Comparison and clinical suitability of eight prediction models for cardiac surgery-related acute kidney injury

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Abstract

Background. Cardiac surgery-related acute kidney injury (CS-AKI) results in increased morbidity and mortality. Different models have been developed to identify patients at risk of CS-AKI. While models that predict dialysis and CS-AKI defined by the RIFLE criteria are available, their predictive power and clinical applicability have not been compared head to head.

Methods. Of 1388 consecutive adult cardiac surgery patients operated with cardiopulmonary bypass, risk scores of eight prediction models were calculated. Four models were only applicable to a subgroup of patients. The area under the receiver operating curve (AUROC) was calculated for all levels of CS-AKI and for need for dialysis (AKI-D) for each risk model and compared for the models applicable to the largest subgroup (n = 1243).

Results. The incidence of AKI-D was 1.9% and for CS-AKI 9.3%. The models of Rahmanian, Palomba and Aronson could not be used for preoperative risk assessment as postoperative data are necessary. The three best AUROCs for AKI-D were of the model of Thakar: 0.75 (95% CI 0.73–0.78), 0.74 (95% CI 0.71–0.76) and 0.70 (95% CI 0.73–0.78), for Thakar, Mehta and both Fortescue and Wijeysundera, respectively. The model of Thakar performed significantly better compared with the models of Mehta, Rahmanian, Fortescue and Wijeysundera (all P-values <0.01) at different levels of severity of CS-AKI.

Conclusions. The Thakar model offers the best discriminative value to predict CS-AKI and is applicable in a preoperative setting and for all patients undergoing cardiac surgery.

Keywords: AKI; cardiothoracic surgery; renal replacement therapy; risk prediction; RIFLE

Introduction

An important risk factor for adverse outcome following cardiac surgery is the development of acute kidney injury (AKI). Several studies show that postoperative renal dysfunction and need for dialysis prolong postoperative hospital and intensive care unit (ICU) length of stay and independently increase morbidity and mortality [1–5]. Not only need for dialysis, but also small decreases in renal function post-cardiac surgery are associated with an increased chance to develop chronic kidney disease [6]. Even a transient, minor elevation of serum creatinine postoperatively is associated with long-term mortality [7]. Therefore, it would be desirable to preoperatively identify patients at risk of renal dysfunction following cardiac surgery.

The need for dialysis after cardiac surgery develops in 1–5% of patients [8, 9]. Depending on the definition used for renal dysfunction, the incidence of cardiac surgery-related AKI (CS-AKI) varies from 1 to 30% [8, 9].

To identify patients at risk for CS-AKI and guide clinical decision-making, several studies have identified risk factors for the development of CS-AKI [2, 3, 10, 11]. Eight prediction models based on these risk factors have been published [12–19]. In 1997, Chertow et al. [12] built and validated the first prediction model consisting of a decision tree using seven preoperative predictors. This prediction decision tree model was later adapted into an additive risk score [20]. From 2005 up to 2011, seven other prediction models were developed which are described in Table 1. These prediction models differ in the patient mix and risk factors used and outcome definitions.

Because of these differences, it is unclear which one of these models demonstrates the highest predictive value concerning the occurrence of CS-AKI, defined by the need for dialysis and the Risk, Injury, Failure, Loss, End-stage Renal Disease (RIFLE) criteria [21].

The aim of our study was to compare the predictive value of these eight prediction models and their suitability as a clinical tool.
Table 1. Predictive models of cardiac surgery-associated AKI

