Predicting kidney disease progression in patients with acute kidney injury after cardiac surgery

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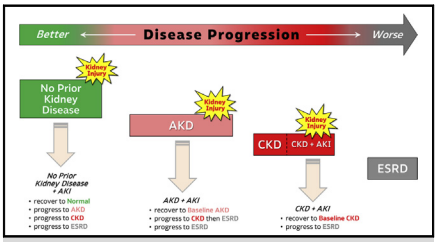
ABSTRACT

Objective: The study objective was to identify patients who are likely to develop progressive kidney dysfunction (acute kidney disease) before their hospital discharge after cardiac surgery, allowing targeted monitoring of kidney function in this at-risk group with periodic serum creatinine measurements.

Methods: Risks of progression to acute kidney disease (a state in between acute kidney injury and chronic kidney disease) were modeled from acute kidney injury stages (Kidney Disease: Improving Global Outcomes) in patients undergoing cardiac surgery. A modified Poisson regression with robust error variance was used to evaluate the association between acute kidney injury stages and the development of acute kidney disease (defined as doubling of creatinine 2-4 weeks after surgery) in this observational study.

Results: Acute kidney disease occurred in 4.4% of patients with no preexisting kidney disease and 4.8% of patients with preexisting chronic kidney disease. Acute kidney injury predicted development of acute kidney disease in a graded manner in which higher stages of acute kidney injury predicted higher relative risk of progressive kidney disease (area under the receiver operator characteristic curve = 0.82). This correlation persisted regardless of baseline kidney function ($P < .001$). Of note, development of acute kidney disease was associated with higher mortality and need for renal replacement therapy.

Conclusions: The degree of acute kidney injury can identify patients who will have a higher risk of progression to acute kidney disease. These patients may benefit from close follow-up of renal function because they are at risk of progressing to chronic kidney disease or end-stage renal disease. (J Thorac Cardiovasc Surg 2018;■:1-9)



After AKI, patients may progress to AKD and then to CKD or end-stage renal disease.

Central Message

AKI definitions can be used to predict AKD, a disease state between AKI and CKD in patients undergoing cardiac surgery.

Perspective

Patients with AKI may sustain further worsening of kidney function that is subchronic (AKD), and some of these patients may progress to CKD. There is no reliable method to predict who with AKI is at risk for developing progressive kidney disease. This study presents a serum creatinine–based predictive model for such at-risk patients.

See Editorial Commentary page XXX.

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Acute kidney injury (AKI) is a common disorder associated with increased morbidity and mortality.[1-4] In cardiac surgery, AKI complicates up to 30% of operations, and 1% to 2% of patients may require postoperative renal replacement therapy (RRT).[2,4] Although AKI may be reversible, some patients develop subclinical or sub-acute kidney disease (AKD) that can lead to progressive kidney disease (Figure 1 and Video 1).

Kidney Disease: Improving Global Outcomes (KDIGO) AKI guidelines termed this subchronic kidney injury as "AKD and disorders." They defined AKD as kidney damage for less than 3 months after AKI, glomerular filtration rate (GFR) less than 60 mL/min/1.73 m^2 for less than 3 months, or a decrease in glomerular filtration rate 35% or more or increase in sCr by more than 50% for less than 3 months[5] (Figure 1 and Table E1).

Although serum creatinine (sCr) is not an ideal biomarker for diagnosing AKI, it is an established marker

Scanning this QR code will take you to the supplemental tables and video for this article.

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Abbreviations and Acronyms

AKD = acute kidney disease
AKI = acute kidney injury
AUC_{ROC} = area under the receiver operator characteristic curve
CABG = coronary artery bypass grafting
CKD = chronic kidney disease
eGFR = estimated glomerular filtration rate
KDIGO = Kidney Disease: Improving Global Outcomes
NKD = no known kidney disease
RRT = renal replacement therapy
sCr = serum creatinine

of chronic kidney disease (CKD), a disease that can be clinically silent and asymptomatic until later stages. Unfortunately, current clinical practice does not require periodic sCr measurements in all postoperative patients after discharge because it is neither clinically indicated nor fiscally prudent. Therefore, our main objective was to determine whether early postoperative changes in sCr (AKI) during the index hospital admission after cardiac surgery could identify a subset of at-risk patients who will progress to CKD or end-stage renal disease via AKD. Identification of such patients before they are discharged from the hospital after cardiac surgery will enable targeted periodic sCr measurements in this at-risk patient group.

