Improving the Identification of Patients at Risk of Postoperative Renal Failure after Cardiac Surgery

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Background: Preoperative renal insufficiency is an important predictor of the need for postoperative renal replacement therapy (RRT). Serum creatinine (sCr) has a limited ability to identify patients with preoperative renal insufficiency because it varies with age, sex, and muscle mass. Calculated creatinine clearance (CrCl) is an alternative measure of renal function that may allow better estimation of renal reserve.

Methods: Data were prospectively collected for consecutive patients who underwent cardiac surgery requiring cardiopulmonary bypass at a tertiary care center. The relation between CrCl (Cockcroft-Gault equation) and RRT was initially described using descriptive statistics, logistic regression, and receiver operating characteristic analysis. Based on these analyses, preoperative renal insufficiency was defined as CrCl of 60 ml/min or less. Preoperative renal function was classified as moderate insufficiency (sCr > 133 μmol/L, mild insufficiency (100 μmol/L ≤ sCr ≤ 133 μmol/L), occult insufficiency (sCr ≤ 100 μmol/L and CrCl ≤ 60 ml/min), or normal function (sCr ≤ 100 μmol/L and CrCl > 60 ml/min). The independent association of preoperative renal function with the need for RRT was subsequently determined using multiple logistic regression.

Results: Of the 10,751 patients in the sample, 137 (1.2%) required postoperative RRT. Approximately 13% of patients with normal sCr had occult renal insufficiency. Occult renal insufficiency was independently associated with RRT (odds ratio, 2.80; 95% confidence interval, 1.39–5.33). The magnitude of this risk was similar to patients with mild renal insufficiency (P = 0.73).

Conclusions: The inclusion of a simple CrCl-based criterion in preoperative assessments may improve identification of patients at risk of needing postoperative RRT.

ACUTE renal failure necessitating renal replacement therapy (RRT) is a severe complication of cardiac surgery. Although no causative relation has been proven, the need for postoperative RRT is independently associated with increased mortality.¹ ² Prognostic risk stratification for RRT, therefore, is an important component of the preoperative assessment of cardiac surgery patients.

Numerous studies have consistently identified preexisting renal insufficiency as an independent predictor of the need for postoperative RRT.²–⁸ Most of these studies, however, did not specify thresholds for defining clinically important preoperative renal insufficiency; furthermore, any specified thresholds were chosen in an arbitrary manner.²–⁸ In addition, most defined thresholds estimated renal function using serum creatinine concentration (sCr).² ⁵ ⁸ Creatinine concentration has important limitations because it varies with factors aside from renal function: age, sex, muscle mass, metabolism, and hyperhydration. Consequently, the glomerular filtration rate (GFR) may be reduced by 75% before sCr becomes abnormal.⁹

Creatinine clearance (CrCl) is an alternative measure of preoperative renal reserve that approximates GFR. Although the direct accurate measurement of CrCl over short time periods is possible in the research setting, it is not a feasible option in clinical practice or larger clinical studies.¹⁰ A more practical solution is to estimate CrCl using sCr-based prediction equations that estimate GFR with moderate accuracy and precision.¹¹ ¹²

To better understand the role of estimated CrCl in prognostic stratification for RRT, we undertook a retrospective cohort observational study of cardiac surgical patients. Creatinine clearance was estimated using the Cockcroft-Gault equation.¹¹ This prediction equation was chosen because it is calculated using readily available clinical data and is reasonably correlated with measured creatinine clearance in cardiac patients.¹³ The association between CrCl and RRT was first examined to determine an optimal CrCl-based cutoff for defining preoperative renal insufficiency. This definition was subsequently applied among patients with normal sCr values to determine whether it was independently associated with the need for postoperative RRT.

