Early detection of postoperative acute kidney injury by Doppler renal resistive index in cardiac surgery with cardiopulmonary bypass

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Editor’s key points

- Acute kidney injury (AKI) is an important cause of morbidity and mortality after cardiac surgery.
- This prospective observational study assessed Doppler renal resistive index (RRI) as a predictor of AKI.
- Increased RRI was a sensitive and specific predictor of AKI after cardiopulmonary bypass.

Background. Acute kidney injury (AKI) is common after cardiac surgery, affecting outcome. Early detection of an AKI marker is likely to speed diagnosis and implementation of measures to preserve renal function. In septic shock and unselected ventilated subjects, an increased Doppler renal resistive index (RRI) is a predictor of AKI. This study aims to determine whether RRI would act similarly in the postoperative setting of cardiac surgery.

Methods. This study included 65 subjects aged more than 60 yr undergoing elective heart surgery with cardiopulmonary bypass (CPB) and at risk of AKI. All presented at least one AKI risk factor [arteritis, diabetes, or serum creatinine (sCr) clearance of 30–60 ml min⁻¹] and were haemodynamically stable without arrhythmia. Doppler RRI was measured in the immediate postoperative period (POP) while subjects were ventilated and sedated. AKI was assessed when sCr increased 30% above the preoperative baseline.

Results. Eighteen subjects developed AKI between days 1 and 4, with six requiring dialysis. RRI in the POP was increased in AKI [RRI: 0.79 (0.08) with AKI vs 0.68 (0.06) without AKI, \(P < 0.001\)], correlating to AKI severity [0.68 (0.06) without AKI, 0.77 (0.08) with AKI but no dialysis, and 0.84 (0.03) with AKI and dialysis, \(P < 0.001\)]. RRI was similar in subjects receiving catecholamines. RRI >0.74 in the POP predicted delayed AKI with high sensitivity and specificity (0.85 and 0.94, respectively). Multivariate analysis showed that AKI was associated with increased RRI and transfusion.

Conclusions. RRI used in the immediate POP after cardiac surgery with CPB enabled prediction of delayed AKI and anticipation of its severity.

Keywords: acute kidney injury; cardiac surgical procedures; early diagnosis; kidney; postoperative period; ultrasonography, Doppler

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Acute kidney injury (AKI) requiring dialysis occurs in up to 6% of cardiac surgery subjects, with less severe renal injury affecting as many as 15%.\(^1\) AKI should be considered a major postoperative complication as it is associated with high mortality rates.\(^2\)–\(^6\) Even in cases of slight renal function impairment,\(^3\)–\(^10\) However, in the perioperative period, early diagnosis of AKI is difficult as an increase in the level of conventional markers, such as serum creatinine (sCr) level or clearance, is delayed.\(^11\) Moreover, AKI may be present even in the case of normal urine output.\(^12\) While new markers might be more sensitive, they have not yet been used in daily practice.\(^13\) An early and simple marker would be welcome in order to detect AKI as soon as possible, thus allowing for optimization of renal condition. The main surrogate for optimization is assumed to be renal hemodynamics,\(^14\) which is often altered when general hemodynamics is still preserved. Prompt correction can normalize renal condition, thus avoiding AKI.

Accordingly, clinical predictive scores for AKI have been proposed in cardiac surgery.\(^15\) More specifically, ultrasound imaging of the renal arteries can be instrumental in the early detection of AKI. Indeed, renal blood flow is decreased at an early stage during acute tubular necrosis as a consequence of protracted intrarenal vasoconstriction.\(^16\) The renal resistive index (RRI), which is used for assessing arterial pulsatility, was shown to correlate with renal vascular resistance.\(^17\)–\(^18\) It can easily be measured using transparietal renal Doppler. Its usefulness in predicting AKI has been demonstrated after renal allografts\(^19\) and in a rabbit model of acute tubular necrosis.\(^20\) More recently, a correlation was found between increased RRI on day 1 and the occurrence of AKI on day 5 in septic shock.\(^21\) Assuming RRI to be a promising tool to predict postoperative renal insufficiency, RRI was measured prospectively in cardiac surgery subjects during the immediate postoperative period (POP). Our aim was to assess whether RRI would predict emergent AKI after cardiac surgery.