We hypothesized that sCr-based AKI stages can predict clinically significant decline in kidney function (development of AKD), defined as doubling of sCr from baseline by 2 to 4 weeks after surgery in patients with no kidney disease and patients with preexisting CKD. Doubling of sCr was used as our outcome because it represents a significant (≥50%) decrease in kidney function and is part of the KDIGO AKD definition. Our primary objective was to investigate whether the degree of AKI (AKI stages) can predict the development of AKD. Our secondary objective was to investigate whether patients who developed AKD had higher mortality and need for RRT after surgery.

MATERIALS AND METHODS

Data Sources, Data Collection, and Patient Characteristics

All patients who underwent cardiopulmonary bypass at Brigham and Women's Hospital from 2006 to 2014 were enrolled in the study. The data for this retrospective study were extracted from our electronic patient medical records using the RPDR query system (Partners Research, Boston, Mass). The authors' institutional review board approved this study, and the need for patient consent was waived.

Patients were divided into 2 groups: those with preoperative normal kidney function (estimated glomerular filtration rate [eGFR] ≥60 mL/min/1.73 m^2) and those with preexisting CKD (eGFR <60 mL/min/1.73 m^2). Preoperative eGFR was estimated by the isotope dilution mass spectrometry traceable Modification of Diet in Renal Disease study equation.[6] Baseline sCr was defined as the closest sCr before surgery within 2 weeks of the operation.

Outcomes of Interest

The primary outcome of interest was development of postoperative AKD. AKD, a subchronic kidney injury state, was defined as doubling of sCr using the peak sCr value during the 2- to 4-week postoperative period relative to preoperative baseline. We did not include AKI as part of the definition of AKD or urine output (Table E1). The highest sCr value available during this specific time period was used rather than the mean because we valued sensitivity at the expense of including false-negatives. Doubling of sCr was used because it met the functional criteria for AKD in the AKI guidelines and represents significant (50% or potentially >50%) loss of renal function.[5] Mortality and need for RRT were secondary outcomes. Alternately, we also defined AKD as a decrease in eGFR 35% or more at the 2- to 4-week postoperative period. This definition was included as part of the functional criteria for AKD in the guidelines. Data using the eGFR criteria are presented in Tables E2 to E4.

According to the guidelines, AKD is defined as kidney injury less than 3 months.[5] We chose this 2- to 4-week time after the surgery because we wanted to predict the development of sustained kidney injury closer to the acute period (ie, possibly during a reversible period) than a more chronic time point (ie, possibly irreversible period). We considered this 2- to 4-week postoperative period a point in time that reflects a period beyond the acute injury phase but before the chronic disease state, thus subchronic. We also chose this specific time because we previously found that early changes in sCr predicted progression of AKI to sustained kidney disease occurring 2 to 4 weeks after surgery in patients undergoing mesothelioma surgery.[7]

Statistical Analysis

Continuous baseline characteristics of patients with no known kidney disease (NKD) and with preexisting CKD were summarized as mean ± standard deviation and compared using Student *t* tests. Categoric variables were reported as absolute numbers (percentage) and analyzed using Fisher exact tests.

After univariate analyses, a multivariate prediction model including age, gender, and surgical type was generated rather than a propensity score-matching model to maintain the generalizability of the prediction model. Surgery type was categorized as the following: coronary artery bypass grafting (CABG); CABG and aortic or mitral valve surgery; valve surgery (without CABG); heart failure surgery (heart transplantation and mechanical assist device); and other (mainly congenital and surgery on the aorta). Other covariates known to be associated with increased risk of renal injury in patients undergoing cardiac surgery, as reoperations, emergency surgery, need for intra-aortic balloon pump, history of diabetes, and hypertension, did not show significance with univariate analysis and were not included in the multivariate prediction model.

A modified Poisson regression with robust error variance was used to estimate the cumulative relative risk of the association between the stages of KDIGO AKI and the development of AKD.[8] The modified Poisson regression was used because it allowed us to obtain cumulative risk ratios directly. Receiver operator characteristic curves were generated to examine the ability of the multivariate regression model using KDIGO AKI definitions to predict the development of AKD.

To evaluate the trend of AKI rates during the study period (2006-2014), patients with no AKI were compared with patients with AKI stage 1 and stages 2 and 3 combined. Linear regression was used to test for linear trend in AKI rates. All statistical analyses were performed using R software version 3.1.2 (R Foundation for Statistical Computing, Vienna, Austria).