Materials and Methods

Data Sources

After approval by the institutional research ethics board was obtained, preoperative, intraoperative, and postoperative data on individuals undergoing cardiac surgery at the Toronto General Hospital (Toronto, Ontario, Canada) were prospectively collected in a clinical registry. This database has been previously described.¹⁴ Attending anesthesiologists, surgeons, and perfusionists collected all preoperative and intraoperative data. A full-time research nurse, who was blinded to the details of this study, adjudicated all outcomes from patients’ med-
ical records. Database accuracy was measured by reab-
stracting the medical records of 200 randomly selected
patients.

Study Sample
The study sample consisted of adults (aged $\geq 18$ yr) who underwent cardiac surgery under cardiopulmonary
bypass between May 1999 and July 2004. Exclusion
criteria included severe preoperative renal dysfunction
(preoperative dialysis dependence or $\text{sCr} > 300 \mu M$) and
infrequent procedures (heart transplantation, ventricular
assist device insertion). Missing data values were im-
puted. An unknown left ventricular ejection fraction was
considered equal to a normal value ($> 60\%$). Missing
values for dichotomous variables were assigned the most
frequent value, whereas continuous variables were as-
signed the median value. Using sample size recommenda-
dions for 10 or more outcome events per predictor variable, a sample of 10,000 patients was deemed suffi-
cient to allow unbiased fitting of up to 10 predictor variables in multiple logistic regression (estimated 1% incidence of postoperative RRT).

General Analysis Issues
Statistical analyses were performed using SAS Version
8.20 (SAS Institute, Cary, NC). All $P$ values were two
tailed, with statistical significance defined by $P \leq 0.05$.
The dependent variable was the need for postoperative
RRT (intermittent hemodialysis or continuous veno-
venous hemodiafiltration). Decisions about implement-
ing RRT were made by consulting nephrologists. The
common indications for RRT at our institution are fluid
overload, metabolic abnormalities (acidosis, hyperkale-
mia), and anuria.

The principal predictor variable for this study was
preoperative renal function. Preoperative renal function
was estimated using both $\text{sCr}$ and CrCl. The $\text{sCr}$ concen-
trations of patients undergoing cardiac surgery at the
Toronto General Hospital are routinely measured before
surgery (within 30 days). The preoperative $\text{sCr}$ was de-
efined as the value closest to surgery. The preoperative
CrCl was calculated using the Cockcroft-Gault equa-
tion. Several other preoperative factors that are asso-
ciated with RRT were considered as potential confound-
ers in multivariable analyses (table 1).

Unadjusted Relation between $\text{CrCl}$ and
Postoperative RRT
To determine the optimum $\text{CrCl}$-based definition of
preoperative renal insufficiency, the unadjusted relation
between $\text{CrCl}$ and postoperative RRT was analyzed using
descriptive statistics, logistic regression, and receiver
operating characteristic (ROC) curve analysis. Patients
were divided into six strata based on $\text{CrCl}$: 20 or less,
21–40, 41–60, 61–80, 81–100, and more than 100 ml/
in. The proportion of individuals requiring RRT within
each stratum was subsequently determined. Exact binom-
ial 95% confidence intervals (CIs) were calculated for
these proportions. The relation between $\text{CrCl}$ (continu-
ous variable) and RRT was subsequently analyzed using
logistic regression. Given that logistic regression as-
sumes a linear relation between $\text{CrCl}$ and the probability
of RRT (logit transformation), restricted cubic spline
analyses were used to derive more accurate estimates of
this relation. Finally, the relation between $\text{CrCl}$ and
RRT was evaluated further using ROC curve analysis. An
ROC curve was used to identify an optimal $\text{CrCl}$-based
threshold for predicting RRT (minimum distance to ideal
sensitivity and specificity values of 1). Based on these
analyses, preoperative renal insufficiency was defined as
a $\text{CrCl}$ of 60 ml/min or less (Results). The sensitivity,
specificity, positive predictive value, negative predictive
value, and accuracy of this threshold were calculated with
associated exact binomial 95% CIs. Accuracy was
declared as the sum of all cells in a two-by-two table.

