Blood Transfusion and the Risk of Acute Kidney Injury After Transcatheter Aortic Valve Implantation

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Background—Blood transfusion is associated with acute kidney injury (AKI) after transcatheter aortic valve implantation (TAVI). We sought to elucidate in more detail the relation between blood transfusion and AKI and its effects on short- and long-term mortality.

Methods and Results—Nine hundred ninety-five patients with aortic stenosis underwent TAVI with the Medtronic CoreValve or the Edwards Valve in 7 centers. AKI was defined by the Valve Academic Research Consortium (absolute increase in serum creatinine ≥0.3 mg/dL [≥26.4 μmol/L] or ≥50% increase ≤72 hours). Logistic and Cox regression was used for predictor and survival analysis. AKI occurred in 20.7% (n=206). The number of units of blood transfusion ≤24 hours was the strongest predictor of AKI (≥5 units, OR, 4.81 [1.45–15.95], 3–4 units, OR, 3.05 [1.24–7.53], 1–2 units, OR, 1.47 [0.98–2.22]) followed by peripheral vascular disease (OR, 1.48 [1.05–2.10]), history of heart failure (OR, 1.43 [1.01–2.03]), leucocyte count ≤72 hours after TAVI (OR, 1.05 [1.02–1.09]) and European System for Cardiac Operative Risk Evaluation (EuroSCORE; OR, 1.02 [1.00–1.03]). Potential triggers of blood transfusion such as baseline anemia, bleeding-vascular complications, and perioperative blood loss were not identified as predictors. AKI and life-threatening bleeding were independent predictors of 30-day mortality (OR, 3.15 [1.56–6.38], OR, 6.65 [2.28–19.44], respectively), whereas transfusion (≥3 units), baseline anemia, and AKI predicted mortality beyond 30 days.

Conclusions—AKI occurred in 21% of the patients after TAVI. The number of blood transfusions but not the indication of transfusion predicted AKI. AKI was a predictor of both short- and long-term mortality, whereas blood transfusion predicted long-term mortality. These findings indicate that outcome of TAVI may be improved by more restrictive use of blood transfusions. (Circ Cardiovasc Interv. 2012;5:680-688.)

Key Words: acute kidney injury ■ anemia ■ blood transfusion ■ predictors ■ transcatheter aortic valve implantation

Transcatheter aortic valve implantation (TAVI) is increasingly used to treat patients with aortic stenosis, who are considered at high risk for surgical aortic valve replacement. Despite its minimally invasive nature, TAVI is invariably associated with a number of complications that may affect outcome. Some of these complications are clinically manifest during the procedure for which immediate actions are taken, whereas others such as acute kidney injury (AKI) are detected later and may have silent, but harmful, prognostic effects. AKI is reported in 12% to 57% of the patients who undergo TAVI and is associated with a 2- to 6-fold increased risk of death during short- and long-term follow-up.

At present, the pathophysiologic mechanisms of AKI after TAVI are unclear. Some studies suggest a direct relation between perioperative blood transfusion and AKI. This may be explained by the fact that in association with the transfusion of red blood cells (RBC) a number of other cellular and molecular substances are administrated that either directly or indirectly (eg, inflammation) induce kidney damage, yet one may question whether the triggers for blood transfusion, such as perioperative blood loss because of bleeding-vascular...
WHAT IS KNOWN
• Perioperative blood transfusion has been associated with acute kidney injury after transcatheter aortic valve implantation.

WHAT THE STUDY ADDS
• Blood transfusion was the most important factor associated with acute kidney injury whereas potential triggers of transfusion, such as baseline anemia, vascular-bleeding complications, blood loss, or severe hypotension, were not.
• Patients with anemia had less decline in hemoglobin after transcatheter aortic valve implantation but received more transfusions as compared with patients without anemia.
• Acute kidney injury was a predictor of both short- and long-term mortality whereas blood transfusion predicted long-term mortality.

clinical, procedural and follow-up data for research in accordance with Institutional Review Board approval. This study complies with the Declaration of Helsinki.

Procedure
TAVI was performed under general or local anesthesia using the Medtronic CoreValve System (26, 29, or 31 mm) or Edwards SAPIEN Valve (20, 23, or 26 mm) via a transfemoral, transapical, transsubclavian, or transaortic approach of which details have been described previously. Details of the prehydration protocol for the various institutions are summarized in online-only Data Supplement.

The amount of contrast and the occurrence of life-threatening arrhythmias (any episode of ventricular tachycardia, ventricular fibrillation, asystole requiring vasopressive drugs, electric defibrillation, or cardiopulmonary resuscitation), any complication leading to severe sustained hypotension, postimplantation balloon dilation, and (Valve Academic Research Consortium-defined) bleeding and vascular complications were recorded during or immediately after TAVI.19

After the procedure, patients were extubated in the catheterization room or after transfer in the cardiac care unit shortly after the procedure or later if clinically indicated. Antiplatelet therapy after Medtronic CoreValve System and Edwards SAPIEN Valve implantation consisted of clopidogrel 75 mg for 6 months and aspirin 80 to 100 mg indefinitely. Patients on oral anticoagulant therapy before TAVI received periprocedural therapeutic anticoagulation with unfractionated heparin or low-molecular-weight heparin in combination with either clopidogrel or aspirin to cover the time with subtherapeutic INR levels. Oral anticoagulation was resumed shortly after TAVI.

Laboratory Measurements and AKI Definition
Preoperative serum creatinine (SCr) values were used to calculate the baseline SCr clearance using the Cockcroft and Gault equation: SCr clearance (mL/min)=(140−age)x(weight kg)÷[72×SCr (mg/dL) (×0.85 for women).20 Chronic kidney disease (CKD) was defined as a calculated SCr clearance <60 mL/min.21,22 Patients with CKD were further classified in tertiles to examine the effect of mild (45.0–60.0 mL/min), moderate (35.0–44.9 mL/min), and severe CKD (<35 mL/min).