<table>
<thead>
<tr>
<th>Model</th>
<th>Inclusion and exclusion criteria</th>
<th>Definition AKI or AKI-D</th>
<th>Variables in additive risk score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fortescue et al. [20]</td>
<td>Inclusion: all cardiac surgery, Exclusion: baseline sCr &gt; 265.2 μmol/L</td>
<td>AKI-D in 30 days</td>
<td>CrCl, IABP, SBP, type of surgery, prior CS, CHF, PVD, LVEF &lt; 35%, COPD*</td>
</tr>
<tr>
<td>Thakar et al. [14]</td>
<td>Inclusion: first cardiac surgery only, Exclusion: preoperative dialysis and previous renal transplant</td>
<td>AKI-D in the postoperative period</td>
<td>Sex, COPD, IDDM, CHF, IABP, LVEF &lt; 35%, Preop Cr, emergency surgery, type of surgery, prior CS</td>
</tr>
<tr>
<td>Mehta et al. [13]</td>
<td>Inclusion: CABG, mitral or aortic valve replacement or both</td>
<td>AKI-D</td>
<td>Age, race, chronic lung disease, NIDDM, IDDM, CHF, recent MI, preop Cr, prior CS, type of surgery, cardiogenic shock</td>
</tr>
<tr>
<td>Aronson et al. [18]</td>
<td>Inclusion: CABG with CPB</td>
<td>'Renal composite event': renal dysfunction: postop sCr &gt; 2mg/dL and increase of at least 0.7mg/dL from baseline. Failure: dialysis or evidence of renal failure at autopsy</td>
<td>Age, CHF, prior MI, Renal disease, PP, ≥ 2 inotropes peri-operative, IABP, CPB &gt; 122 min</td>
</tr>
<tr>
<td>Brown et al. [17]</td>
<td>Inclusion: CABG, Exclusion: eGFR &lt; 60 mL/min</td>
<td>AKI-D</td>
<td>Age, sex, DM, PVD, hypertension, IABP, white blood count, prior CABG</td>
</tr>
<tr>
<td>Wijeysundera et al. [16]</td>
<td>Inclusion: elective CABG, valve replacement or both, Exclusion: serum creatinine &gt;3.0 mg/dL or previous renal transplant</td>
<td>In patients with preop sCr &lt; 1.5 mg/dL: sCr &gt; 2 mg/dL. In patients with preop sCr &gt; 1.5 mg/dL: sCr increase &gt;50% from baseline</td>
<td>DM, IABP, LVEF &lt; 40%, eGFR, prior CS, other surgery than CABG, non-elective procedure</td>
</tr>
<tr>
<td>Palomba et al. [15]</td>
<td>Inclusion: cardiac surgery with CPB, Exclusion: preoperative dialysis and serum creatinine &gt;3.4 mg/dL</td>
<td>AKI-D</td>
<td>Age, CHF, preop Cr, preop glucose, combined surgery, CPB &gt; 120 min, postop LCO, postop CVP &gt; 14 cmH2O</td>
</tr>
<tr>
<td>Rahmanian et al. [19]</td>
<td>Inclusion: all cardiac surgery with CPB, Exclusion: preoperative dialysis</td>
<td>AKI-D</td>
<td>Age, DM, CHF, PVD, recent MI, AF, PH, preop Cr, CPB &gt; 120 min</td>
</tr>
</tbody>
</table>

AF, atrial fibrillation; AKI, acute kidney injury; AKI-D, acute kidney injury requiring dialysis; CABG, coronary artery bypass graft; CHF, congestive heart failure according to New York Heart Association; COPD, chronic obstructive pulmonary disease; CPB, cardiopulmonary bypass; CrCl, creatine clearance; CVP, central venous pressure; IABP, intra-aortic balloon pump; IDDM, insulin-dependent diabetes mellitus; LVEF, left ventricular ejection fraction; NIDDM, non-insulin-dependent diabetes mellitus; PH, pulmonary hypertension; postop LCO, postoperative low cardiac output; Preop Cr, preoperative creatinine; prior CS, prior cardiac surgery; PP, pulse pressure; PVD, peripheral vascular disease; recent MI, recent myocardial infarction; SBP, systolic blood pressure.

*Pulmonary rates were discounted because of poor reliability and frequent missings in documentation.

