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Improving the Prediction of Cardiac Surgery–Associated Acute Kidney Injury

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Introduction: Acute kidney injury (AKI) is a potentially fatal complication of cardiac surgery. The inability to predict cardiac surgery-associated AKI is a major barrier to prevention and early treatment. Current clinical risk models for the prediction of cardiac surgery-associated AKI are insufficient, particularly in patients with preexisting kidney dysfunction.

Methods: To identify intraoperative variables that might improve the performance of a validated clinical risk score (Cleveland Clinic Score, CCS) for the prediction of cardiac surgery-associated AKI, we conducted a prospective cohort study in 289 consecutive elective cardiac surgery patients at a tertiary care center. We compared the area under the receiver operator characteristic curve (AUC) of a base model including only the CCS with models containing additional selected intraoperative variables including mean arterial pressure, hematocrit, duration of procedure, blood transfusions, and fluid balance. AKI was defined by the Kidney Disease Improving Global Outcomes 2012 criteria.

Results: The CCS alone gave an AUC of 0.72 (95% confidence interval, 0.62–0.82) for postoperative AKI. Nadir intraoperative hematocrit was the only variable that improved AUC for postoperative AKI when added to the CCS (AUC = 0.78; 95% confidence interval, 0.70–0.87; $P = 0.002$). In the subcohort of patients without preexisting chronic kidney disease (n = 214), where the CCS underperformed (AUC, 0.60 [0.43–0.76]), the improvement with the addition of nadir hematocrit was more marked (AUC, 0.74 [0.62–0.86]). Other variables did not improve discrimination.

Discussion: Nadir intraoperative hematocrit is useful in improving discrimination of clinical risk scores for AKI, and may provide a target for intervention.

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Acute kidney injury (AKI) is an important complication of cardiac surgery and is associated with significantly increased morbidity,[1–4] mortality,[1,2,4–10] and health care costs.[5] AKI occurs in up to 18% of patients undergoing cardiac surgery, with 2% of all patients requiring renal replacement therapy.[4] Although overall mortality for cardiac surgery is typically between 2% and 3%,[6,11] this rate doubles with even mild postoperative AKI, and approaches 60% for AKI severe enough to require dialysis.[5–10,12] In addition, cardiac surgery-associated AKI (CSA-AKI) is associated with increased rates of infection,[13] dysfunction in multiple other organ systems,[2–4,14] longer ICU and hospital length of stay,[2] and long-term kidney disease.[1]

CSA-AKI is believed to originate intraoperatively,[15] the cumulative result of ischemic insults,[15–19] systemic inflammation,[20–23] and oxidative stress,[17,22,24,25] ultimately resulting in progression to tubular necrosis. Animal models consistently demonstrate the potential to abrogate or prevent AKI with a variety of pharmaceutical approaches targeting these mechanisms,[26–30] provided the treatment is instituted before significant tubular cell death occurs.[15] In the context of CSA-AKI, for example, the application of this early treatment paradigm requires diagnosis and treatment of AKI intraoperatively, at the time of the incipient injury.[31–34] Unfortunately, timely intraoperative diagnosis of AKI is not yet feasible. Serum creatinine, the

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current standard for AKI diagnosis, takes several days to reach diagnostic thresholds.[34] Even novel urinary biomarkers lack adequate discrimination to guide therapy when measured intraoperatively.[35]

An alternative approach to "real-time" diagnosis is to use clinical variables measured before or at the time of surgery to predict risk of postoperative AKI. Provided the risk model is sufficiently accurate, such a prediction tool could be used to guide the implementation of more intensive renoprotective efforts and surveillance in patients at highest risk. Importantly, better risk prediction could improve pretest probabilities for novel diagnostic tests of CSA-AKI, thereby improving the performance of early diagnostic markers and possibly paving the way for more specific, targeted therapies. A number of predictive models based on preoperative risk factors[9,35–40] have been developed for CSA-AKI. Of these, the Cleveland Clinic Score (CCS, often called the Thakar score) is the best validated and most predictive of these tools (Table 1).[41] Originally developed to predict renal replacement therapy after cardiac surgery, the CCS has since been validated for the prediction of less severe CSA-AKI.[36–38]

Despite its usefulness, the CCS does not incorporate potentially useful intraoperative information. The score is also heavily influenced by preoperative kidney dysfunction, and is less discriminatory in patients with normal preoperative kidney function. We hypothesized that the performance of the CCS could be improved by the incorporation of easily measured intraoperative variables capturing the aspects of adequacy of organ perfusion, such as intraoperative blood pressure, hematocrit, urine output, blood transfusion, and fluid administration.

Table 1. Cleveland Clinic Score

Risk factor	Points
Female gender	1
Congestive heart failure	1
Left ventricular ejection fraction <35%	1
Preoperative use of intra-aortic balloon pump	2
Chronic obstructive pulmonary disease	1
Insulin-requiring diabetes	1
Previous cardiac surgery	1
Emergency surgery	2
Surgery type:	
Coronary artery bypass grafting only	0
Valve repair/replacement only	1
Coronary artery bypass grafting + valve	2
Any other cardiac surgery	2
Preoperative creatinine:	
107 to <186 μM (1.2 to <2.1 mg/dl)	2
≥186 μM (≥2.1 mg/dl)	5
Maximum score	17

METHODS

The University of Manitoba Human Research Ethics Board and the Saint Boniface General Hospital Research Review Committee approved our research protocol, and all patients provided informed consent.

Study Design

We employed an observational prospective cohort design. All adult patients scheduled for elective cardiac surgery at a tertiary care center (Saint Boniface General Hospital, Winnipeg, Canada) were considered for inclusion. Patient recruitment occurred between June 2012 and July 2014. Exclusion criteria included age < 18 years, chronic kidney disease of stage V or greater (Modification of Diet in Renal Disease estimated glomerular filtration rate < 15 ml/min per 1.73 m^2), currently on dialysis for any indication, previous kidney transplant, or planned off-pump procedure.

Data Collection

Data were abstracted from patient charts as well as from the Manitoba Cardiac Surgery Database for the duration of hospital stay from time of entry to the operating room to hospital discharge. All data were collected according to routine clinical practice. Baseline data and demographics were recorded during the presurgical clinic visit and/or on admission to hospital. Mean arterial pressure (MAP) was monitored via an arterial catheter and recorded by the anesthetist at 5-minute intervals. Data on hematocrit from intraoperative arterial blood gas panels were abstracted at the following times: (i) at time of arterial line placement, (ii) on initiation of cardiopulmonary bypass (CPB), (iii) 1 hour after the commencement of CPB, and (iv) at arrival to postoperative ICU. Surgery duration was recorded in the intraoperative record. Pump time and cross clamp time were recorded in the perfusion record. Use of blood products was recorded in a transfusion log. Volume inputs were recorded by the anesthesiologist and perfusionist. Urine outputs for the entire operative period as well as outputs specific to the period while on CPB were recorded intraoperatively by nursing staff. Creatinine was measured at arrival to ICU and in the morning of each postoperative day, along with other routine bloodwork.

Primary Exposure Variables of Interest

The CCS, a well-validated AKI risk score, was calculated based on the relevant preoperative variables for each patient (Table 1). Nadir hematocrit was defined as the lowest of the 4 hematocrits measured during the operation at the time points described above. Average MAP was defined as the average of all MAP readings recorded during surgery. The total number of