Estimated creatinine clearance instead of plasma creatinine level as prognostic test for postoperative renal function in patients undergoing coronary artery bypass surgery

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Abstract

Background: Preoperative renal failure is a risk factor for adverse events in cardiac surgery. Serum creatinine (SCr) is the most used test for renal failure. However, patients can have significantly decreased glomerular filtration rates with normal SCr levels. More accurate approximation of renal function can be obtained using the Cockroft—Gault equation to calculate an estimated creatinine clearance (CrCl) rate from SCr.

Methods: This study included 627 patients undergoing an isolated CABG between January 2003 and September 2004. CrCl was calculated using the Cockroft—Gault formula. Patients were divided in group A-SCr, 576 patients (91.1%) with a good renal function, SCr/C20 < 1.20 mg/dL for women and < 1.40 mg/dL for men, and a group B-SCr, with impaired renal function, 51 patients (8.1%). CrCl/50 mL/min was chosen to reflect renal impairment. Group A-CrCl (555 patients, 88.5%) had a normal renal function and group B-CrCl (72 patients, 11.5%) an impaired renal function. The studied outcomes were hospital mortality, hospital morbidity, and postoperative renal failure.

Results: There was no statistical significant difference between A-SCr and B-SCr group according to the studied outcomes. On the contrary, using the CrCl there was a statistical significant difference between A-CrCl and B-CrCl for the percentage of postoperative renal failure 10 patients (1.8%) versus 5 patients (6.9%) (p = 0.00), hospital morbidity 75 patients (13.5%) versus 16 patients (22.2%) (p = 0.04). Hospital mortality, 11 patients (2%) versus 4 patients (5.6%), was not significantly (p = 0.06) different. Postoperative dialysis, four patients (0.7%) versus three patients (4.2%) (p = 0.00), stroke, three patients (0.5%) versus three patients (4.2%) (p = 0.00), and hospital stay (7.6 days vs 11.0 days) (p = 0.01) were significantly different. Conclusion: This study documents that the association between preoperative renal failure and adverse outcomes after CABG is stronger with the estimated CrCl than with the routinely used SCr. Routine estimation or measurement of glomerular filtration rate should be preferred to SCr as screening method for the detection of higher risk patients undergoing CABG.

Keywords: Coronary artery disease; Heart surgery; Postoperative; Renal function

1. Introduction

Preoperative renal failure has been correlated with increased risk of adverse outcome after cardiac surgery [1—5]. Renal function is mostly estimated by a standard method, using serum creatinine level. However, this is not a sensitive marker, because of its dependency on other parameters like muscle mass, age, gender, race, and metabolism [6,7].

Recently, the association between preoperative renal impairment and adverse events after cardiac surgery was shown stronger when renal function was estimated by creatinine clearance (CrCl) than when using serum creatinine (SCr) level [8].

The aim of our study is to investigate whether creatinine clearance as reference for renal function is superior to identify preoperative patients at risk undergoing surgical myocardial revascularization (CABG).

2. Patients and methods

2.1. Patients

With the aid of our database, Coronary Surgery Database Radboud Hospital (CORRAD), a registry that stores pre-, peri-, and postoperative data as well as follow-up data of all patients undergoing myocardial revascularization, we identified 627 patients undergoing an isolated myocardial revascularization (CABG) between January 2003 and September 2004. Table 1 presents the variables studied and their definitions.

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2.2. Renal function

2.2.1. Serum creatinine

In all patients serum creatinine level in μmol/L was determined preoperatively. For the total group the mean Scr in μmol/L was 91.4 ± 20.6, range 50–202, median 88. These values were converted to mg/dL (divided by a conversion factor 88.4) 1.03 ± 0.23, range 0.57–2.2, median 1.0.

Based on our standard values for Scr the total population was divided in two groups: group A-Scr: 576 patients (91.9%), with good renal function, Scr <1.20 mg/dL (106 μmol/L) for women and <1.40 mg/dL (124 μmol/L) for men, and group B-Scr, with impaired renal function, 51 (8.1%) patients.