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Methods

Subject selection
This prospective, observational study was approved by our institutional review board, which waived the requirement for written informed consent as renal Doppler echography is an existing feature of our routine practice during ‘office hours’. The study was conducted during a 6 month period (April 2009–September 2009), in the context of the immediate POP after cardiac surgery. We included consecutive subjects with at least two of the following known risk factors for AKI: age >60 yr, arteritis defined by severe lower limb arteriopathy or carotid stenosis >50%, diabetes, valvular or combined surgery, and preoperative intra-aortic balloon pump. Exclusion criteria were the following: chronic renal dysfunction (sCr clearance <30 ml min⁻¹), renal artery stenosis, endocarditis, emergent surgery, nephrotoxic treatment, or non-sinus cardiac rhythm. Indeed, cardiac arrhythmia hinders RRI assessment. Inclusion was decided after haemodynamic assessment using a Swan–Ganz catheter, provided that haemodynamic stability was achieved [mean arterial pressure (MAP) >65 mm Hg] with fluid loading or catecholamine infusion (dobutamine or norepinephrine) as needed.

For each subject, basic characteristic data, standard treatments, logistic EuroScore, and main surgery features were recorded.

RRI measurement
RRI measurement was performed by trained sonographers (G.B., P.B., J.H., and J.J.C.) using a 5 MHz pulsed wave Doppler probe (VIVID7™, GE Healthcare, Chalfont St Giles, UK). Investigators were blinded to subject characteristics, with inclusion criteria and subject data being checked and collected by an independent investigator (L.B.). Velocity in interlobar or cortico-medullar arteries was assessed three to five times in each kidney. For each artery, RRI was calculated as RRI=(peak systolic velocity−end-diastolic velocity)/peak systolic velocity (Fig. 1) as the average of all values.

Procedure
RRI was assessed before operation in the first 25 subjects and after operation in the entire population. Immediately after arrival in the intensive therapy unit (ITU), standard haemodynamic parameters were optimized, and ventilation without PEEP was adjusted to obtain a PaCO₂ in the range of 4.7−5.3 kPa in order to standardize renal blood flow. Thereafter, RRI measurements were performed in all subjects (n=65) after a 20 min steady-state period under the residual effects of general anaesthesia. All postoperative measurements were performed within the first 45 min upon the arrival of subjects in the ITU.

Follow-up
The following data were collected intraoperatively: surgery type, duration of cardiopulmonary bypass (CPB), need for transfusion, and urine output; upon arrival in the ITU (day 0): RRI measurement, MAP, heart rate, PaCO₂, serum lactate, venous blood saturation of O₂ (SvO₂), indexed cardiac output, right atrial pressure, serum total proteins, haematocrit, proportion of subjects receiving norepinephrine or dobutamine; and during postoperative days spent in the ITU: volume loading with crystalloids and colloids on day 0 and mean urine output on days 1−3. These data along with the characteristic features of the subject population are summarized in Table 1.

In addition, sCr value, which was assessed before operation as a reference value, was reassessed at arrival in the ITU and then daily each morning, until peak sCr value was reached. AKI was defined as an increase of more than 30% between preoperative and peak sCr values (the highest of all postoperative sCr values). Outcome variables, such as the need for renal replacement therapy (RRT), length of stay in the ITU and hospital, and mortality on day 30, were also recorded. The RIFLE score on the first operative day (day 1) was computed according to three levels (risk, injury, and failure) depending on the increase in sCr and diuresis.

Validation of investigator performance
Before the study, all three investigators performed a series of 20 blind RRI assessments in unselected ITU subjects. Intra-observer reproducibility of measurements and inter-observer reliability were assessed by the intraclass correlation coefficients and their 95% confidence intervals. These parameters were higher than 95% and ranged from 84% to 99%, respectively.