Adjusted Relation between Preoperative Renal
Function and Postoperative RRT
The unadjusted associations between potential predic-
tor variables and RRT were initially determined using
appropriate tests (t test, Mann–Whitney U test, chi-
square test, Fisher exact test). Patients were divided into
four categories on the basis of preoperative renal func-
tion. Moderate renal insufficiency (class 4) was defined as
a preoperative $\text{sCr}$ greater than 133 $\mu M$ (1.5 mg/dl).
This degree of preoperative renal insufficiency is inde-
dependently associated with perioperative mortality and
morbidity after cardiac surgery. Mild renal insuffi-
ciency (class 3) was defined as 100 $\mu M < \text{sCr} \leq 133$ $\mu M$.
The 100-$\mu M$ value was chosen because it is the upper
limit of the normal $\text{sCr}$ range at our institution; fur-
more, it is the threshold above which many clinicians
would interpret renal function as being abnormal. Oc-
cult renal insufficiency (class 2) was defined as a normal
$\text{sCr} (\leq 100 \mu M)$ with an abnormal $\text{CrCl} (\leq 60 \text{ ml/min})$.
Normal renal function (class 1) included all individuals
with both normal $\text{sCr} (\leq 100 \mu M)$ and $\text{CrCl} (> 60$
ml/min).

The independent association of preoperative renal
function (classes 1–4) with postoperative RRT was de-
termined using multiple logistic regression. The refer-
cence group against which other levels of renal function
were compared was class 1 (normal renal function). In
addition to preoperative renal function, we considered
13 other variables, which were previously identified as
independent predictors of postoperative RRT, as poten-
tial confounders. These variables were age, sex, diabetes
mellitus requiring insulin or oral hypoglycemic agents,
systemic hypertension (requiring medication), chronic
obstructive pulmonary disease (requiring daily oral or
inhaled medication), vascular disease (history of stroke,
renal function

comorbid disease

Table 1. Characteristics of Study Sample and Subgroups (Stratified by Preoperative Renal Function)