Materials and methods

All consecutive patients (aged >18 years) who underwent cardiac surgery with cardiopulmonary bypass and were admitted to the ICU of the Radboud University Nijmegen Medical Centre between October 2006 and January 2009 were included. When more than one cardiac operation was performed during the same ICU admission, only the risk factors related to the first operation were recorded. Patients were excluded if they received preoperative dialysis, were recipients of a kidney transplant or died within 24 h after cardiac surgery, as the development of CS-AKI could not be evaluated in these patient groups. The regional Medical Ethical Committee approved the study and waived the need for informed consent, in view of the observational nature of this study.

Data collection

Data on preoperative risk factors, surgery and postoperative complications were collected from the cardio-thoracic database, hospital databases and medical records.

In addition to the risk factors needed for the different models, we registered preoperative serum creatinine (sCr), available daily sCr for 6 days postoperative and need for dialysis within 6 days following cardiac surgery. When preoperative sCr was not available, the first postoperative sCr was used (1.15% of 1388 patients). All creatinine values were checked by an independent researcher to improve the validity of the results. Prior to cardiac surgery, the estimated glomerular filtration rate (eGFR) of each patient was calculated with the Cockcroft–Gault equation [22].

For each patient, the prediction scores were calculated as in the original studies. Patients who did not meet the original inclusion criteria for a certain model were excluded for analysis of that specific model, as is shown in Figure 1. As the original model of Chertow [12] is a recursive partitioning tree, the additive risk score based on the logistic regression as published by Fortescue et al. [20] was used. In this model, the risk factor pulmonary rates were discounted because of poor reliability [23] and frequent missing values in documentation.

Definition cardiac surgery-associated AKI

We compared the predictive value of the models on a uniformly defined outcome, although the definitions of AKI and the time frame for it to develop differ among the original studies. The presence and type of AKI was assessed for each individual patient using the last sCr value before surgery and the highest postoperative sCr or the initiation of dialysis (continuous venovenous haemofiltration or intermittent haemodialysis) within 6 days following surgery. The initiation of dialysis was considered AKI-dialysis (AKI-D). A relative increase in sCr of 50, 100, and 200% or initiation of dialysis were thresholds for classification in, respectively, the AKI-Risk, AKI-Injury and AKI-Failure classes of the RIFLE criteria [24]. The urine output criteria from the RIFLE criteria were not used. The initiation of dialysis was started at the discretion of the attending physician, based on the criteria for initiation of dialysis that were standardized by the Acute Dialysis Quality Initiative (ADQI) consensus [25].
All patients operated on cardiopulmonary bypass from October 2006 to January 2008, n=1409

- Exclusion, n=20
  - Died <24 hours postoperative, n=6
  - Preoperative dialysis, n=10
  - Renal transplant receiver, n=3
  - Infrequent procedure, n=1
  - Missing data, n=1

Total cohort, n=1388
- Chertow
- Thakar
- Wijeysundera
- Rahmanian

Fig. 1. Flowchart of study cohort and subgroup selection.

**Statistical analysis**
Categorical variables are reported as frequencies with percentage; continuous variables are reported as median with inter-quartile range. Categorical variables are reported as frequencies with percentage; continuous variables were tested for significance with the χ² test; the continuous variables with the Mann–Whitney U, as appropriate. Logistic regression was used to assess the importance of the individual risk factors in the prediction of AKI-D. A selection of independent variables with a significant univariate relationship to AKI-D were included in a logistic regression.

The receiver operating curve (ROC) is a plot of sets of values of sensitivity versus 1-specificity for each given value in an ordinal score. The area under the ROC (AUROC) is a statistic for goodness of the predicting score system. The AUROC for each model was calculated for the prediction of AKI-D, as well as AKI-Risk, AKI-Injury and AKI-Failure. We compared the AUROCs for AKI-D and AKI-Risk, AKI-Injury and AKI-Failure of the prediction model with the best performance with the other prediction models. As our data are based on tests on the same individuals, they are correlated and therefore a non-parametric approach is used with the DeLong non-parametric method [26]. This comparison was performed for all patients who underwent coronary artery bypass grafting (CABG), aortic valve replacement (AVR), mitral valve replacement (MVR) or CABG with either AVR or MVR, as these patients were included in the models of Palomba and Mehta (n=1243, 90% of the present study population). The models of Brown and Aronson were excluded from statistical comparison of AUROC as they were applicable to patients with CABG only; including them in the comparison would exclude 40% of the study population.