AKI was defined according to the Valve Academic Research Consortium recommendations as an absolute (≤72 hours) reduction in kidney function and defined as: (1) an absolute increase in the highest value of SCr ≥0.3 mg/dL (≥26.4 μmol/L) or (2) a percentage increase in the highest value of SCr ≥50% (1.5-fold from baseline). AKI severity was further classified as stage I (increase in SCr of 150%–200% or increase of ≥203 mg/dL [≥22.6 μmol/L]), stage II (increase in SCr of 200%–300%), or stage III (increase in SCr of ≥300% or increase of ≥24.0 mg/dL [≥235 μmol/L]) with an acute increase of ≥0.5 mg/dL (≥4.4 μmol/L). Patients receiving renal replacement therapy (hemodialysis, peritoneal dialysis, or hemofiltration) during hospitalization or within 30 days after the procedure were considered to be classified as stage III.23

Preoperative hemoglobin (Hb) values were used to define baseline anemia according to the American College of Physicians and WHO criteria as a Hb level <13 g/dL in men and <12 g/dL in women.24 Patients with anemia were classified in tertiles to assess the effects of mild (12.0–12.99 g/dL in men; 11.30–11.99 g/dL in women), moderate (10.80–11.99 g/dL in men; 10.23–11.29 g/dL in women), and severe anemia (<10.80 g/dL in men; <10.23 g/dL in women).

Data on RBC transfusions were recorded by the institution’s blood bank laboratory and used to determine the corrected Hb drop ≤24 hours after TAVI according to the modified Lande field equation.24,25 In this equation 1 unit of packed RBCs is considered to represent 1 g/dL of Hb and, therefore, the net Hb drop corresponds to the addition of the number of packed RBC to the baseline-minus-measured nadir Hb.12

Follow-Up
After hospital discharge, mortality data were collected by contacting the civil registries or the referring physician or general practitioner...
and was complete in 98.4% of the 937 patients who survived the first 30 days (median [interquartile range] follow-up time; 12 [4–23] months). Death at any time during the follow-up period was classified as cardiac or noncardiac according to the Valve Academic Research Consortium criteria.19

**Statistical Analysis**

Details of data completeness and management are summarized in online-only Data Supplement. Categorical variables are presented as frequencies and percentages and were compared with the χ² test or Fisher exact test. The normality of distributions was assessed with the Shapiro-Wilk test; comparison of continuous variables was done by using the Student t test or Wilcoxon rank-sum test when appropriate. A stepwise logistic regression analysis including all variables from Tables 1 and 2 exhibiting \( P < 0.10 \) in the univariable analysis was used to determine the predictive factors of AKI and 30-day mortality. Two interaction terms were tested to evaluate synergistic effects of (1) baseline anemia and Hb drop ≤24 hours and (2) baseline CKD and contrast load.10 A stepwise Cox regression analysis including all variables from Tables 1 and 2 exhibiting \( P < 0.10 \) in the Cox univariable analysis was used to determine the predictive factors of long-term mortality in patients who survived the first 30 days after TAVI (landmark analysis). For the purpose of this study, diabetes mellitus, hypertension, and peripheral vascular disease were considered as risk factors for AKI.