Statistical analysis
Main data are expressed as mean (sd) or median (25th−75th percentiles). The study population was divided into two groups according to the occurrence or absence of postoperative AKI. Patient characteristic and outcome variables were compared between the two groups using parametric or non-parametric tests depending on the normality of distribution.

Fig 1 Example of RRI measurement (RRI=0.55). The Doppler beam is angled to match the artery long axis.
Table 1  Subject characteristics according to postoperative renal status. LOS, length of stay. *Comparison between data of the present study (AKI vs no AKI). †Significantly different from the subjects included in the study ($P=0.02$). All other numbers in the same column do not differ from the study population. ‡In addition to basal perfusion which is standardized (30 ml kg$^{-1}$ 24 h$^{-1}$). Values in italics indicate significant $P$-values. ARA, angiotensine receptor angagonist; CABG, coronary artery bypass graft; RRI, renal resistive index; MAP, mean arterial pressure; $P_{aCO_2}$, arterial partial pressure in CO$_2$; $SvO_2$, mixed venous blood saturation in O$_2$.

<table>
<thead>
<tr>
<th>Patient characteristics and preoperative period</th>
<th>All subjects operated on during the study period ($n=316$)</th>
<th>Subjects of the present study</th>
<th>P-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr) (25th – 75th percentiles)</td>
<td>70 (65 – 75)$^f$</td>
<td>74 (69 – 78)</td>
<td>0.57</td>
</tr>
<tr>
<td>Gender (% men)</td>
<td>66</td>
<td>63</td>
<td>0.38</td>
</tr>
<tr>
<td>Arteritis (%)</td>
<td>15</td>
<td>13</td>
<td>0.003</td>
</tr>
<tr>
<td>Diabetes (%)</td>
<td>23</td>
<td>23</td>
<td>0.53</td>
</tr>
<tr>
<td>Converting enzyme inhibitors (%)</td>
<td></td>
<td>54</td>
<td>1</td>
</tr>
<tr>
<td>ARA II (%)</td>
<td>8</td>
<td>22</td>
<td>0.2</td>
</tr>
<tr>
<td>Diuretics (%)</td>
<td>43</td>
<td>23</td>
<td>0.07</td>
</tr>
<tr>
<td>Statins (%)</td>
<td>60</td>
<td>55</td>
<td>0.15</td>
</tr>
<tr>
<td>Logistic EuroScore (dimensionless) (25th – 75th percentiles)</td>
<td>6.1 (4 – 6)</td>
<td>5.3 (4 – 5)</td>
<td>0.03</td>
</tr>
<tr>
<td>Indexed creatinine clearance (ml min$^{-1}$)</td>
<td>69 (27)</td>
<td>72 (17)</td>
<td>0.003</td>
</tr>
<tr>
<td>Serum creatinine (µmol litre$^{-1}$)</td>
<td>94 (32)</td>
<td>79 (19)</td>
<td>0.002</td>
</tr>
<tr>
<td>Ejection fraction (%)</td>
<td>59 (12)</td>
<td>63 (11)</td>
<td>0.12</td>
</tr>
<tr>
<td>Serum total proteins (g litre$^{-1}$)</td>
<td>74 (6)</td>
<td>76 (6)</td>
<td>0.02</td>
</tr>
<tr>
<td>Haematocrit (%)</td>
<td>41 (4)</td>
<td>41 (3)</td>
<td>0.08</td>
</tr>
<tr>
<td>Intraoperative period</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CABG (%)</td>