2.2.2. Creatinine clearance

Creatinine clearance was calculated following the Cockroft–Gault formula [9].

For the total group the mean CrCl in mL/min was 74.48, range 27.32–165.27, median 73.67.

A CrCl value of <50 mL/min was chosen to reflect renal impairment [7]. The total population was divided in group CrCl-A, 555 patients (88.5%) with a normal renal function and group CrCl-B, 72 patients (11.5%) with an impaired renal function.

2.3. Surgical technique

Six hundred and one patients (95.9%) were operated using standard cardio-pulmonary bypass technique, aortic and right atrial cannulation, hypothermia (28–32 °C), and myocardial protection using St Thomas’ Hospital cardioplegia. Twenty-six patients (4.16%) were operated ‘off-pump’. For the patients operated on-pump, the mean time on the extra-corporal circulation time (ECC time) was 91.6 ± 31.9 min, range 24–300, median 85 ± 18.8 min, and the mean aortic cross-clamp time (AoX time) was 53.3 min, range 10–140, with a median of 51 min. For the total group, there was a mean of 1.9 ± 0.4 grafts, range 1–4, with a median of 2 and a mean of 3.3 ± 1.0 distal anastomoses, range 1–7, with a median of 3. Off all patients, 564 (90%) received at least one arterial graft.

2.4. Outcome

The studied outcomes were hospital mortality and hospital morbidity, postoperative renal failure, and postoperative dialysis.

Hospital mortality in our study was defined as all cardiac related and non-cardiac related mortality during hospital stay in the Radboud University Medical Center.

Hospital morbidity was defined as ventilatory support for more than 3 days, wound problems (sternal dehiscence with refixation, mediastinitis), low cardiac output (need for inotropic support for at least 12 h, and/or a cardiac index below 2.2 L/min/m²) and postoperative renal, neurological, pulmonary, gastrointestinal, and vascular complications resulting in a prolonged hospital stay.

Postoperative renal failure was defined as all patients with a renal dysfunction, serum creatinine ≥1.7 mg/dL (150 μmol/L) and/or patients requiring dialysis. Postoperative dialysis, as separate outcome was also studied.

2.5. Statistical analysis

Characteristics of patients are presented as percentage for dichotome variables, as mean ± standard deviation (SD) for numeric variables. Differences in percentages were tested with the chi-square test, and numerical variables were tested with the t-test. Regression analysis was used to evaluate the relation between the studied outcomes and Scr and CrCl. Statistical significance was assumed at p ≤ 0.05, p = 0.00 means p < 0.01.
3. Results

The postoperative incidences, hospital mortality, morbidity, renal failure, and dialysis for the whole of our population were 2.4% (15/627), 14.5% (91/627), 2.3% (15/627), and 1.2% (7/627), respectively. These percentages are in concordance with other studies [8,10].

3.1. Preoperative data

Table 2 presents the preoperative data for the different groups. Because of the selection based on serum creatinine and creatinine clearance there is a statistical significant difference between groups A and B.

Between the SCr-A and SCr-B group there is only a significant difference in percentage of patients with a history of neurological disease ($p = 0.03$). Between the groups CrCl-A and CrCl-B, there is a significant difference for age ($p < 0.001$), sex ($p = 0.02$), BMI ($p < 0.00$), and a history of pulmonary disease ($p < 0.00$). Otherwise, there is no difference as well for preoperative comorbidity as for preoperative cardiac variables.

3.2. Perioperative data

Univariate analysis shows no significant differences for number of grafts, distal anastomoses, use of at least one arterial graft, aortic cross-clamp time, and ECC time. (Table 3)

3.3. Postoperative data

Univariate analysis shows no significant differences between the SCr-A and SCr-B according to the studied outcomes, hospital mortality, morbidity, and renal failure. Also other registered postoperative variables, perioperative myocardial infarction,
low cardiac output, reintervention, neurological, pulmonary and wound problems, hospital stay, ventilation time, and intensive care stay showed no differences.