**Table 1. Baseline Characteristics of Patients With and Without AKI After TAVI**

<table>
<thead>
<tr>
<th></th>
<th>Entire Cohort (n=995)</th>
<th>No AKI (n=789)</th>
<th>AKI (n=206)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age, y, median (IQR)</strong></td>
<td>82 (77–86)</td>
<td>82 (78–86)</td>
<td>82 (77–86)</td>
<td>0.42</td>
</tr>
<tr>
<td><strong>Male sex, no (%)</strong></td>
<td>497 (50)</td>
<td>393 (50)</td>
<td>104 (50)</td>
<td>0.86</td>
</tr>
<tr>
<td><strong>Height, cm, mean±SD</strong></td>
<td>164±10</td>
<td>164±10</td>
<td>165±10</td>
<td>0.31</td>
</tr>
<tr>
<td><strong>Weight, kg, mean±SD</strong></td>
<td>72±15</td>
<td>71±15</td>
<td>73±16</td>
<td>0.092</td>
</tr>
<tr>
<td><strong>Body mass index, mean±SD</strong></td>
<td>26.4±5.0</td>
<td>26.3±4.8</td>
<td>26.9±5.5</td>
<td>0.14</td>
</tr>
<tr>
<td><strong>Body surface area, mean±SD</strong></td>
<td>1.79±0.21</td>
<td>1.79±0.21</td>
<td>1.82±0.22</td>
<td>0.097</td>
</tr>
<tr>
<td><strong>New York Heart Association class ≥III, no (%)</strong></td>
<td>806 (81)</td>
<td>631 (80)</td>
<td>175 (85)</td>
<td>0.11</td>
</tr>
<tr>
<td><strong>Previous cerebrovascular event, no (%)</strong></td>
<td>198 (20)</td>
<td>155 (20)</td>
<td>43 (21)</td>
<td>0.71</td>
</tr>
<tr>
<td><strong>Previous myocardial infarction, no (%)</strong></td>
<td>262 (26)</td>
<td>201 (26)</td>
<td>61 (30)</td>
<td>0.23</td>
</tr>
<tr>
<td><strong>Previous coronary artery bypass graft surgery, no (%)</strong></td>
<td>267 (27)</td>
<td>214 (27)</td>
<td>53 (26)</td>
<td>0.68</td>
</tr>
<tr>
<td><strong>Previous percutaneous coronary intervention, no (%)</strong></td>
<td>303 (31)</td>
<td>239 (30)</td>
<td>64 (31)</td>
<td>0.83</td>
</tr>
<tr>
<td><strong>Congestive heart failure, no (%)</strong></td>
<td>577 (58)</td>
<td>442 (56)</td>
<td>135 (66)</td>
<td>0.010</td>
</tr>
<tr>
<td><strong>Diabetes mellitus, no (%)</strong></td>
<td>274 (28)</td>
<td>218 (28)</td>
<td>56 (27)</td>
<td>0.90</td>
</tr>
<tr>
<td><strong>Hypertension, no (%)</strong></td>
<td>772 (78)</td>
<td>603 (76)</td>
<td>169 (82)</td>
<td>0.085</td>
</tr>
<tr>
<td><strong>Peripheral vascular disease, no (%)</strong></td>
<td>301 (30)</td>
<td>222 (28)</td>
<td>79 (39)</td>
<td>0.004</td>
</tr>
<tr>
<td><strong>Chronic obstructive pulmonary disease, no (%)</strong></td>
<td>281 (28)</td>
<td>217 (28)</td>
<td>64 (31)</td>
<td>0.31</td>
</tr>
<tr>
<td><strong>Creatinine, median (IQR)</strong></td>
<td>100 (81–129)</td>
<td>99 (81–126)</td>
<td>106 (80–139)</td>
<td>0.12</td>
</tr>
<tr>
<td><strong>Chronic kidney disease, no (%)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mild*</td>
<td>243 (24)</td>
<td>198 (25)</td>
<td>45 (22)</td>
<td>0.40</td>
</tr>
<tr>
<td>Moderate*</td>
<td>250 (25)</td>
<td>203 (26)</td>
<td>47 (23)</td>
<td>0.20</td>
</tr>
<tr>
<td>Severe*</td>
<td>242 (24)</td>
<td>184 (23)</td>
<td>58 (28)</td>
<td>0.31</td>
</tr>
<tr>
<td><strong>Hemoglobin, mean±SD</strong></td>
<td>12.2±3.8</td>
<td>12.2±4.2</td>
<td>12.0±1.7</td>
<td>0.42</td>
</tr>
<tr>
<td><strong>Anemia, no (%)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mild†</td>
<td>200 (20)</td>
<td>157 (20)</td>
<td>43 (21)</td>
<td>0.82</td>
</tr>
<tr>
<td>Moderate†</td>
<td>192 (19)</td>
<td>150 (19)</td>
<td>42 (20)</td>
<td>0.20</td>
</tr>
<tr>
<td>Severe†</td>
<td>175 (18)</td>
<td>136 (17)</td>
<td>39 (19)</td>
<td>0.19</td>
</tr>
<tr>
<td><strong>Leucocyte count (×10⁹ cells/L), mean±SD</strong></td>
<td>7.3±2.0</td>
<td>7.3±2.2</td>
<td>7.2±2.1</td>
<td>0.55</td>
</tr>
<tr>
<td><strong>Atrial fibrillation, no (%)</strong></td>
<td>265 (27)</td>
<td>209 (27)</td>
<td>56 (27)</td>
<td>0.82</td>
</tr>
<tr>
<td><strong>Permanent pacemaker, no (%)</strong></td>
<td>133 (13)</td>
<td>100 (13)</td>
<td>33 (16)</td>
<td>0.21</td>
</tr>
<tr>
<td><strong>Left ventricular ejection fraction ≤35%, no (%)</strong></td>
<td>157 (16)</td>
<td>116 (15)</td>
<td>41 (20)</td>
<td>0.068</td>
</tr>
<tr>
<td><strong>Aortic valve area, cm², mean±SD</strong></td>
<td>0.66±0.19</td>
<td>0.66±0.20</td>
<td>0.66±0.17</td>
<td>0.89</td>
</tr>
<tr>
<td><strong>Peak gradient, mean±SD</strong></td>
<td>71±25</td>
<td>71±25</td>
<td>71±26</td>
<td>0.93</td>
</tr>
<tr>
<td><strong>Mitral regurgitation grade ≥III, no (%)</strong></td>
<td>118 (12)</td>
<td>102 (13)</td>
<td>16 (8)</td>
<td>0.041</td>
</tr>
<tr>
<td><strong>Aortic regurgitation grade ≥III, no (%)</strong></td>
<td>86 (9)</td>
<td>71 (9)</td>
<td>15 (7)</td>
<td>0.44</td>
</tr>
<tr>
<td><strong>Logistic Euroscore, median (IQR)</strong></td>
<td>17 (11–30)</td>
<td>15 (10–28)</td>
<td>22 (12–35)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

**AKI** indicates acute kidney injury; **TAVI**, transcatheter aortic valve implantation; and **IQR**, interquartile range.

*Chronic kidney disease was defined as a calculated creatinine clearance <60 mL/min; mild 45.0 to 60.0 mL/min, moderate 35.0 to 44.9 mL/min and severe <35 mL/min.

†Anemia was defined as Hb <13 g/dL in men and <12 g/dL in women,23 mild anemia 12.0 to 12.99 g/dL in men and 11.30 to 11.99 g/dL in women, moderate anemia 10.80 to 11.99 g/dL in men and 10.23 to 11.29 g/dL in women, and severe anemia <10.80 g/dL in men and <10.23 g/dL in women.
Table 2. Perioperative Results for Patients With and Without AKI After TAVI