For the best performing model, the sensitivity and specificity for several cut-off points were calculated. A two-sided P-value of <0.05 indicates statistical significance. The data were analysed using SPSS 17.0 and MedCalc® version 11.3.1.0 (MedCalc Software, Mariakerke, Belgium).

**Results**

**Cohort characteristics**
The study population consisted of 1409 eligible patients; of which, 21 patients were excluded. Six patients died within 24 h, 10 patients received preoperative dialysis, there were three renal transplant patients, one patient with missing data and one patient was excluded for an infrequent procedure with an emergency transfer to a heart transplantation centre, resulting in a study population of 1388 (Figure 1). A second, independent investigator checked the data of all patients. Baseline characteristics and risk factors of the total patient cohort, specified by the patients with AKI-D and without AKI-D, are shown in Table 2. AKI-D occurred in 27 patients (1.9%). CS-AKI as classified by the RIFLE occurred in 129 (9.3%) patients, of which 65 (4.7%) developed AKI-Risk, 32 (2.3%) developed AKI-Injury and 32 (2.3%) AKI-Failure. In multivariate logistic regression, preoperative creatinine, preoperative use of intra-aortic balloon pump, cerebrovascular disease, diabetes mellitus, cardiopulmonary bypass time and left ventricular ejection fraction estimated <40% were independently associated with development of AKI-D.

**Clinical applicability**
The model of Fortescue, Thakar, Wijeysundera and Rahmanian was applicable to all patients (n = 1388, 100%). The other models were applicable to a selected group of patients, i.e. for Mehta (n = 1247, 90%), Palomba (n = 1244, 90%), Brown (n = 763, 55%) and Aronson (n = 833, 61%), as shown in Figure 1. The models of Fortescue, Wijeysundera, Thakar, Mehta and Brown use preoperative data only, whereas the models of Palomba, Aronson and Rahmanian require peri-operative (i.e. duration of cardiopulmonary bypass and use of preoperative inotropic agents) and/or postoperative (i.e. low cardiac output and central venous pressure) data (Table 1).

**Prediction of AKI-D, AKI-Risk, AKI-Injury and AKI-Failure using the separate models**
The occurrence of AKI-D and the AUROC for each model and for each level of severity of CS-AKI are available as Supplementary data. Out of the group of 833 patients suitable for using the model of Aronson, one patient developed AKI-D. Therefore, a reliable calculation of the AUROC was not possible. Except for the model of Rahmanian, all the models performed well with an AUROC >0.8. Lesser severe CS-AKI was more difficult to predict than more severe CS-AKI and the need for dialysis for all models.

**Comparison of the AUROC for prediction of AKI-D, AKI-Risk, AKI-Injury and AKI-Failure**
The model with the highest AUROC was statistically tested against the other models. Therefore, the AUROC of Thakar was compared with that of Mehta, Fortescue, Wijeysundera, Palomba and Rahmanian (Table 3). Thakar
performed significantly better than Mehta and Rahmanian in predicting AKI-D (P = 0.009 and 0.007, respectively). In predicting AKI-Risk, Thakar performed significantly better than Fortescue, Wijeysundera and Rahmanian (P = 0.009, 0.006 and <0.001, respectively). Thakar performed only significantly superior to Rahmanian for
predicting AKI-Injury and AKI-Failure (P < 0.001 and 0.004, respectively).