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Class 1 (sCr ≤ 100 μM and CrCl &gt; 60 ml/min, n = 6,743 (63%))</th>
<th>Class 2 (sCr ≤ 100 μM and CrCl ≤ 60 ml/min, n = 1,008 (9%))</th>
<th>Class 3 (100 μM &lt; sCr ≤ 133 μM, n = 2,357 (22%))</th>
<th>Class 4 (sCr &gt; 133 μM, n = 643 (6%))</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yr</td>
<td>62 ± 12</td>
<td>59 ± 12</td>
<td>73 ± 7</td>
<td>66 ± 11</td>
</tr>
<tr>
<td>Female sex</td>
<td>2,787 (26)</td>
<td>1,641 (24)</td>
<td>700 (69)</td>
<td>324 (14)</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>79 ± 16</td>
<td>81 ± 15</td>
<td>61 ± 9</td>
<td>81 ± 15</td>
</tr>
<tr>
<td>Renal function</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Creatinine concentration, μM</td>
<td>92 ± 26</td>
<td>80 ± 13</td>
<td>85 ± 10</td>
<td>112 ± 9</td>
</tr>
<tr>
<td>Creatinine clearance, ml/min</td>
<td>82 ± 31</td>
<td>97 ± 27</td>
<td>51 ± 7</td>
<td>64 ± 19</td>
</tr>
<tr>
<td>Comorbid disease</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes mellitus requiring medication</td>
<td>2,381 (22)</td>
<td>1,446 (21)</td>
<td>183 (18)</td>
<td>552 (23)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>5,891 (55)</td>
<td>3,410 (51)</td>
<td>605 (60)</td>
<td>1,400 (59)</td>
</tr>
<tr>
<td>Chronic obstructive pulmonary disease</td>
<td>427 (4)</td>
<td>237 (4)</td>
<td>42 (4)</td>
<td>115 (5)</td>
</tr>
<tr>
<td>Cerebrovascular disease</td>
<td>968 (9)</td>
<td>492 (7)</td>
<td>96 (10)</td>
<td>270 (11)</td>
</tr>
<tr>
<td>Peripheral vascular disease</td>
<td>1,421 (13)</td>
<td>689 (10)</td>
<td>152 (15)</td>
<td>399 (17)</td>
</tr>
<tr>
<td>Cerebrovascular and/or peripheral vascular disease</td>
<td>2,066 (19)</td>
<td>1,035 (15)</td>
<td>219 (22)</td>
<td>561 (24)</td>
</tr>
<tr>
<td>Surgical details</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Coronary angiography within 72 h before surgery</td>
<td>779 (7)</td>
<td>477 (7)</td>
<td>85 (8)</td>
<td>178 (8)</td>
</tr>
<tr>
<td>Active endocarditis</td>
<td>88 (0.8)</td>
<td>42 (0.6)</td>
<td>8 (0.8)</td>
<td>22 (0.9)</td>
</tr>
<tr>
<td>Previous cardiac surgery</td>
<td>856 (8)</td>
<td>525 (8)</td>
<td>66 (7)</td>
<td>193 (8)</td>
</tr>
<tr>
<td>Preoperative intraaortic balloon pump</td>
<td>217 (2)</td>
<td>124 (2)</td>
<td>22 (2)</td>
<td>50 (2)</td>
</tr>
<tr>
<td>Operative procedure</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CABG or ASD repair alone</td>
<td>7,005 (65)</td>
<td>4,434 (66)</td>
<td>603 (60)</td>
<td>1,574 (67)</td>
</tr>
<tr>
<td>Valve repair alone</td>
<td>1,755 (16)</td>
<td>1,164 (17)</td>
<td>172 (17)</td>
<td>332 (14)</td>
</tr>
<tr>
<td>Complex procedures</td>
<td>1,991 (19)</td>
<td>1,145 (17)</td>
<td>233 (23)</td>
<td>451 (19)</td>
</tr>
<tr>
<td>Timing of surgery</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Elective</td>
<td>6,392 (59)</td>
<td>4,322 (64)</td>
<td>539 (53)</td>
<td>1,240 (53)</td>
</tr>
<tr>
<td>Urgent</td>
<td>4,158 (39)</td>
<td>2,303 (34)</td>
<td>452 (45)</td>
<td>1,073 (46)</td>
</tr>
<tr>
<td>Emergent</td>
<td>201 (2)</td>
<td>118 (2)</td>
<td>17 (2)</td>
<td>44 (2)</td>
</tr>
<tr>
<td>Outcomes</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>In-hospital mortality</td>
<td>180 (1.7)</td>
<td>66 (1.0)</td>
<td>34 (3.4)</td>
<td>48 (2.0)</td>
</tr>
<tr>
<td>Need for renal replacement therapy</td>
<td>137 (1.2)</td>
<td>29 (0.4)</td>
<td>13 (1.3)</td>
<td>37 (1.6)</td>
</tr>
</tbody>
</table>

Data are presented as mean ± SD or number of patients (%).

ASD = atrial septal defect; CABG = coronary artery bypass graft; CrCl = creatinine clearance; sCr = serum creatinine.