<table>
<thead>
<tr>
<th>Intraoperative or ≤24 h</th>
<th>No AKI (n=789)</th>
<th>AKI (n=206)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Access strategy, no (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Transfemoral</td>
<td>561 (71)</td>
<td>130 (63)</td>
<td>0.002</td>
</tr>
<tr>
<td>Transapical</td>
<td>210 (27)</td>
<td>67 (33)</td>
<td></td>
</tr>
<tr>
<td>Transsubclavian</td>
<td>18 (2)</td>
<td>6 (3)</td>
<td></td>
</tr>
<tr>
<td>Transaortic</td>
<td>0</td>
<td>3 (2)</td>
<td></td>
</tr>
<tr>
<td>Circulatory support, no (%)</td>
<td>20 (3)</td>
<td>9 (4)</td>
<td>0.16</td>
</tr>
<tr>
<td>Prosthesis size, mm, no (%)*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>20, 23, 26</td>
<td>517 (66)</td>
<td>146 (71)</td>
<td>0.12</td>
</tr>
<tr>
<td>29, 31</td>
<td>272 (34)</td>
<td>59 (29)</td>
<td>0.12</td>
</tr>
<tr>
<td>Any complication leading to severe sustained hypotension, no (%)</td>
<td>24 (3)</td>
<td>8 (4)</td>
<td>0.54</td>
</tr>
<tr>
<td>Life-threatening arrhythmia, no (%)</td>
<td>29 (4)</td>
<td>10 (5)</td>
<td>0.44</td>
</tr>
<tr>
<td>Postimplantation balloon dilation, no (%)</td>
<td>130 (16)</td>
<td>39 (19)</td>
<td>0.41</td>
</tr>
<tr>
<td>Contrast volume, mL, mean±SD</td>
<td>142±97</td>
<td>158±96</td>
<td>0.052</td>
</tr>
<tr>
<td>Duration of procedure, min, mean±SD</td>
<td>99 (70–156)</td>
<td>105 (70–173)</td>
<td>0.32</td>
</tr>
<tr>
<td>Major vascular complication, no (%)</td>
<td>55 (7)</td>
<td>26 (13)</td>
<td>0.008</td>
</tr>
<tr>
<td>Bleeding complication, no (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Life threatening or major, no (%)</td>
<td>104 (13)</td>
<td>37 (18)</td>
<td>0.080</td>
</tr>
<tr>
<td>Life threatening</td>
<td>39 (5)</td>
<td>15 (7)</td>
<td>0.19</td>
</tr>
<tr>
<td>RBC transfusion, no (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>632 (80)</td>
<td>133 (64)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>1–2 units</td>
<td>137 (17)</td>
<td>54 (26)</td>
<td></td>
</tr>
<tr>
<td>3–4 units</td>
<td>14 (2)</td>
<td>11 (5)</td>
<td></td>
</tr>
<tr>
<td>≥5 units</td>
<td>6 (1)</td>
<td>8 (4)</td>
<td></td>
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<tr>
<td>Hemoglobin drop—uncorrected for RBC TF, g/dL, mean±SD</td>
<td>2.3±4.1</td>
<td>2.3±1.7</td>
<td>0.94</td>
</tr>
<tr>
<td>Hemoglobin drop—corrected for RBC TF, g/dL, mean±SD</td>
<td>2.7±4.3</td>
<td>3.2±2.7</td>
<td>0.12</td>
</tr>
<tr>
<td>Postoperative ≤72 h</td>
<td></td>
<td></td>
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<tr>
<td>Serum creatinine (μmol/L), median (IQR)</td>
<td></td>
<td></td>
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<tr>
<td>Preprocedural</td>
<td>99 (81–126)</td>
<td>106 (80–139)</td>
<td>0.12</td>
</tr>
<tr>
<td>Postprocedural</td>
<td>83 (67–106)</td>
<td>172 (122–229)</td>
<td>&lt;0.001</td>
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<tr>
<td>Creatinine clearance (mL/min), mean±SD</td>
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<tr>
<td>Preprocedural</td>
<td>48±20</td>
<td>50±27</td>
<td>0.49</td>
</tr>
<tr>
<td>Postprocedural</td>
<td>63±37</td>
<td>33±29</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Leucocyte count (&gt;10⁹ cells/L), mean±SD</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Preprocedural</td>
<td>7.3±2.2</td>
<td>7.2±2.1</td>
<td>0.55</td>
</tr>
<tr>
<td>Postprocedural</td>
<td>11.7±4.8</td>
<td>13.0±4.9</td>
<td>0.001</td>
</tr>
<tr>
<td>Hemoglobin (g/dL), mean±SD</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Preprocedural</td>
<td>12.2±4.2</td>
<td>12.0±1.7</td>
<td>0.42</td>
</tr>
<tr>
<td>Postprocedural</td>
<td>9.4±1.5</td>
<td>9.1±1.5</td>
<td>0.011</td>
</tr>
<tr>
<td>RBC transfusion, no (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>515 (65)</td>
<td>98 (48)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>1–2 units</td>
<td>209 (27)</td>
<td>63 (31)</td>
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</tbody>
</table>

Table 2. (Continued).

<table>
<thead>
<tr>
<th>In-hospital</th>
<th>No AKI (n=789)</th>
<th>AKI (n=206)</th>
<th>P Value</th>
</tr>
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<tr>
<td>Circulatory support, no (%)</td>
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<td>0.16</td>
</tr>
<tr>
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<td>10 (5)</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Life threatening or major, no (%)</td>
<td>104 (13)</td>
<td>37 (18)</td>
<td>0.080</td>
</tr>
<tr>
<td>Life threatening</td>
<td>39 (5)</td>
<td>15 (7)</td>
<td>0.19</td>
</tr>
<tr>
<td>RBC transfusion, no (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>632 (80)</td>
<td>133 (64)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>1–2 units</td>
<td>137 (17)</td>
<td>54 (26)</td>
<td></td>
</tr>
<tr>
<td>3–4 units</td>
<td>14 (2)</td>
<td>11 (5)</td>
<td></td>
</tr>
<tr>
<td>≥5 units</td>
<td>6 (1)</td>
<td>8 (4)</td>
<td></td>
</tr>
<tr>
<td>Hemoglobin drop—uncorrected for RBC TF, g/dL, mean±SD</td>
<td>2.3±4.1</td>
<td>2.3±1.7</td>
<td>0.94</td>
</tr>
<tr>
<td>Hemoglobin drop—corrected for RBC TF, g/dL, mean±SD</td>
<td>2.7±4.3</td>
<td>3.2±2.7</td>
<td>0.12</td>
</tr>
</tbody>
</table>

Table 2. (Continued).

<table>
<thead>
<tr>
<th>Mortality</th>
<th>No AKI (n=789)</th>
<th>AKI (n=206)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤30 days</td>
<td>28 (4)</td>
<td>30 (15)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>≤30 days cardiac</td>
<td>14 (2)</td>
<td>17 (8)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>&gt;30 days†</td>
<td>140 (18)</td>
<td>59 (34)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>&gt;30 days cardiac‡</td>
<td>61 (8)</td>
<td>26 (15)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

AKI indicates acute kidney injury; TAVI, transcatheter aortic valve implantation; RBC, red blood cell; TF, transfusion.

†N=937 patients survived ≥30 days after TAVI of which 199 patients died at a median of 12 (IQR: 4–23) months after TAVI.
‡The cause of death was missing or unknown in 27 of the 199 deaths (14%; n=8 in AKI group, n=19 in no AKI group).

Results

The baseline patient characteristics and perioperative details of the total population and of the patients with and without AKI are summarized in Tables 1 and 2, respectively. AKI occurred in 20.7% (n=206) of the patients of whom 3.1% (n=31) received renal replacement therapy. Details of AKI (stages I–III) and other changes in renal function are depicted in Figure 1. Patients with AKI had a significantly higher mortality at 30 days and during follow-up (Table 2).

