Prediction of acute kidney injury within 30 days of cardiac surgery

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Objective: To predict acute kidney injury after cardiac surgery.

Methods: The study included 28,422 cardiac surgery patients who had had no preoperative renal dialysis from June 2001 to June 2009 in 18 hospitals. Logistic regression analyses were undertaken to identify the best combination of risk factors for predicting acute kidney injury. Two models were developed, one including the preoperative risk factors and another including the pre-, peri-, and early postoperative risk factors. The area under the receiver operating characteristic curve was calculated, using split-sample internal validation, to assess model discrimination.

Results: The incidence of acute kidney injury was 5.8% (1642 patients). The mortality for patients who experienced acute kidney injury was 17.4% versus 1.6% for patients who did not. On validation, the area under the curve for the preoperative model was 0.77, and the Hosmer-Lemeshow goodness-of-fit *P* value was .06. For the postoperative model area under the curve was 0.81 and the Hosmer-Lemeshow *P* value was .6. Both models had good discrimination and acceptable calibration.

Conclusions: Acute kidney injury after cardiac surgery can be predicted using preoperative risk factors alone or, with greater accuracy, using pre-, peri-, and early postoperative risk factors. The ability to identify high-risk individuals can be useful in preoperative patient management and for recruitment of appropriate patients to clinical trials. Prediction in the early stages of postoperative care can guide subsequent intensive care of patients and could also be the basis of a retrospective performance audit tool. (J Thorac Cardiovasc Surg 2014;147:1875-83)

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Postoperative renal dysfunction, also known as acute kidney injury (AKI), is a recognized and serious complication of cardiac surgery that increases in-hospital mortality, morbidity, length of stay, and hospital costs after surgery.[1] Identifying patients who are at high risk of developing AKI after cardiac surgery will potentially enable improved treatment decisions and support more informed patient education processes.

The incidence of AKI has varied, depending on the definition used, the postoperative period of the studies, and the specific population studied. Hence, it has been difficult to compare the results of published studies. Nevertheless, the incidence of postoperative AKI appears to range from 1% to 30%, with in-hospital mortality varying from 14% to 60%.[2-4] Postoperative renal replacement therapies (RRTs) are required for approximately 1% to 5% of cardiac surgery patients,[5] with in-hospital mortality rates reportedly up to 70% in these patients.[2,4]

Several risk factors for postoperative AKI have been identified, including diabetes mellitus, congestive heart failure, intra-aortic balloon pump (IABP) use, preoperative serum creatinine, age, left main coronary stenosis, peripheral vascular disease, and cardiopulmonary bypass duration.[3,5-7] Other possible risk factors for which the evidence has been less consistent include female gender, chronic obstructive pulmonary disease, infective endocarditis, emergent surgery, and crossclamp time.[2-4,6-10] Although some risk prediction tools have been proposed, they have included different combinations of risk factors, and a recent review found an absence of general agreement on the use of prediction models for AKI after cardiac surgery.[11] Indeed, they concluded that additional studies are required to predict milder AKI not requiring dialysis.

From 2001, the Australian and New Zealand Society of Cardiac and Thoracic Surgeons (ANZSCTS) registry of

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Abbreviations and Acronyms

AKI	= acute kidney injury
ANZSCTS	= Australian and New Zealand Society of Cardiac and Thoracic Surgeons
AUC	= area under the receiver operating characteristic curve
BIC	= Bayesian information criteria
HL-*P*	= Hosmer-Lemeshow *P* value
IABP	= intra-aortic balloon pump
MSE	= mean square error
NYHA	= New York Heart Association
RBC	= red blood cell
RRT	= renal replacement therapy

cardiac surgical procedures has collected outcomes, including complications after cardiac surgery, and collecting extensive patient, clinical, and surgical information.[12] The aim of the present study was to use the ANZSCTS registry to identify the best combination of patient and surgical risk factors for predicting AKI as defined by either RRT or a substantially increased serum creatinine after cardiac surgery.

METHODS

Study Population

The ANZSCTS registry recorded data for 32,279 patients who had undergone cardiac surgery from 2001 to 2009 in 18 hospitals in Australia. The patient demographics and clinical and surgery variables were collected by the registry.[12] From the existing data and the data availability in the registry, 38 pre-, peri-, and early postoperative variables potentially related to the development of AKI were chosen for consideration and are listed in Table 1. The early postoperative variables were those for which the value would typically be known within 24 hours of surgery.