transient ischemic attacks, carotid disease, aortoiliac disease, or femoropopliteal disease), left ventricular ejection fraction (four classes: > 60%, 41–60%, 21–40%, and ≤ 20%), recent coronary angiography (within 72 h of surgery), active endocarditis, previous cardiac surgery, preoperative intraaortic balloon pump use, procedure type (three classes: coronary artery bypass or atrial septal defect repair, valve surgery alone, and other procedures), and timing of surgery. Two timing of surgery was classified into three categories: elective, urgent (cannot leave hospital without surgery), and emergent (surgery required within 12 h of presentation). To conform to the underlying assumptions of logistic regression, age was transformed to a continuous variable restricted between 60 to 80 yr. Thus, ages below 60 yr were considered equal to 60 yr; similarly, ages above 80 yr were considered equivalent to 80 yr. Backward stepwise variable selection was used to construct the final regression model (criterion for selection: $P < 0.05$). The associations of independent predictors with RRT in the final model were expressed as odds ratios with 95% CIs. The variation in the dependent variable (RRT) attributable to each independent predictor was estimated by the likelihood ratio chi-square statistic; a larger chi-square statistic implied a more important role in explaining variation in the dependent variable. Model discrimination was measured using the c statistic, which is equivalent to the area under the ROC curve. Model calibration was estimated using the Hosmer-Lemeshow statistic (higher $P$ values imply that the model fit the observed data better). The validity of the final model was further described using bootstrap techniques. Initially, 1,000 computer-generated samples, each including 10,571 individuals, were derived from the study sample by random selection with replacement. The bootstrap samples were used to estimate the 95% CI for the $c$ statistic of the final model.
The reliability of the independent predictors included in the final model was also described using bootstrap bagging. In summary, 1,000 bootstrap samples were generated as described above. Within each bootstrap sample, forward stepwise variable selection (criterion for inclusion: $P < 0.05$) was employed using all 14 potential independent variables. The reliability of predictor variables in the final regression model was estimated by how often they were retained as independent predictors in the bootstrap samples. Reliable predictors were expected to be retained in a higher proportion of bootstrap samples.

Results

During the study period, 10,940 patients underwent cardiac surgical procedures under cardiopulmonary bypass. A total of 189 patients were excluded because of preoperative dialysis dependence, severe preoperative renal insufficiency (sCr $> 300 \mu M$), or ineligible procedures. The final sample consisted of 10,751 individuals. Within this sample, 54 patients (0.5%) had missing values in one or more data elements. All missing values were replaced using imputation, as described previously. Exclusion of patients with missing data did not alter the magnitude or significance of the results. Database accuracy exceeded 95%.

Overall rates of in-hospital mortality and RRT were 1.7% ($n = 180$) and 1.2% ($n = 137$), respectively (table 1). Among patients requiring postoperative RRT, 47% ($n = 65$) died in the hospital. Despite a moderate negative correlation between sCr and CrCl (Pearson correlation coefficient $R = -0.56; P < 0.001$), the range of CrCl values among patients with normal sCr ($\leq 100 \mu M$) was wide (fig. 1). When the study sample was classified into six strata based on CrCl, the rate of RRT remained below 1% until the preoperative CrCl decreased below 60 ml/min (fig. 1). Similarly, when restricted cubic splines and logistic regression were used to analyze the relation between CrCl (continuous variable) and RRT, the risk of RRT seemed to increase appreciably when CrCl was 60 ml/min or less (fig. 2). In ROC curve analyses, the area under the curve for the relation between CrCl and RRT was 0.77 (95% CI, 0.73–0.82). The optimal threshold for predicting RRT was a CrCl of 60 ml/min or less, with a sensitivity and specificity of 0.64 (95% CI, 0.56–0.72) and 0.76 (95% CI, 0.75–0.76), respectively. Clinically important preoperative renal dysfunction was therefore defined as a CrCl of 60 ml/min or less. This threshold had an overall accuracy of 0.76 (95% CI, 0.75–0.76). Given the low prevalence of RRT in our sample, the threshold had a relatively low positive predictive value (0.03; 95% CI, 0.03–0.04) but high negative predictive value (0.99; 95% CI, 0.99–1.00).