Predictors of AKI

By univariable analysis, patients with AKI had a higher prevalence of congestive heart failure (66 versus 56%, P=0.004) and peripheral vascular disease (39 versus 28%, P=0.004) explaining a higher operative risk (Logistic EuroSCORE 22
versus 15%, \( P < 0.001 \), Table 1). They also more often underwent transapical TAVI (33 versus 27%, \( P = 0.002 \)) and suffered more major vascular complications (13 versus 7%, \( P = 0.008 \), Table 2). Despite the latter, there was no difference in perioperative blood loss (corrected Hb drop) between patients with and without AKI, yet patients with AKI received significantly more blood transfusions within 24 and 72 hours after TAVI. Because baseline anemia might affect the decision to administer blood transfusion, the mean Hb drop and number of blood transfusions for patients with no and with various degrees of baseline anemia was analyzed (Figure 2A–2B); patients with severe baseline anemia had 2.4 times less blood loss but on average received 2.3-fold more units of blood transfusions in comparison with patients without anemia before TAVI (\( P < 0.001 \)). Neither contrast use (\( P = 0.052 \)) nor any of the interaction terms (baseline anemia and Hb drop \( \leq 24 \) hours, \( P = 0.31 \); baseline CKD and contrast load, \( P = 0.10 \)) were significantly associated with AKI.

**Figure 1.** Changes in creatinine \( \leq 72 \) hours after transcatheter aortic valve implantation.

**Figure 2.** Mean percent Hb drop and mean number of blood transfusions \( \leq 24 \) and \( \leq 72 \) hours after transcatheter aortic valve implantation (TAVI) grouped according to various degrees of baseline anemia. Baseline anemia was defined as Hb <13 g/dL in men and <12 g/dL in women\(^\text{23} \); mild anemia 12.0 to 12.99 g/dL in men and 11.30 to 11.99 g/dL in women, moderate anemia 10.80 to 11.99 g/dL in men and 10.23 to 11.29 g/dL in women, and severe anemia <10.80 g/dL in men and <10.23 g/dL in women. Hb indicates hemoglobin. **A,** Mean percent Hb drop \( \leq 24 \) and \( \leq 72 \) hours after TAVI. Percent Hb drop \( \leq 24 \) h = (baseline Hb–nadir Hb \( \leq 24 \) h)/baseline Hb; Percent Hb drop \( \leq 72 \) h = (baseline Hb–nadir Hb \( \leq 72 \) hours)/baseline Hb. **B,** Mean number of blood transfusions \( \leq 24 \) and \( \leq 72 \) hours after TAVI. AKI indicates acute kidney injury.
Table 3.  Independent Predictors of AKI After TAVI

<table>
<thead>
<tr>
<th>Variable</th>
<th>OR (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>RBC transfusion ≤24 h</td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>Reference</td>
<td></td>
</tr>
<tr>
<td>1–2 units</td>
<td>1.47 (0.98–2.22)</td>
<td>0.064</td>
</tr>
<tr>
<td>3–4 units</td>
<td>3.05 (1.24–7.53)</td>
<td>0.015</td>
</tr>
<tr>
<td>≥5 units</td>
<td>4.81 (1.45–15.95)</td>
<td>0.010</td>
</tr>
<tr>
<td>Peripheral vascular disease</td>
<td>1.48 (1.05–2.10)</td>
<td>0.026</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>1.43 (1.01–2.03)</td>
<td>0.042</td>
</tr>
<tr>
<td>Maximum leucocyte count ≤72 h</td>
<td>1.05 (1.02–1.09)</td>
<td>0.001</td>
</tr>
<tr>
<td>Logistic EuroSCORE (per % increase)</td>
<td>1.02 (1.00–1.03)</td>
<td>0.006</td>
</tr>
</tbody>
</table>

AKI indicates acute kidney injury; TAVI, transcatheter aortic valve implantation; RBC, red blood cell.

In a descending order of the magnitude of the OR, we found by multivariable analysis that the number of units of blood transfusion ≤24 hours was the strongest predictor of AKI (≥5 units, OR, 4.81 [1.45–15.95]; 3–4 units, OR, 3.05 [1.24–7.53]; 1–2 units, OR, 1.47 [0.98–2.22]), followed by peripheral vascular disease (OR, 1.48 [1.05–2.10]), congestive heart failure (OR, 1.43 [1.01–2.03]), leucocyte count ≤72 hours after TAVI (OR, 1.05 [1.02–1.09]), and Logistic EuroSCORE (OR, 1.02 [1.00–1.03]). Potential triggers of blood transfusion such as baseline anemia, bleeding-vascular complications, and perioperative blood loss (corrected Hb drop) were not identified as independent predictors of AKI (Table 3).

Prognostic Implications

Independent predictors of 30-day mortality consisted of perioperative life-threatening bleeding (OR, 6.65 [2.28–19.44]), aortic regurgitation post-TAVI (OR, 4.80 [1.78–12.96]), AKI (OR, 3.15 [1.56–6.38]), leucocyte count ≤72 hours (OR, 1.13 [1.06–1.20]), and Logistic EuroSCORE (OR, 1.04 [1.02–1.06]). Mortality during follow-up in patients who survived the first 30 days was determined by a mix of patient-related variables and by the administration of blood transfusion for ≤24 hours (≥5 units, HR, 2.54 [1.34–4.81], 3–4 units, HR, 2.03 [1.26–3.24], 1–2 units, HR, 1.32 [0.94–1.86]) in addition to AKI (HR, 1.57 [1.13–2.17], Table 5). Kaplan–Meier survival estimates for increasing severity of AKI, baseline anemia, and number of transfusions are shown in Figure 3.

Table 4.  Independent Predictors of Mortality ≤30 Days After Transcatheter Aortic Valve Implantation

<table>
<thead>
<tr>
<th>Variable</th>
<th>OR (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Life-threatening bleeding</td>
<td>6.65 (2.28–19.44)</td>
<td>0.001</td>
</tr>
<tr>
<td>Post operative aortic regurgitation grade ≥Ⅲ</td>
<td>4.80 (1.78–12.96)</td>
<td>0.002</td>
</tr>
<tr>
<td>Acute kidney injury</td>
<td>3.15 (1.56–6.38)</td>
<td>0.001</td>
</tr>
<tr>
<td>Maximum leucocyte count ≤72 h (per 10⁹ cells/L increase)</td>
<td>1.13 (1.06–1.20)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Logistic EuroSCORE (per % increase)</td>
<td>1.04 (1.02–1.06)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>RBC transfusion ≤24 h</td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>Reference</td>
<td>0.72</td>
</tr>
<tr>
<td>1–2 units</td>
<td>0.76 (0.33–1.75)</td>
<td>0.51</td>
</tr>
<tr>
<td>3–4 units</td>
<td>0.31 (0.03–3.06)</td>
<td>0.31</td>
</tr>
<tr>
<td>≥5 units</td>
<td>1.01 (0.15–6.73)</td>
<td>0.99</td>
</tr>
</tbody>
</table>

RBC denotes red blood cell.