<td>27</td>
<td>25</td>
<td>0.26</td>
</tr>
<tr>
<td>Valve replacement (%)</td>
<td>52</td>
<td>51</td>
<td>0.39</td>
</tr>
<tr>
<td>Mixed (%)</td>
<td>12</td>
<td>23</td>
<td>0.33</td>
</tr>
<tr>
<td>Transfusion (%)</td>
<td>21</td>
<td>13</td>
<td>0.001</td>
</tr>
<tr>
<td>Cardiopulmonary bypass (min)</td>
<td>142 (56)</td>
<td>103 (29)</td>
<td>0.002</td>
</tr>
<tr>
<td>Urine output (ml)</td>
<td>465 (218)</td>
<td>436 (208)</td>
<td>0.63</td>
</tr>
<tr>
<td>Immediate postoperative period (day 0, 30 min after arrival in the ITU)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RRI (dimensionless)</td>
<td>0.68 (0.06)</td>
<td>0.79 (0.08)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>MAP (mm Hg)</td>
<td>75 (12)</td>
<td>81 (10)</td>
<td>0.017</td>
</tr>
<tr>
<td>Heart rate (beats min$^{-1}$)</td>
<td>79 (14)</td>
<td>78 (13)</td>
<td>0.52</td>
</tr>
<tr>
<td>$P_{aCO_2}$ (mm Hg)</td>
<td>37 (4)</td>
<td>39 (4)</td>
<td>0.11</td>
</tr>
<tr>
<td>Serum lactate (mmol litre$^{-1}$)</td>
<td>1.1 (0.4)</td>
<td>1.2 (0.05)</td>
<td>0.44</td>
</tr>
<tr>
<td>$SvO_2$ (%)</td>
<td>66 (6)</td>
<td>70 (8)</td>
<td>0.28</td>
</tr>
<tr>
<td>Indexed cardiac output (litre min$^{-1}$ m$^{-2}$)</td>
<td>2.2 (0.7)</td>
<td>2.4 (0.5)</td>
<td>0.57</td>
</tr>
<tr>
<td>Right atrium pressure (mm Hg)</td>
<td>10 (4)</td>
<td>10 (3)</td>
<td>0.43</td>
</tr>
<tr>
<td>Serum total proteins (g litre$^{-1}$)</td>
<td>46 (6)</td>
<td>45 (6)</td>
<td>0.53</td>
</tr>
<tr>
<td>Haematocrit (%)</td>
<td>35 (4)</td>
<td>35 (5)</td>
<td>0.75</td>
</tr>
<tr>
<td>Norepinephrine (%)</td>
<td>49</td>
<td>44</td>
<td>1</td>
</tr>
<tr>
<td>Dobutamine (%)</td>
<td>6</td>
<td>22</td>
<td>0.09</td>
</tr>
<tr>
<td>Postoperative period (D$_1$ – D$_3$)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Crystalloids$^2$ (D$_0$) (ml)</td>
<td>0 (0 – 0)</td>
<td>0 (0 – 1000)</td>
<td>0.16</td>
</tr>
<tr>
<td>Colloids (D$_0$) (ml)</td>
<td>800 (0 – 1500)</td>
<td>1000 (125 – 1500)</td>
<td>0.41</td>
</tr>
<tr>
<td>Mean urine output (D$_1$) (ml h$^{-1}$ kg$^{-1}$) (25th – 75th percentiles)</td>
<td>0.67 (0.56 – 0.79)</td>
<td>0.65 (0.47 – 0.84)</td>
<td>0.14</td>
</tr>
<tr>
<td>Mean urine output (D$_2$) (ml h$^{-1}$ kg$^{-1}$) (25th – 75th percentiles)</td>
<td>0.52 (0.38 – 0.65)</td>
<td>0.48 (0.39 – 0.72)</td>
<td>0.6</td>
</tr>
<tr>
<td>Mean urine output (D$_3$) (ml h$^{-1}$ kg$^{-1}$) (25th – 75th percentiles)</td>
<td>0.59 (0.41 – 1.06)</td>
<td>0.61 (0.42 – 1.40)</td>
<td>0.5</td>
</tr>
</tbody>
</table>

Continued
The EuroScore and length of ITU and hospital stays were presented as median (inter-quartile range) and compared after logarithmic transformation. Qualitative data were compared using the $\chi^2$ test.