The prevalence of occult renal dysfunction (sCr $\leq 100 \mu M$ and CrCl $\leq 60 \text{ ml/min}$) was 9% ($n = 1,008$). Approximately 13% of individuals with normal sCr were subsequently found to have occult renal dysfunction (CrCl $\leq 60 \text{ ml/min}$). These individuals were more likely to be elderly females with low body weights (table 1). In comparison with individuals with normal renal function, patients with occult renal dysfunction experienced more than a threefold increased risk of mortality and RRT (table 1).

In unadjusted analyses, the following variables had significant associations with RRT: sex, age, weight, sCr,
CrCl, diabetes mellitus, cerebrovascular disease, peripheral vascular disease, vascular disease, left ventricular ejection fraction, recent coronary angiography, previous cardiac surgery, preoperative intraaortic balloon pump use, procedure type, and timing of surgery (table 2).

In multiple logistic regression analyses, preoperative renal function, diabetes mellitus, left ventricular ejection fraction, previous cardiac surgery, procedure type, and timing of surgery were independently associated with RRT (table 3). All predictor variables that were included in the final model were also retained in more than 50% of 1,000 bootstrap samples (table 3). The final model had good discrimination ($c$ statistic, 0.87; 95% CI, 0.83–0.89) and calibration (Hosmer-Lemeshow statistic, 7.33; $P = 0.50$). Occult renal dysfunction (class 2) was independently associated with RRT (odds ratio, 2.80; 95% CI, 1.39–5.33; $P = 0.003$). The magnitude of this increased risk was similar to that of patients with mild renal dysfunction (odds ratio, 3.14; 95% CI, 1.92–5.19; $P < 0.001$). There was no significant difference between occult and mild renal dysfunction with regard to risk of RRT ($P = 0.73$).

Discussion

This study found that the risk of postoperative RRT increases appreciably when CrCl decreases below 60 ml/min, even if sCr is normal. If this criterion is incorporated into preoperative assessments, 13% of individuals with normal sCr values ($\leq 100 \mu M$) would be identified as being at increased risk of needing perioperative RRT. Patients with occult renal dysfunction were disproportionately elderly women with low body weights. Occult renal dysfunction has an important impact on perioperative outcomes. It is associated with a greater than threefold increase in the unadjusted risk of perioperative mortality and RRT. Furthermore, it is independently as-
associated with perioperative RRT to the same extent as mild renal dysfunction (100 µM < sCr ≤ 133 µM). These findings confirm the importance of including an estimate of GFR in both clinical practice and research.

The current study has important strengths. First, a large accurate prospectively collected database was used. Second, the outcome of interest (need for RRT) was clear and clinically relevant. Third, the logistic re-

Table 3. Independent Predictors of the Need for Postoperative Renal Replacement Therapy

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>No Renal Replacement Therapy, n = 10,614</th>
<th>Renal Replacement Therapy, n = 137</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Preoperative renal function</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>sCr ≤ 100 µM and CrCl &gt; 60 ml/min</td>
<td>1*</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>sCr ≤ 100 µM and CrCl ≤ 60 ml/min</td>
<td>2.80</td>
<td>1.39–5.33</td>
<td>0.003</td>
</tr>
<tr>
<td>100 µM &lt; sCr ≤ 133 µM</td>
<td>3.14</td>
<td>1.92–5.19</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>sCr &gt; 133 µM</td>
<td>15.23</td>
<td>9.57–24.71</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td><strong>Comorbid disease</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes mellitus requiring medication</td>
<td>2.46</td>
<td>1.67–3.60</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Left ventricular ejection fraction</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt; 60%</td>
<td>1*</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>21–60%</td>
<td>1.48</td>
<td>0.99–2.25</td>
<td>0.06</td>
</tr>
<tr>
<td>≤ 20%</td>
<td>2.61</td>
<td>1.32–4.95</td>
<td>0.004</td>
</tr>
<tr>
<td><strong>Operative details</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Previous cardiac surgery</td>
<td>1.71</td>
<td>1.02–2.79</td>
<td>0.04</td>
</tr>
<tr>
<td>Operative procedure</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CABG or ASD repair alone</td>
<td>1*</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Valve repair alone</td>
<td>1.58</td>
<td>0.77–3.02</td>
<td>0.19</td>
</tr>
<tr>
<td>Complex procedures</td>
<td>3.52</td>
<td>2.37–5.24</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Timing of surgery</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Elective</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urgent</td>
<td>1.76</td>
<td>1.19–2.60</td>
<td>0.005</td>
</tr>
<tr>
<td>Emergent</td>
<td>9.91</td>
<td>5.22–18.11</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

* Reference group.