Discussion

In this multicenter study including 995 patients who underwent TAVI we found that AKI occurred in 21% of the patients and that the number of perioperative blood transfusions was the strongest predictor of AKI but not the clinical indications of transfusion (ie, baseline anemia, perioperative vascular-bleeding complications, or blood loss). AKI was a predictor of both short- and long-term mortality, whereas blood transfusion predicted long-term mortality.

The frequency of AKI after TAVI has been reported to vary between 12% and 57% in previous but smaller series of patients using various definitions of AKI.2–10 The herein reported point estimate of 21% most likely reflects the incidence of AKI encountered in clinical practice, given the sample size and the multicenter nature of this study. Irrespective of the true value, AKI poses a clinical problem as it is associated with an increased mortality at 30 days and beyond. This has also been shown by others and suggests that the outcome of TAVI may be improved by—among others—implementing all measures to prevent AKI.5–10

For that purpose it is essential to understand the pathophysiologic mechanism(s) of AKI after TAVI. Unfortunately, a clinical study such as this one cannot do so, yet the analysis of the association between AKI and patient- and procedure-related variables that are readily available (eg, patient demographics) or subject to change or improvement (eg, execution of procedure) may be helpful.

With respect to execution of the procedure, the findings of this study indicate that AKI and, therefore, outcome may be improved by a more careful use of blood transfusions. As mentioned, the number of blood transfusions was found...
to be the strongest predictor of AKI with a distinct gradient of risk. The relation between AKI and transfusion is consistent with other reports that studied patients who underwent TAVI or cardiac surgery, yet, such a strong relationship between AKI and the number of transfusions has not been reported. Noteworthy, we also found that the clinical triggers upon which one may decide to administer blood during TAVI were not associated with AKI. If true, this suggests that one should be more restrictive in the use of blood transfusions during TAVI and that the need of unequivocal criteria for the decision of blood transfusion is advocated. This is illustrated by the findings that patients without anemia had a 2.4 times greater Hb drop in comparison with patients with severe baseline anemia. This may be explained by a different patient and procedure planning in addition to differences in the execution of TAVI (i.e., control of hemostasis) in patients with different baseline risks. Interventions that reduce perioperative transfusions may protect against AKI, especially in anemic patients.

The absence of a relationship between AKI and the indications for transfusion in addition to the fact that we did not find a relationship between AKI and periprocedural complications leading to hypotension supports a direct harmful effect of transfusion on the kidneys. It is known that preserved RBCs suffer structural or functional changes including reduced deformability and increased aggregability, all of which—particularly in older patients with impaired renal function—might induce (further) renal dysfunction. Also the coadministration of proinflammatory molecules may play a role either directly or indirectly by inducing inflammation. This may explain the relation found in this and other studies between postoperative leucocyte count and AKI. At variance with percutaneous coronary intervention (PCI), we found a borderline association between contrast load and AKI in the univariable analysis, yet contrast load was not found to be an independent predictor. The absence of an association cannot be explained by a restrictive use of contrast in the present population considering the mean values and standard deviations (142±97 and 158±96 mL) although this may be an issue of sample size as a result of which a significant statistical difference was not detected. The current findings suggest that unlike PCI, contrast has only a minor effect on the development of AKI in patients who undergo TAVI.

With respect to the patient-related variables and, thus, patient selection, it is unlikely that we will exclude patients with peripheral vascular disease because TAVI was specifically developed for patients who are too high a risk for aortic
valve replacement. These patients often have widespread atherosclerosis including the peripheral circulation. It remains to be seen how additional pre- and postoperative care may avoid AKI such as optimal perioperative hydration.

Apart from perioperative blood transfusion and AKI, we found a number of other predictors of early and late mortality after TAVI. In accordance with previous series, we found severe bleeding and postoperative aortic regurgitation to be associated with a 5-fold increased risk of early death,23 whereas severe baseline anemia, peripheral vascular disease, heart failure, male sex, and atrial fibrillation were independent predictors of late death.23,34 These findings confirm the importance of appropriate patient selection to improve outcome after TAVI.

Limitations
This multicenter observational assessment in a large series of patients may estimate the frequency of AKI and its predictors but it cannot elucidate the precise pathophysiologic mechanism(s). This is needed to propose in greater detail improvements in patient and procedure planning and execution in addition to eventual changes in postoperative care. We also acknowledge the formulation of the research question during and after the data collection and the absence of a specified case report form. As a result, despite a high degree of completeness (online-only Data Supplement), the timing of the collection of the individual variables may not be consistent, which may affect the precision of the current findings. In addition, there was no uniform protocol of blood transfusion, as a result of which we are not able to unravel the true triggers of transfusion, thereby precluding specific propositions of improvement.

Conclusions
AKI occurred in 21% of the patients after TAVI. The number of blood transfusions, but not the indication of transfusion, predicted AKI. AKI was a predictor of both short- and long-term mortality, whereas blood transfusion predicted long-term mortality. These findings indicate that the outcome of TAVI may be improved by a more restrictive use of blood transfusions.

Disclosures
Dr Rodés-Cabau is a consultant for and received funding from Edwards Lifesciences Inc; Drs Kefer and van Garssen are physician proctors for Edwards Lifesciences Inc; Drs Bosmans and de Jaegere are physician proctors for Medtronic CoreValve Inc, MN.

References

Nuis et al. Blood Transfusion and AKI After TAVI. 687...


