Introduction

Cardiac surgery is the second most frequent form of acute kidney injury (AKI) in critically ill patients [1]. Therefore, AKI is a common complication after cardiac surgery and is associated with an increased morbidity and mortality [2]. Difficulties in prediction and early identification of AKI have hindered the ability to develop preventive and therapeutic measures for this syndrome. We tested the hypothesis that a urine test measuring insulin-like growth factor-binding protein 7 (TIMP7) and tissue inhibitor of metalloproteinases-2 (TIMP2), both inducers of G1 cell cycle arrest, a key mechanism implicated in acute kidney injury (AKI), could predict AKI in cardiac surgery patients.

Methods

We studied 50 patients at high risk for AKI undergoing cardiac surgery with cardiopulmonary bypass (CPB). Serial urine samples were analyzed for [TIMP2]*[IGFBP7] concentrations. The primary outcome measure was AKI as defined by international consensus criteria following surgery. Furthermore, we investigated whether urine [TIMP2]*[IGFBP7] could predict renal recovery from AKI prior to hospital discharge.

Results

Clinical characteristics

<table>
<thead>
<tr>
<th></th>
<th>Total (n=50)</th>
<th>AKI (n=14)</th>
<th>Non-AKI (n=36)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>71 ± 12</td>
<td>71 ± 12</td>
<td>71 ± 12</td>
<td>0.944</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>26 (52%)</td>
<td>9 (64%)</td>
<td>17 (47%)</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>24 (48%)</td>
<td>5 (36%)</td>
<td>19 (53%)</td>
<td></td>
</tr>
<tr>
<td>Previous smoking</td>
<td>1.5 ± 0.5</td>
<td>1.7 ± 0.6</td>
<td>1.2 ± 0.2</td>
<td>0.065</td>
</tr>
<tr>
<td>eGFR (ml/min/1.73m²)</td>
<td>51 ± 11</td>
<td>50 ± 16</td>
<td>53 ± 12</td>
<td>0.884</td>
</tr>
<tr>
<td>Concomitant</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>48 (96%)</td>
<td>24 (168)</td>
<td>24 (168)</td>
<td>0.006</td>
</tr>
<tr>
<td>Congestive Heart Failure (%)</td>
<td>40 (80%)</td>
<td>20 (140)</td>
<td>20 (140)</td>
<td>0.039</td>
</tr>
<tr>
<td>Diabetes (%)</td>
<td>20 (40%)</td>
<td>10 (71%)</td>
<td>10 (28%)</td>
<td>0.055</td>
</tr>
<tr>
<td>COPD (%)</td>
<td>15 (30%)</td>
<td>7 (50%)</td>
<td>8 (22%)</td>
<td>0.200</td>
</tr>
<tr>
<td>Chronic Kidney Disease (%)</td>
<td>15 (30%)</td>
<td>7 (50%)</td>
<td>8 (22%)</td>
<td>0.486</td>
</tr>
<tr>
<td>Previous heart surgery (%)</td>
<td>6 (12%)</td>
<td>3 (21%)</td>
<td>3 (8%)</td>
<td>0.235</td>
</tr>
<tr>
<td>Left ventricular EF (%)</td>
<td>70 (140)</td>
<td>35 (100)</td>
<td>35 (100)</td>
<td>0.008</td>
</tr>
<tr>
<td>LVEF (mean)</td>
<td>140 ± 40</td>
<td>140 ± 40</td>
<td>140 ± 40</td>
<td>0.053</td>
</tr>
<tr>
<td>Length of ICU stay (days)</td>
<td>8 ± 2</td>
<td>12 ± 3</td>
<td>4 ± 1</td>
<td>0.001</td>
</tr>
<tr>
<td>Length of hospital stay (days)</td>
<td>10 ± 2</td>
<td>24 ± 9</td>
<td>34 ± 1</td>
<td>0.001</td>
</tr>
</tbody>
</table>

ROC curves for the maximum early composite and the 4 h value

(A) This figure displays the receiver operating characteristic (ROC) curve for the maximum early composite (maximum value from the first 24 postoperative hours) for [TIMP2]*[IGFBP7]. (B) This figure displays the receiver operating characteristic (ROC) curves for the 4h values of [TIMP2]*[IGFBP7] (black solid line) and NGAL (gray dashed line).

Conclusions

In summary, our results indicate that TIMP2 and IGFBP7 are early predictive urinary biomarkers of AKI after cardiac surgery. The combination of these two biomarkers may allow for the reliable early prediction of AKI at all times after CPB. The course of urinary TIMP2 and IGFBP7 concentrations appears to be useful for predicting renal recovery following cardiac surgery.

References