The sensitivity and specificity for several cut-off values for the model of Thakar are reported in Table 4. The optimal cut-off value is 3, with a sensitivity of 83% and a specificity of 87%. Previous comparisons of models predicting cardiac surgery-associated AKI are illustrated in Table 5.

### Discussion

In the present study, we compared the eight available prediction models of CS-AKI defined by the RIFLE criteria and need for dialysis for the first time. Four of these models (Fortescue, Thakar, Wijeysundera and Rahmanian) were applicable to all patients undergoing cardiac surgery including cardiopulmonary bypass. Two models (Mehta and Palomba) were applicable to those with CABG only. We report that the model of Thakar exerts the highest predictive value. This difference was statistically significant compared with the models of Fortescue, Wijeysundera, Rahmanian and Mehta. Although there was no statistical difference in the prediction of CS-AKI of the Palomba model and the model of Thakar, the model of Palomba is not useful in the preoperative setting. The model of Thakar combines the best predictive power and usefulness in the preoperative setting in all patients undergoing cardiac surgery.

### Comparison with other comparative studies

Although to our knowledge, head-to-head comparison of the eight available prediction models has not been performed previously, some prediction models of CS-AKI have been compared with other models before [16, 27–29]. The incidence of AKI-D in our study cohort was comparable to the incidence reported in these studies, which ranged from 1.0 to 3.8%. Our observation that the model of Thakar has the highest predictive power of predicting CS-AKI is in accordance with other comparative studies [27–29]. Remarkably, we observed a better predictive performance for all the models compared with previous studies. There may be several explanations for this. First, we defined a fixed time frame of 6 days following surgery in which dialysis had to be initiated in order to be classified as cardiac surgery-related AKI-D. Some other studies did not set this time frame; therefore, dialysis could have been initiated later on, increasing the chance of other renal insults to have occurred (e.g. sepsis, nephrotoxic drugs or contrast), not directly related to the cardiac surgery. Second, the renal replacement therapy was initiated by the discretion of the attending physician. In our hospital, this decision is based on the criteria for initiation of dialysis that were standardized by the ADQI consensus [25]. Differences in thresholds for initiation of dialysis between hospitals could result in different scores in prediction of dialysis.

The models of Aronson, Brown and Palomba were designed to predict AKI, not AKI-D, and their ability to predict AKI-D was not studied before. In contrast to the higher predictive scores for the prediction of AKI-D than in the original studies [15, 17, 18], we found much lower predictive scores for the prediction of less severe AKI than in the original studies. This is likely due to a difference in definition of AKI. In the original studies, AKI was defined as a renal composite event based on initiation of dialysis.

### Table 4. Sensitivity and specificity of cut-off values for the model of Thakar

<table>
<thead>
<tr>
<th>Cut-off value</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>Positive likelihood ratio</th>
<th>Negative likelihood ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>100</td>
<td>53.8</td>
<td>2.2</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>94.4</td>
<td>75.0</td>
<td>3.8</td>
<td>0.07</td>
</tr>
<tr>
<td>3</td>
<td>83.3</td>
<td>86.5</td>
<td>6.2</td>
<td>0.19</td>
</tr>
<tr>
<td>4</td>
<td>55.6</td>
<td>93.5</td>
<td>8.5</td>
<td>0.48</td>
</tr>
<tr>
<td>5</td>
<td>55.6</td>
<td>97.2</td>
<td>20.1</td>
<td>0.46</td>
</tr>
<tr>
<td>6</td>
<td>38.9</td>
<td>99.1</td>
<td>43.4</td>
<td>0.62</td>
</tr>
<tr>
<td>7</td>
<td>22.2</td>
<td>99.6</td>
<td>54.6</td>
<td>0.78</td>
</tr>
<tr>
<td>8</td>
<td>16.7</td>
<td>99.8</td>
<td>102.3</td>
<td>0.83</td>
</tr>
<tr>
<td>9</td>
<td>5.6</td>
<td>99.9</td>
<td>68.2</td>
<td>0.95</td>
</tr>
<tr>
<td>10</td>
<td>0</td>
<td>100</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>

The scoring range is 0–17.

