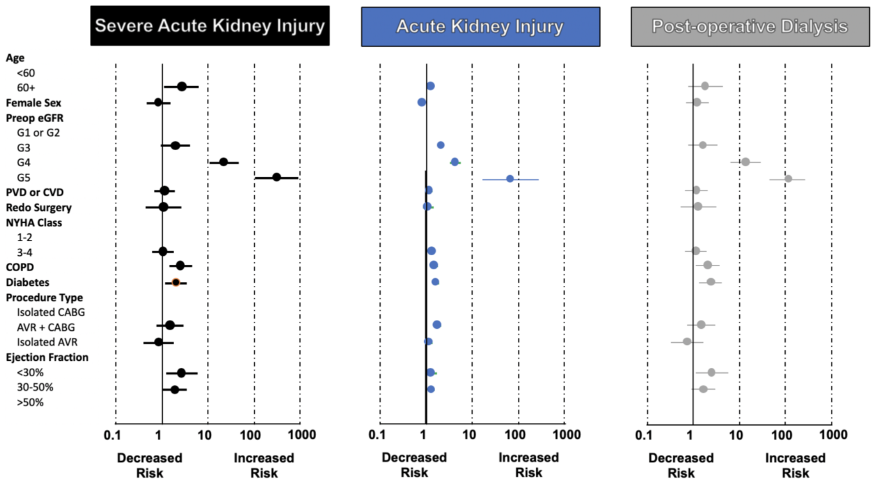

Figure 1. Adjusted predictors of AKI, severe AKI and need for post-operative dialysis after multivariable adjustment (visualized as relative odds with 95% confidence intervals).

Table 1. Staging of AKI as per Kidney Disease-Improving Outcomes (KDIGO) 2012 Guidelines	Table 1. Staging of AKI a
AKI Stage	Definition
Stage 1	Increase in serum creatini
Stage 2	Increase in serum creatini
Stage 3	Increase in serum creatini

Table 2. Staging of GFR as per Kidney Disease-Improving Outcomes 2012 Guidelines utilizing the CKD-EI
GFR category
G1
G2
G3a
G3b
G4
G5

Table 3. Baseline characteristics of patients categorized based on AKI following non-emergent cardiac surgery.	Table 3. B
Variable	**Overall (**
Age (yrs), Means ± SD	66.8 ± 10.
<60	1610 (24%)
60-69	2297 (34.2
70-79	2077 (30.9
80	729 (10.9%
Female	1600 (23.8
KDIGO staging (PREoperative eGFR) using CKD-EPI formula instead of RIFLE	
G1 or G2	4487 (66.8

Table 3. Baseline characteristics of patients categorized based on AKI following non-emergent cardiac surgery.	Table 3. B
G3	1960 (29.2
G4	228 (3.4%)
G5	38 (0.6%)
PVD &/or CVD, N (%)	1539 (22.9
Redo N, (%)	369 (5.5%)
Intra op IABP N (%)	57 (0.8%)
NYHA	
Class I or II	3861 (57.5
Class III or IV	2852 (42.5
COPD	893 (13.3%
Diabetes	2586 (38.5
Active endocarditis	19 (0.3%)
Procedure Type	
Isolated CABG	4766 (71%
Isolated AVR	1251 (18.6
AVR + CABG	696 (10.4%
Cardioplegia Type	
No Cardioplegia	68 (1%)
Antegrade Only	4811 (71.8
Retrograde Only	466 (7%)
Both	1351 (20.2
Urgency	
Elective	3192 (47.5
In-house	3521 (52.5
Clamp Time	
>90 min	2144 (31.9
Incomplete Revascularization	53 (0.8%)

CABG – Coronary artery bypass grafting, CKD- Chronic Kidney Disease Epidemiology Collaboration, COPD – chronic obstructive lung disease, CVD – cerebrovascular disease, IABP – intra-aortic balloon pump, NYHA – New York Heart association functional class, PVD – peripheral vascular disease

Table 4. Unadjusted postoperative outcomes among AKI vs non-AKI subgroups	Table 4. Unadjusted postoperative outco
	AKI (n=1489)
AKI Stage	
0	0 (0%)
1	1409 (94.6%)
2	7 (0.5%)
3	73 (4.9%)
Postoperative dialysis	63 (4.2%)
In-hospital Mortality	108 (7.3%)
Low Cardiac Output Syndrome	272 (18.3%)
Reoperation for Bleeding	122 (8.2%)
Postoperative Tamponade	86 (5.8%)
Reintubation	130 (8.7%)
Prolonged Ventilation	508 (34.1%)
Transfusion of Blood Products	818 (54.9%)

Table 5. Scorecard for Preoperative Estimation of Severe AKI Risk After Non-emergent Cardiac Surgery
5a. Predictors of Severe AKI

Table 5. Scoreca
5a. Predictors o

Risk Factor	**Score**
Age (y)	
60+	1
GFR	
G3	1
G4	4.5
G5	9
PVD CVD	0.5
COPD	1.5
Diabetes	1
AVR + CABG	0.5
EF	
<30%	1.5
30-50%	1

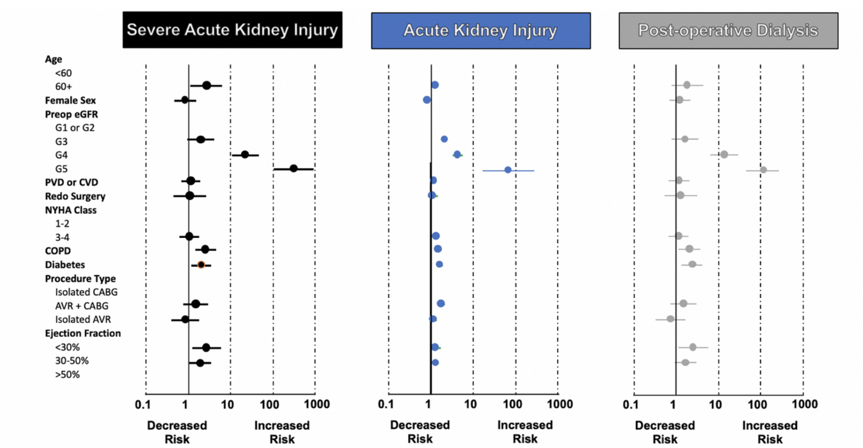

Figure 1. Adjusted predictors of AKI, severe AKI and need for post-operative dialysis after multivariable adjustment (visualized as relative odds with 95% confidence intervals).