Blood Transfusion and the Risk of Acute Kidney Injury After Transcatheter Aortic Valve Implantation

Rutger-Jan Nuis, Josep Rodés-Cabau, Jan-Malte Sinning, Leen van Garsse, Joelle Kefer, Johan Bosmans, Antonio E. Dager, Nicolas van Mieghem, Marina Urena, Georg Nickenig, Nikos Werner, Jos Maessen, Parla Astarci, Sergio Perez, Luis M. Benitez, Eric Dumont, Ron T. van Domburg and Peter P. de Jaegere

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### Supplement A. Causes of death of patients not participating in the study because of death <72 hr after TAVI

<table>
<thead>
<tr>
<th>Cause</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sudden death</td>
<td>5 (22)</td>
</tr>
<tr>
<td>Electromechanical dissociation</td>
<td>4 (17)</td>
</tr>
<tr>
<td>Major vascular complication</td>
<td>3 (13)</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>2 (9)</td>
</tr>
<tr>
<td>Mesenteric artery thrombosis</td>
<td>2 (9)</td>
</tr>
<tr>
<td>Severe aortic regurgitation</td>
<td>2 (9)</td>
</tr>
<tr>
<td>Annulus rupture</td>
<td>1 (4)</td>
</tr>
<tr>
<td>Stroke</td>
<td>1 (4)</td>
</tr>
<tr>
<td>Heart failure</td>
<td>1 (4)</td>
</tr>
<tr>
<td>Induction of anesthesia</td>
<td>1 (4)</td>
</tr>
<tr>
<td>Cardiac tamponade</td>
<td>1 (4)</td>
</tr>
</tbody>
</table>
**Supplement B. Prehydration protocol per institution**

<table>
<thead>
<tr>
<th>Institution</th>
<th>Cut-off value: eGFR (ml/min) or serum creatinine (mg/dl)</th>
<th>Saline</th>
<th>N-acetylcysteine</th>
<th>Bicarbonate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rotterdam ThoraxCenter</td>
<td>eGFR &lt;45 * and &lt;60 †</td>
<td>0.9% §</td>
<td>no</td>
<td>no</td>
</tr>
<tr>
<td>Quebec Heart and Lung Institute</td>
<td>eGFR &lt;45 * and &lt;60 †</td>
<td>0.9% §</td>
<td>yes</td>
<td>no</td>
</tr>
<tr>
<td>University Hospital Bonn</td>
<td>eGFR &lt;60</td>
<td>0.9% §</td>
<td>no</td>
<td>no</td>
</tr>
<tr>
<td>University Hospital Maastricht</td>
<td>eGFR &lt;45 ‡</td>
<td>0.9% §</td>
<td>yes</td>
<td>yes</td>
</tr>
<tr>
<td>University Hospital Saint-Luc</td>
<td>eGFR &lt;60</td>
<td>0.45%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>University Hospital Antwerp</td>
<td>creatinine &gt;1.5</td>
<td>0.9% §</td>
<td>no</td>
<td>no</td>
</tr>
<tr>
<td>Angiografia de Occidente</td>
<td>eGFR &lt;45</td>
<td>0.9% §</td>
<td>yes</td>
<td>no</td>
</tr>
</tbody>
</table>

* * In the absence of diabetes  
† In the presence of diabetes and/or ≥ 2 other risk factors for impaired renal function after contrast agents (e.g. age>75, heart failure)  
‡ All other patients (eGFR ≥ 45 ml/min) received 1 L lactated Ringer’s solution and N-acetylcysteine at the time of induction  
§12–16 ml/kg 4–6 hr before and after TAVI  
|| 1 ml/kg/h 12h before and after TAVI

eGFR denotes estimated glomerular filtration rate
Supplement C. Data completeness and management

The data of each institution were collected and examined for missing data or extreme values, and contributing units were asked to complete or correct data. Data for each variable were ≥98% complete, except for NYHA class (97.5%), pre-operative left ventricular ejection fraction (95%), contrast volume (91%), and procedure time and post-operative echocardiography (89%). Of the 937 patients who survived the first 30 days, follow-up mortality data were complete in 98.4%; 199 patients died and the cause of death was confirmed in 172 patients (86%) and missing or unknown in 27 patients (14%).
### Supplement D. Univariable prediction models of AKI, 30-day mortality and late mortality after TAVI