Data are presented as mean ± SD or number of patients (%).

ASD = atrial septal defect; CABG = coronary artery bypass graft; CrCl = creatinine clearance; sCr = serum creatinine.
gression analyses adhered to sample size recommendations for 10 or more outcome events per predictor variable. Fourth, the regression analyses were further strengthened by internal bootstrap validation. Finally, our analyses clearly demonstrate that the use of the CrCl threshold of 60 ml/min or less would enable clinicians to identify approximately 10% of the surgical population that would otherwise be misclassified as low risk for requiring postoperative RRT.

Our finding that CrCl has important advantages over sCr is consistent with previous research. The ability of sCr to identify outpatients with impaired renal function that would otherwise be misclassified as low risk for threshold of 60 ml/min or less would enable clinicians to strengthened by internal bootstrap validation. Finally, the use alternative predictions for 10 or more outcome events per predictor variable. Fourth, the regression analyses were further strengthened by the use of CrCl, as opposed to sCr. The definition of clinically significant preoperative renal impairment (CrCl ≤ 60 ml/min) identified in the current study is also in accord with the literature.

**Limitations**

There are several limitations to be considered when interpreting our results. First, the use alternative prediction equations (e.g., Modification of Diet in Renal Disease equation) may have improved correlation between estimated CrCl and GFR. The Modification of Diet in Renal Disease equation was not applied in the current study because the prospective clinical registry did not capture all required variables. It is unlikely that this limitation significantly affected our results, given that our analyses focused on the association between estimated CrCl and clinical outcomes, not GFR. Second, the Cockcroft-Gault equation introduces more complexity to the preoperative assessment than sCr alone. Nonetheless, its use may be facilitated through the use of nomograms or personal digital assistant software. Third, given that these data originated from a single center, further external validation is still needed. Fourth, as opposed to calculating CrCl, clinicians could simply interpret sCr in light of sex, age, and weight. However, this process would entail that clinicians consider different sCr cutoffs for a 60-yr-old, 50-kg man; a 70-yr-old, 100-kg woman; and a 45-yr-old, 50-kg man. Such a strategy would introduce considerably more complexity to the preoperative assessment process than simply calculating CrCl and comparing it against a single threshold (60 ml/min). Finally, given that our clinical registry is limited to in-hospital data, the long-term implications of postoperative RRT after hospital discharge remain unknown.

**Clinical Implications**

The assessment of preoperative renal function involves interplay between sCr, age, sex, and muscle mass. The current study suggests that clinicians should estimate the CrCl of all cardiac surgery patients using their closest preoperative sCr. Individuals with CrCl values below 60 ml/min should be deemed to have clinical important preoperative renal insufficiency, regardless of their sCr concentration. This strategy would allow clinicians to readily identify 10% of the surgical population who are at increased risk of perioperative renal insufficiency despite having normal sCr values.

The incorporation of a CrCl threshold (≤ 60 ml/min) in the preoperative assessment would therefore facilitate identification of high-risk patients for potential renal-protective interventions. Although vasoactive agents seem to have limited efficacy in preserving renal function, therapies targeting other pathogenic mechanisms (ischemia–reperfusion injury, suboptimal hematocrit) may hold promise. In addition, these same high-risk patients may be ideal candidates for recruitment into clinical trials of novel renal-protective therapies.

**References**