Multivariate logistic regression (forward step) was performed on the three variables reaching the lowest $P$-value in univariate analysis and being clinically pertinent (RRI, transfusion, and duration of CPB). As only 18 cases of AKI occurred, due to the rule of using one variable per 10 cases, the model was set to only retain the two most significant variables reaching a $P$-value of 0.05.

Receiver operating characteristic (ROC) curves were constructed in order to assess the diagnostic value of RRI and other surrogate markers as predictors of AKI.

Statistical analysis was performed using SPSS 15™ (SPSS Inc., Chicago, IL, USA).

Results

Among the 316 subjects undergoing cardiac surgery with CPB during the study period, 66 met the inclusion criteria. One subject experiencing haemorrhagic shock in the second postoperative hour was excluded from the study, resulting in 65 subjects completing the study. The data of these 65 subjects were used for analysis.

In total, 18 subjects presented AKI, six of whom required dialysis. Peak sCr occurred in all subjects within the first four postoperative days: it was observed in 60% of subjects on the day after surgery (day 1), 26% on day 2, 11% on day 3, and 3% on day 4. The delay in reaching postoperative sCr peak correlated with the degree of AKI observed after operation, which was graded according to three levels (0, none; 1, AKI without dialysis; and 2, AKI with dialysis) ($r=0.80$, $P<10^{-3}$).

Preoperative measurement of RRI was performed in the first 25 subjects. No significant difference was found in preoperative RRI values between the six subjects with postoperative AKI and the 19 subjects without AKI ($0.68 \pm 0.06$ compared with $0.69 \pm 0.07$, respectively). However, RRI significantly increased in postoperative AKI subjects, but not in those without AKI (Fig. 2).

The distribution of immediate postoperative RRI among groups is shown in Figure 3. It should be noted that RRI measurements in the right and left kidneys were similar and so they were pooled. RRI significantly differed between the subjects with or without AKI ($0.79 \pm 0.08$ compared with $0.68 \pm 0.06$, respectively, $P<0.001$). Finally, RRI was similar in subjects who received vasopressors and those who did not, although a significant inverse correlation was found between RRI and MAP in the immediate POP ($r=0.39$, $P<10^{-3}$).

Preoperative sCr and sCr clearance differed significantly between subjects with or without postoperative AKI (Table 1). However, ROC curves (Fig. 5) showed that RRI at the threshold level of 0.74 achieved a higher level of sensitivity and specificity (0.94 and 0.89, respectively) in predicting postoperative AKI than standard variables such as preoperative sCr, sCr clearance, indexed diuresis, and MAP. It is noteworthy that the indexed urine output, which is universally used as a simple clinical parameter, was surpassed by RRI in predicting postoperative AKI. Although other surrogate haemodynamic predictors of AKI (SVO2, right atrial pressure, and indexed cardiac output measured within 45 min upon arrival in the ITU) were tested, they failed to be predictors of AKI as area under the curve (AUC) did not significantly differ from 0.5 (range of $P 0.15–0.28$).
Univariate analysis showed that AKI significantly correlated with RRI, arteritis, logistic EuroScore, preoperative indexed sCr clearance, serum total proteins, transfusion, duration of CPB, MAP at arrival in the ITU, and length of ITU stay (Table 1). After including the three variables reaching the lowest significant P-value in multivariate analysis and allowing the model to only retain the two variables with the greater association level, RRI and, to a lesser extent, transfusion were the most significant predictive variables (Table 2).

We observed a significant proportional relationship between AKI stages according to the RIFLE score (no AKI, injury, and failure) and the three AKI categories (no AKI, RRI 0.65 to 0.75, 0.75 to 0.85, 0.85 to 0.95) and MAP on day 0, that is, during the first 40 min, after operation (r=0.39, P<0.001).
AKI without RRT, and AKI with RRT) defined based on a 30% postoperative increase in sCr ($\chi^2$ test, $P<10^{-3}$).