### Table 5. Comparative studies of models predicting cardiac surgery-associated AKI

<table>
<thead>
<tr>
<th>Author</th>
<th>Centre</th>
<th>n</th>
<th>Country</th>
<th>Compared against</th>
<th>AKI-D (%)</th>
<th>AKI-D AUROC</th>
<th>Definition AKI</th>
<th>AKI (%)</th>
<th>AKI AUROC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wijeysundera et al. [16]</td>
<td>M</td>
<td>10 751</td>
<td>Canada</td>
<td>Wijeysundera</td>
<td>1.3</td>
<td>0.78 and 0.78</td>
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<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Chertow</td>
<td></td>
<td>0.68 and 0.70</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Thakar</td>
<td></td>
<td>0.81 and 0.80</td>
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<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Mehta</td>
<td>0.75 and 0.78</td>
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<td>N/A</td>
<td>N/A</td>
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<td></td>
<td></td>
<td></td>
<td>Thakar</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Wijeysundera</td>
<td></td>
<td>0.82</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
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<tr>
<td>Candela-Toha et al. [27]</td>
<td>S</td>
<td>1780</td>
<td>Spain</td>
<td>Thakar</td>
<td>1.0</td>
<td>0.66</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Modified Thakar</td>
<td></td>
<td>0.67</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Heise et al. [28]</td>
<td>S</td>
<td>3508</td>
<td>Germany</td>
<td>Thakar</td>
<td>2.1</td>
<td>0.86</td>
<td>sCr&gt;2.0 mg/dL</td>
<td>3.9</td>
<td>0.81</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Mehta</td>
<td></td>
<td>0.81</td>
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<td>0.76</td>
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<tr>
<td></td>
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<td></td>
<td>Wijeysundera</td>
<td></td>
<td>0.79</td>
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<td>0.75</td>
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<tr>
<td>Englberger et al. [29]</td>
<td>S</td>
<td>12 096</td>
<td>USA</td>
<td>Thakar</td>
<td>2.1</td>
<td>0.86</td>
<td>sCr&gt;2.0 mg/dL</td>
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<td></td>
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<td></td>
<td>Wijeysundera</td>
<td></td>
<td>0.79</td>
<td></td>
<td></td>
<td>0.75</td>
</tr>
</tbody>
</table>

M, multicentre; S, single centre; AKI-D, acute kidney injury requiring dialysis; AUROC, area under the receiver operating curve; AKI, acute kidney injury; sCr, serum creatinine; CrCl, creatinine clearance; N/A, not applicable.
of dialysis or absolute or relative increases in sCr and estimated GFR [17, 18].

Risk factors used in the predictive models
There have been many studies that identified risk factors of CS-AKI [2, 3, 10, 11]. In this study, we found a significant relationship with predicting AKI-D for patients with cerebral vascular disease, pulmonary disease and pulmonary hypertension, preoperative renal disease and reduced GFR, prior cardiac surgery, type of surgery, reduced left ventricular function and congestive heart failure, emergency surgery, cardiogenic shock and need for intra-aortic balloon pump, mitral valve regurgitation, prolonged CPB and cross-clamp time, postoperative elevated central venous pressure and low cardiac output. The higher scoring models (AUROC >0.85: Fortescue, Thakar, Mehta, Wijeysundera and Palomba) all used six or more of these risk factors in their model. The other three models (Brown, Aronson and Rahmanian) with a lower performance used only two to four of the risk factors that were significantly related to AKI-D in the present study.

Three models (Aronson, Palomba and Rahmanian) use pre- and postoperative data, consequently postponing the estimation of risk on CS-AKI to the postoperative phase, when renal damage already could have occurred and thereby limiting the possibilities to take preventive measures. These kinds of models are, therefore, not suitable to assess the risk of CS-AKI in the preoperative phase. In addition, we report that these models do not perform better than those that only use preoperative data. So, adding pre- and postoperative data does not increase the predictive power, but does weaken the clinical usefulness as preoperative application is impossible.