On the contrary, using the creatinine clearance, there is a statistical significant difference between the two groups for the percentage of hospital morbidity \((p = 0.04)\), renal failure \((p = 0.00)\), dialysis \((p = 0.00)\), three of the four studied outcomes. Hospital mortality was not significantly \((p = 0.06)\) different between CrCl-A and CrCl-B. Postoperative dialysis \((p = 0.00)\), neurological \((p = 0.00)\), wound problems \((p = 0.00)\), and hospital stay \((p = 0.01)\) were also statistical significant different between CrCl-A and CrCl-B (Table 4).

Regression analysis (Table 5) shows a statistical significant relation between the CrCl group and postoperative renal failure and dialysis. The analysis for hospital morbidity just did not reach statistical significance \((p = 0.051)\). With the SCr-group there is no statistical significant relation.

### Table 3

**Perioperative variables**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Serum creatinine</th>
<th>Creatinine clearance</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Scr-A n = 576 (%)</td>
<td>Scr-B n = 51 (%)</td>
</tr>
<tr>
<td>Off pump</td>
<td>24 (4.1)</td>
<td>2 (3.9)</td>
</tr>
<tr>
<td>ECL, mean ± SD</td>
<td>87.9 ± 36.5</td>
<td>90.1 ± 33.0</td>
</tr>
<tr>
<td>AoX, mean ± SD</td>
<td>50.5 ± 21.5</td>
<td>53.2 ± 21.2</td>
</tr>
<tr>
<td>Grafts, mean ± SD</td>
<td>1.9 ± 0.4</td>
<td>2.0 ± 0.4</td>
</tr>
<tr>
<td>Distal anast mean ± SD</td>
<td>3.2 ± 1.0</td>
<td>3.4 ± 0.9</td>
</tr>
<tr>
<td>Use of minimal 1 art. graft</td>
<td>524 (91)</td>
<td>46 (90)</td>
</tr>
</tbody>
</table>

### Table 4

**Postoperative variables**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Serum creatinine</th>
<th>Creatinine clearance</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Scr-A n = 576 (%)</td>
<td>Scr-B n = 51 (%)</td>
</tr>
<tr>
<td>Peri-MI</td>
<td>29 (5.0)</td>
<td>1 (2.0)</td>
</tr>
<tr>
<td>LCO</td>
<td>23 (4.0)</td>
<td>2 (3.9)</td>
</tr>
<tr>
<td>Reintervention</td>
<td>43 (7.5)</td>
<td>2 (3.9)</td>
</tr>
<tr>
<td>Hospital mortality</td>
<td>13 (2.3)</td>
<td>2 (3.9)</td>
</tr>
<tr>
<td>Complications</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Renal failure</td>
<td>12 (2.1)</td>
<td>3 (5.9)</td>
</tr>
<tr>
<td>Dialysis</td>
<td>7 (1.2)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Neurological</td>
<td>6 (1.0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Pulmonary</td>
<td>48 (8.3)</td>
<td>4 (7.8)</td>
</tr>
<tr>
<td>Wound</td>
<td>16 (2.8)</td>
<td>1 (2.0)</td>
</tr>
<tr>
<td>Hospital morbidity</td>
<td>84 (14.6)</td>
<td>7 (13.7)</td>
</tr>
<tr>
<td>Hospital stay (days)</td>
<td>7.8 ± 10.2</td>
<td>10.2 ± 15.3</td>
</tr>
<tr>
<td>ICU-stay (days)</td>
<td>2.4 ± 6.5</td>
<td>3.3 ± 9.5</td>
</tr>
<tr>
<td>Ventilation time (days)</td>
<td>1.0 ± 4.1</td>
<td>0.9 ± 1.4</td>
</tr>
</tbody>
</table>

### 4. Discussion

Our study shows that the association between preoperative renal function and postoperative renal failure is stronger with the estimated creatinine clearance than with serum creatine levels.