The potential risk factors, New York Heart Association (NYHA) class (2713 missing) and number of red blood cell (RBC) units (4241 missing), were not considered owing to the number of missing values. However, the use of RBCs (yes vs no) was considered.

Patients requiring preoperative renal dialysis ($n = 521$) and those with missing data for postoperative renal function ($n = 86$) and any of the variables listed in Table 1 ($n = 3250$) were excluded. The data from the remaining 28,422 patients were used in the statistical analysis.

Three published models for predicting AKI[13-15] were applied to the ANZSCTS registry data, and their performance was measured using the area under the receiver operating characteristic curve (AUC). Some variables in these models had different definitions in the ANZSCTS registry.

The present research project was undertaken after approval from the ANZSCTS Research Committee, which governs access to data from the registry. Ethical approval for the use of de-identified registry data for secondary research purposes, such as our project, had previously been provided by each participating institution's ethics review committee.

Outcome Definition

Development of AKI was defined by at least 2 of the following measures within 30 days after surgery: (1) increased serum creatinine to greater than 200 μmol/L (2.26 mg/dL), (2) a doubling or greater increase in serum creatinine over the preoperative value, and (3) a new requirement for RRT.

Statistical Analysis

First, the data set was randomly divided in 2, forming a model creation data set ($n = 17{,}095$, 60% of total patients) and a model validation data set ($n = 11{,}327$). Next, 1000 bootstrap[16] samples (each 17,095 in size) were selected, with replacement from the model creation data set, and a logistic regression model for AKI incorporating all variables under consideration was applied to each of the 1000 samples. The number of times each candidate variable was significant ($P \leq .05$) in the 1000 models was recorded.

The first candidate model included the risk factors significant in all 1000 bootstrap samples. Next, a sequence of other candidate models, each with 1 variable more than the previous, were identified as the remaining variables were added to the model in rank order according to the number of times they were significant in the 1000 bootstrap samples.

Using the creation data set, the AUC,[17] Bayesian information criteria (BIC),[17] Hosmer-Lemeshow *P* value (HL-*P*),[17] and prediction mean square error (MSE)[17] were calculated for each of the candidate models. These 4 criteria were used to select a final model (the percentage of bootstrap samples in which an association was significant was not used for this purpose).

The prediction performance of the selected model was assessed by calculating the AUC, HL-*P*, and MSE using the validation data set. Finally, point scores proportional to the regression coefficient were assigned to the risk factors included in the final model. Next, for each patient, a risk score was calculated, and the average predicted risks for the different groups of patients are reported.

The statistical software package Stata, version 11 (StataCorp, College Station, Tex), was used for the present analysis.

RESULTS

A total of 32,279 cardiac operations were performed during the 8-year study period. The prevalence of AKI in the 3250 patients who were excluded because of missing data for pre-, peri-, and early postoperative variables was 5.8% ($n = 189$), not different from that for the included patients. In the 28,422 included patients, the mean age was 66 years, and 27% were women. AKI occurred in 1642 patients (5.8%), and the 30-day mortality rate for patients who developed AKI was 17.4% (compared with 1.6% for patients without AKI). Table 1 includes an additional description of the pre-, peri-, and early postoperative characteristics for patients with and without AKI. From the data listed in Table 1, it can be seen that patients who developed postoperative AKI were slightly older and more often had diabetes, hypertension, peripheral vascular disease, respiratory disease, infective endocarditis, and previous myocardial infarction. More patients with postoperative AKI had congestive heart failure, arrhythmia, cardiogenic shock, the need for resuscitation and the use of inotropes on the day of surgery, or had undergone a previous cardiothoracic intervention (surgical or percutaneous). The bypass and crossclamp times were longer on the average in the group that developed AKI. IABP use and the use of RBCs were also more common in that group (Table 1).

All variables from the 3 published models,[13-15] except for ejection fraction, race, and NYHA class, were among the variables considered for inclusion in the models we developed, although some variables had slightly different definitions. The ejection fraction was missing for 72% of the ANZSCTS patients. Two methods were used to