**Discussion**

The main finding of our study was the ability of RRI to predict AKI with a high level of sensitivity and specificity at an early stage after cardiac surgery, that is, upon arrival in the ITU. This parameter outperformed conventional sCr-related markers, whose increase was shown to be delayed after operation. Moreover, RRI correlated with the severity of renal dysfunction.

The incidence of AKI in our study subjects was 28%, with 9% requiring dialysis. These results are similar to the overall incidence found in our department in subjects undergoing cardiac surgery during the same period (31% with 7% requiring dialysis), although we applied inclusion criteria to subjects at risk of AKI. These data must be compared with the finding taken from a recent large multicentre epidemiological study in a cardiac surgery setting, involving 24 Spanish centres. This study reported an overall rate of 3.5% for postoperative dialysis (range: 1.0–6.5%), including subjects with a mean age of 67 yr.27 Our overall dialysis rate was above this reported range, which might be explained by the 3 yr higher mean subject age, consistent with the role of age in the rate of dialysis.28 Our RRI threshold of 0.74 for predicting AKI in the cardiac surgery setting is similar to that found in human septic shock21 and approaches the predictive values (RRI >0.70) reported in humans29 30 and in a rabbit model of AKI.20 Our RRI threshold (RRI >0.83) for subjects requiring dialysis is in line with that of another study involving nine subjects with severe acute tubular necrosis requiring dialysis as a consequence of crush injury.31

As an early indicator of AKI, RRI contrasts with other markers using an increase in sCr either alone3 25 or in combination with urine output, such as RIFLE.26 Indeed, RRI is used for assessing instant renal perfusion, which only subsequently results in accumulation of sCr and reduced urine output.11 Based on our data, RRI allows the diagnosis of AKI to be anticipated by 1–2 days on average. Routine evaluation of RRI in subjects at risk of AKI could encourage clinicians to maximize renal-sparing actions such as hydration33 34 and optimization of renal perfusion pressure.35 36 These are the sole approaches shown to exhibit protective effects in subjects undergoing cardiac surgery, presenting with septic shock, and following radiocontrast agent injections.3 Such a prompt response to AKI would not be possible if the therapeutic strategy is based on delayed criteria, such as the increase in sCr or sustained oliguria. Moreover, a routine assessment of RRI immediately after surgery could help refine the indications for hydration and fluid loading, which favour haemodilution, thereby increasing the likelihood of blood transfusion, which were shown to increase mortality after cardiac surgery.27 38

Preoperative RRI was similar in subjects who subsequently developed AKI and those who did not, although it was only measured in the first 25 subjects. As preoperative renal ultrasonography was difficult to perform, we decided not to conduct this measurement in the remaining subjects. Although it is not possible to rule out a preoperative increase in RRI in all subjects, the results related to subjects in whom it was measured do not support such an increase. A lack of correlation between RRI and sCr before injury was previously noted in septic shock subjects.21 39 This suggests that RRI is a distinct marker of acute injury rather than a reflection of pre-existing chronic renal insufficiency. We found a significant correlation between RRI and MAP immediately after surgery. This was not linked to the administration of vasopressors as AKI and non-AKI subjects had similar rates of use of vasopressors. These findings are in line with those of Lerolle and colleagues,21 who concluded that the effects of catecholamine on RRI reflect the physiological post-glomerular vasoconstriction that occurs with arterial hypotension as a physiological means to preserve glomerular filtration. In contrast, RRI appears to reflect the vasoconstriction induced by acute kidney dysfunction.40

Our subject population corresponded to only 20% (65 out of 316) of those who underwent routine cardiac surgery during the study period. Indeed, inclusion criteria favoured selection of subjects at increased risk of AKI. We were unable to include more subjects due to a lack of investigators trained in RRI measurement (13%), notably in the evenings and on weekends. However, the main characteristic data of our subject population were comparable with those of all subjects undergoing cardiac surgery during the study period, with the exception of older age; average.