Over the years there is an increasing percentage of patients with renal dysfunction undergoing CABG [3,11,12]. The relation between preoperative and postoperative renal dysfunction on one side and adverse outcome in cardiac surgery is well documented [3,5,11]. Renal function is also indicated as a level 1 variable for prognostic information in patients undergoing a CABG and included in most risk stratification models [1,2,4,13]. Serum creatinine (SCr) levels are mostly used as screening test for renal function [1,4]. Several reports, however, question the use of SCr, because it may underestimate mild or moderate degree of renal dysfunction and SCr levels can be normal even when renal function is impaired [6,7]. Recently, the impact of mild renal dysfunction and outcomes after coronary artery bypass grafting was described [10]. Creatinine clearance measuring the glomerular filtration rate is a more accurate estimate of renal function. CrCl can be measured from a timed urine collection or by using the Cockroft–Gault formula [9]. By estimation of the CrCl using the Cockroft–Gault equation, variables as age, weight (BSA), and gender are included in the evaluation of renal function.
4.1. Renal function and pre- and perioperative patients characteristics

Using SCr as screening test for renal function there does not seem to be a statistical significant difference in pre- and perioperative characteristics between patients with and without elevated SCr. By using the CrCl, there is a significant difference in mean age, gender, BMI, hypertension, and preoperative pulmonary disease. The differences in mean age, gender, and BMI can be expected because these variables are used in the Cockcroft–Gault formula. Hypertension is a variable related with the occurrence of renal insufficiency and the significant higher incidence of pulmonary disease can be related with older age and higher BMI of the CrCl-B group. The cardiac preoperative and the perioperative variables show no difference between the different groups.

4.2. Renal function and postoperative outcome

Using serum creatinine as indicator for renal function, there is no significant difference between patients with or without elevated SCr. However, by using the creatinine clearance, there is a significant difference for the studied outcomes, with exception for hospital mortality. Even other variables, as neurological or wound complications, and length of hospital stay, show a significant higher incidence in the CrCl-B group. Regression analysis confirmed the relation between the creatinine clearance level ≤50 mL/min and postoperative renal complications (odds 4.2), dialysis (odds 5.9).

This report is a confirmation of another study postulating that the association between preoperative renal impairment and adverse events after cardiac surgery is stronger when renal function is estimated by creatinine clearance than when using serum creatinine levels [8]. Complementary in our study is that we suggest a creatinine clearance level of ≤50 mL/min, which is useful as predictor for postoperative renal failure and/or dialysis. Wang propose a cut-off point of 58 mL/min for renal failure requiring dialysis. We chose a cut-off for normal renal function of 50 mL/min to reduce the likelihood of elderly, an increasing group patients undergoing CABG, being erroneously classified as having abnormal renal function. On the other hand, our choice of this relative low cut-off point can be the reason that we have no significant relation with hospital mortality, because the other study proposed a cut-off point of 66 mL/min for mortality [8].

Of course, our patient population is relatively small and most patients had a relatively good renal function. More studies with more patients are needed to evaluate the real value of creatinine clearance as reference for renal function with a superior relation to unfavorable outcomes in cardiac surgery. On the other hand, even in our small patient population, it is clear that the use of creatinine clearance calculated according to the Cockcroft–Gault equation is superior for identifying patients at risk for postoperative renal failure and dialysis. Therefore, we also suggest that creatinine clearance should be considered in preoperative risk assessment of renal function instead of serum creatinine.

In conclusion, our study shows that using a creatinine clearance level ≤50 mL/min, calculated from the serum creatinine following the Cockcroft–Gault formula results in a better identification of postoperative morbidity and a significant relation with postoperative renal failure and dialysis in patients undergoing cardiac surgery.

References