Application in research and clinical practice
It has been proposed that the prediction of AKI in cardiac surgery can be helpful for three different purposes [30]. First of all, in the preoperative setting, it can support informed decision-making. However, one should be careful with interpretation of these scores as the positive predictive value is limited due to the infrequent occurrence of AKI. For example; when scoring ≥6 on the Thakar model (specificity 0.985), the chance of AKI-D is 24% in our population. The second purpose of predicting CS-AKI is raising awareness of the vulnerability of these patients, which can trigger the initiation of preventative strategies and earlier recognition and treatment. We can imagine that for patients with high risk for renal damage, an interdisciplinary team of cardiac surgeons, anesthesiologists and nephrologists could prevent renal damage. There is some evidence that haemodynamic and fluid optimization have beneficial effects [31]. Although there are some promising agents that are currently being investigated, no pharmacological interventions with definitive proven clinical effect are currently known [31, 32]. Finally, the prediction of CS-AKI can be used for research purposes, e.g. the identification of biomarkers of kidney damage, investigation of preventive and therapeutic interventions and studies on the recovery from AKI.

Strengths and limitations
The strength of this study is the inclusion of all the models that are currently available. By a comparison, we aimed to answer which of these models performed best in one single population. Thereby, we did not only aim to predict AKI-D, but less severe AKI stages as defined by the RIFLE criteria as well.

Some limitations of our study need to be addressed. A weakness in scoring patients on risk factors is the dependency on medical records in which medical history can be incomplete, especially in emergency cases. However, over 90% of the data were derived by hand from medical records, while the remainder were retrieved from correspondence and electronic patient information. Therefore, the medical history, as it was known at the time of the decision of the surgery, was available for our research. So, any systematic error based on incomplete medical history would give the clinician the same over- or underestimation of the risk of CS-AKI. Also, in 165 patients (11.8%), preoperative creatinine was not available the week before surgery. In 122 cases, serum creatinine weeks to months prior to surgery was used, assuming renal function to be stable prior to surgery. In 16 patients, this was not available either, so that the first serum creatinine postoperative was used. Of the other 27 patients, we retrieved preoperative creatinine values from correspondence of the referring hospital. Next, although monitored, urine production was not necessarily documented for all patients during follow-up, and was therefore not available for analysis. It must be emphasized that anuria and oliguria are clinically important signs of AKI, and patients presenting with oliguria are likely to have a rise in creatinine within days. In this retrospective analysis with a duration of 6 days, patients with significant oliguria are likely identified based on rises in their creatinine value.

Also, it has to be considered that initiation of dialysis is not a hard endpoint. Although protocolized, the initiation of dialysis is up to the judgement of the attending physician and criteria for starting dialysis may differ between centres, which could have led to an over- or underprediction of AKI-D [33]. Therefore, we used any severity of CS-AKI as a second endpoint which is independent of clinical decisions.

Finally, one has to take into account that differently defined outcomes were used than in the original studies. Therefore, applied models may perform differently than in the original study. We feel this is appropriate, as we use standardized and widely used outcome definitions (such as the RIFLE criteria) to compare between studies.

Conclusion
The model of Thakar predicts the development of cardiac surgery-associated AKI best. It is an easy-to-use tool, which can be applied in the preoperative stage, with variables that are readily available in a standard preoperative work up. It can predict which patients are at risk not only for need of dialysis, but also less severe forms of CS-AKI.
Supplementary data

Supplementary data are available online at http://ndt.oxfordjournals.org.

Acknowledgements. The authors thank Tijn Bouw for monitoring the database. S.H. was supported by a postdoc startup grant from the Dutch Kidney Foundation.

Conflict of interest statement. None declared.

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Received for publication: 19.4.2012; Accepted in revised form: 8.10.2012