<table>
<thead>
<tr>
<th>Variable</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Univariable predictors of AKI</strong></td>
<td></td>
</tr>
<tr>
<td>RBC transfusion ≤24 hr</td>
<td></td>
</tr>
<tr>
<td>none</td>
<td>reference</td>
</tr>
<tr>
<td>1-2 units</td>
<td>1.87 (1.30-2.70)</td>
</tr>
<tr>
<td>3-4 units</td>
<td>3.73 (1.66-8.41)</td>
</tr>
<tr>
<td>≥ 5 units</td>
<td>6.34 (2.16-18.56)</td>
</tr>
<tr>
<td>RBC transfusion ≤72 hr</td>
<td></td>
</tr>
<tr>
<td>none</td>
<td>reference</td>
</tr>
<tr>
<td>1-2 units</td>
<td>1.30 (0.70-2.39)</td>
</tr>
<tr>
<td>3-4 units</td>
<td>0.79 (0.24-2.65)</td>
</tr>
<tr>
<td>≥ 5 units</td>
<td>6.22 (2.59-14.94)</td>
</tr>
<tr>
<td>Major vascular complication</td>
<td>1.93 (1.18-3.16)</td>
</tr>
<tr>
<td>Body mass index</td>
<td>1.82 (0.90-3.70)</td>
</tr>
<tr>
<td>Peripheral vascular disease</td>
<td>1.60 (1.16-2.20)</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>1.53 (1.10-2.12)</td>
</tr>
<tr>
<td>Left ventricular ejection fraction ≤35%</td>
<td>1.44 (0.97-2.14)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1.41 (0.95-2.09)</td>
</tr>
<tr>
<td>Maximum leucocyte count ≤72 hr</td>
<td>1.05 (1.02-1.08)</td>
</tr>
<tr>
<td>Logistic EuroSCORE</td>
<td>1.02 (1.01-1.03)</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>1.01 (1.00-1.02)</td>
</tr>
<tr>
<td>Baseline creatinine</td>
<td>1.00 (1.00-1.01)</td>
</tr>
<tr>
<td><strong>Univariable predictors of 30-day mortality</strong></td>
<td></td>
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<tr>
<td>RBC transfusion ≤24 hr</td>
<td></td>
</tr>
<tr>
<td>none</td>
<td>reference</td>
</tr>
<tr>
<td>1-2 units</td>
<td>1.36 (0.71-2.60)</td>
</tr>
<tr>
<td>3-4 units</td>
<td>1.62 (0.37-7.11)</td>
</tr>
<tr>
<td>≥ 5 units</td>
<td>7.45 (2.24-24.81)</td>
</tr>
<tr>
<td>Bleeding complication</td>
<td></td>
</tr>
<tr>
<td>life-threatening or major</td>
<td>3.26 (1.82-5.82)</td>
</tr>
<tr>
<td>life-threatening</td>
<td>6.31 (3.16-12.61)</td>
</tr>
<tr>
<td>RBC transfusion ≤72 hr</td>
<td></td>
</tr>
<tr>
<td>none</td>
<td>reference</td>
</tr>
<tr>
<td>1-2 units</td>
<td>1.30 (0.70-2.39)</td>
</tr>
<tr>
<td>3-4 units</td>
<td>0.79 (0.24-2.65)</td>
</tr>
<tr>
<td>≥ 5 units</td>
<td>6.22 (2.59-14.94)</td>
</tr>
<tr>
<td>Acute kidney injury</td>
<td>4.63 (2.70-7.95)</td>
</tr>
<tr>
<td>Aortic regurgitation grade ≥ III</td>
<td>4.11 (1.72-9.83)</td>
</tr>
<tr>
<td>Life-threatening arrhythmias</td>
<td>3.16 (1.27-7.88)</td>
</tr>
<tr>
<td>Circulatory support</td>
<td>3.59 (1.32-9.78)</td>
</tr>
<tr>
<td>---------------------</td>
<td>------------------</td>
</tr>
<tr>
<td>Chronic kidney disease</td>
<td></td>
</tr>
<tr>
<td>none</td>
<td>reference</td>
</tr>
<tr>
<td>mild</td>
<td>1.07 (0.44-2.63)</td>
</tr>
<tr>
<td>moderate</td>
<td>1.26 (0.54-2.97)</td>
</tr>
<tr>
<td>severe</td>
<td>3.01 (1.42-6.38)</td>
</tr>
<tr>
<td>Baseline anemia</td>
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<td>none</td>
<td>reference</td>
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<tr>
<td>mild</td>
<td>1.52 (0.71-3.25)</td>
</tr>
<tr>
<td>moderate</td>
<td>2.17 (1.07-4.38)</td>
</tr>
<tr>
<td>severe</td>
<td>1.91 (0.91-4.03)</td>
</tr>
<tr>
<td>Major vascular complication</td>
<td>2.54 (1.23-5.24)</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>2.03 (1.18-3.50)</td>
</tr>
<tr>
<td>Previous myocardial infarction</td>
<td>1.78 (1.02-3.08)</td>
</tr>
<tr>
<td>Left ventricular ejection fraction ≤35%</td>
<td>1.77 (0.94-3.31)</td>
</tr>
<tr>
<td>Previous percutaneous coronary intervention</td>
<td>1.67 (0.97-2.86)</td>
</tr>
<tr>
<td>Transapical access</td>
<td>1.63 (0.94-2.83)</td>
</tr>
<tr>
<td>Maximum leucocyte count ≤72 hr</td>
<td>1.08 (1.03-1.12)</td>
</tr>
<tr>
<td>Logistic EuroSCORE</td>
<td>1.03 (1.02-1.04)</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>1.03 (1.00-1.06)</td>
</tr>
<tr>
<td>Baseline creatinine</td>
<td>1.01 (1.00-1.01)</td>
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<tr>
<td>Maximum creatinine ≤72 hr</td>
<td>1.00 (1.00-1.00)</td>
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<tr>
<td>Procedure duration (min)</td>
<td>1.00 (1.00-1.01)</td>
</tr>
<tr>
<td>Baseline peak gradient</td>
<td>0.99 (0.97-1.00)</td>
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</tbody>
</table>

### Univariable predictors of late mortality *

<table>
<thead>
<tr>
<th>RBC transfusion ≤72 hr</th>
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<tbody>
<tr>
<td>none</td>
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<tr>
<td>1-2 units</td>
<td>1.49 (1.09-2.04)</td>
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<tr>
<td>3-4 units</td>
<td>2.07 (1.34-3.21)</td>
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<tr>
<td>≥5 units</td>
<td>2.85 (1.55-5.24)</td>
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<tr>
<td>Baseline anemia</td>
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<tr>
<td>none</td>
<td>reference</td>
</tr>
<tr>
<td>mild</td>
<td>0.99 (0.63-1.54)</td>
</tr>
<tr>
<td>moderate</td>
<td>1.73 (1.19-2.51)</td>
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<tr>
<td>severe</td>
<td>2.67 (1.87-3.81)</td>
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<tr>
<td>Acute kidney injury</td>
<td>2.02 (1.49-2.74)</td>
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<tr>
<td>Congestive heart failure</td>
<td>1.99 (1.45-2.72)</td>
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<tr>
<td>Peripheral vascular disease</td>
<td>1.90 (1.42-2.53)</td>
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<tr>
<td>Chronic kidney disease</td>
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<tr>
<td>none</td>
<td>reference</td>
</tr>
<tr>
<td>mild</td>
<td>0.77 (0.49-1.20)</td>
</tr>
<tr>
<td>moderate</td>
<td>1.13 (0.78-1.67)</td>
</tr>
</tbody>
</table>
severe 1.70 (1.16-2.50)
Male gender 1.50 (1.13-1.99)
Left ventricular ejection fraction ≤ 35% 1.48 (1.04-2.09)
Life-threatening or major bleeding 1.45 (1.03-2.06)
Chronic obstructive pulmonary disease 1.41 (1.08-1.89)
Atrial fibrillation 1.40 (1.04-1.88)
Previous stroke 1.36 (0.99-1.87)
Height 1.03 (1.01-1.04)
Logistic EuroSCORE 1.02 (1.01-1.03)
Baseline peak gradient 0.99 (0.99-1.00)
Body mass index 0.97 (0.94-1.00)
Minimum hemoglobin ≤ 72 hrs 0.91 (0.83-1.01)

* N=937 patients survived >30 days after TAVI of which 199 patients died at a median of 12 [4-23] months following TAVI

RBC denotes red blood cell