The selected criterion of a 30% increase in sCr from baseline to assess AKI differed slightly from the threshold used in RIFLE. RIFLE is a multi-criteria classification used to assess AKI that defines AKI as occurring when sCr exceeds the reference value by more than 150% or when urine output is lower than 0.5 ml kg$^{-1}$ h$^{-1}$ for over 6 h.32 However, RIFLE has not been used in cardiac surgery.3 25 Using this criterion to define AKI, we found that an RRI >0.74 is very close to that reported by other authors in non-surgical subjects.21 41 Accordingly, it suggests that the choice of a 30% increase in sCr used to define AKI is of minor importance and compares well with results from studies using RIFLE criteria.

RRI depends on several inter-related parameters (vascular resistance and heart rate). Indeed, increased resistance (hypocapnic vasoconstriction) and decreased heart rate (decreased end-diastolic Doppler flow velocity) were shown to raise RRI. We purposely excluded arrhythmic subjects from our study, and heart rate was very similar in both

**Table 2** Multivariate forward stepwise analysis (entering the three parameters which correlated the most with AKI in univariate analysis)

<table>
<thead>
<tr>
<th></th>
<th>B</th>
<th>P-value</th>
<th>OR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>RRI</td>
<td>24.2</td>
<td>0.001</td>
<td>3.4 × 10$^{10}$</td>
<td>10$^{-3}$ – 10$^{17}$</td>
</tr>
<tr>
<td>Transfusion</td>
<td>2.2</td>
<td>0.036</td>
<td>9.0</td>
<td>1.1 – 70.8</td>
</tr>
<tr>
<td>Constant</td>
<td>–27.7</td>
<td></td>
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</tr>
</tbody>
</table>
groups. Moreover, we kept $P_aCO_2$ within a narrow range in all subjects. Thus, we assume that the dependence of RRI on heart rate and CO$_2$-related vasoconstriction were sufficiently controlled so as to limit bias in RRI assessment. While we did not control for MAP, we found that there was an inverse correlation between MAP and RRI. Despite MAP being significantly lower in the AKI group, it was rejected as a contributing factor in the multivariate analysis. However, the area under the ROC curve for MAP significantly differed from the equivalence line. Accordingly, RRI changes plausibly reflect intrinsic renal arteriolar properties resulting from AKI, with MAP exerting only a marginal influence. However, as no pharmaceutical agent has been approved for preserving kidney function after cardiac surgery, MAP optimization remains an essential option, along with off-pump coronary bypass or minimally invasive surgery (e.g. percutaneous valve replacement). As regards future studies, our data suggest that raising MAP in an attempt to preserve preoperative renal function would be a reasonable approach.

We selected subjects presenting an increased preoperative risk for AKI after cardiac surgery. Extrapolation of our findings to low-risk subjects is of obvious interest. In a study of 37 septic shock subjects, an RRI >0.74 was the threshold that best predicted AKI on day 5, in line with our study results. In 51 subjects ventilated in intensive care unit, an RRI >0.79 achieved the best discriminative power to detect subjects likely to develop persistent AKI on day 3. Hence, our data closely match those of published literature, supporting the use of a threshold value of RRI, >0.74–0.79, in predicting AKI.

The factors related to AKI in multivariate analysis are in line with previous literature. Transfusion is a known risk factor for AKI owing to the vasoconstricting properties of free haemoglobin from haemolysis of packed blood cells and during CPB. Its effects marginally add to RRI, which remains a significant predictor of AKI.

In conclusion, our study showed that RRI was useful in the early detection of AKI after cardiac surgery. RRI should be assessed in the immediate POP, when residual anaesthesia and artificial ventilation allow for maintaining $P_aCO_2$ within a narrow range. This requirement makes RRI unsuitable for predicting AKI in spontaneously breathing or arrhythmic subjects. Assessing RRI might allow for optimizing renal function immediately on admission to the ITU.

**Conflict of interest**
None declared.

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The authors performed this study in the course of their normal duties as full-time employees of public healthcare institutions. The clinical department of L.B. provided funds for the data analysis.

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