Impact of AKI and transfusions on outcome in adult cardiac surgery

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Disclosure

Medtronic/Covidien
Nordic Pharma
Sorin
Overall mortality in cardiac surgery

- Overall mortality 2-3%
- US and EU data incomparable
- Huge variation in practice

STS database Blue Book 2015; Local data Vumc 2015.
Complication rates: context is changing

- Improvement of extracorporeal circuits and cardiopulmonary bypass strategies
- Improvement of surgical techniques
- Patient blood management
- Collaboration in chain of care
Complications in cardiac surgery

- Pulmonary infections / edema
- Blood transfusions
- Acute kidney injury
- Systemic inflammatory response
- Myocardial infarction
- Cerebrovascular events
Complications in cardiac surgery

- Erythrocytes are required for normal coagulation
- A low hemoglobin level is associated with a reduced oxygen carrying capacity

Blood transfusions

Acute kidney injury

- Result of impaired vascular perfusion, local hypoxia and inflammation
Modulators of blood viscosity

Blood viscosity increases:
• Drop in temperature
• Low flow states

Blood viscosity decreases:
• Hemodilution
Viscosity and capillary perfusion

Salazar Vázquez Biorheology 2009.
Blood transfusions recruit the microcirculation during cardiac surgery

12 patients - SDF

Functional capillary density

Before

After BTX

Hb content (AU)

Before

After BTX

Before

After BTX

Hb oxygenation (%)

Before

After BTX

Yuruk, Ince et al. Transfusion 2011
UK-based study between 1996-2003
Associative analysis of blood transfusion and outcome
More than 8000 patients
Blood transfusion and outcome

The risk for complications and cost increases in patients receiving allogeneic blood transfusions.

This increase is marginal in patients receiving 2 or less units of blood products.

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Table 3. Estimates of the Increase in Effects of Transfusion With Increasing Number of Units of RBCs

<table>
<thead>
<tr>
<th>RBCs Transfused, U</th>
<th>Infection Outcome</th>
<th>Ischemic Outcome</th>
<th>Relative Increase in Cost*</th>
<th>Portion of Study Population, %</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Odds Ratio</td>
<td>95% CI</td>
<td>Odds Ratio</td>
<td>95% CI</td>
</tr>
<tr>
<td>Any</td>
<td>3.73</td>
<td>2.32–5.07</td>
<td>4.05</td>
<td>2.63–5.70</td>
</tr>
<tr>
<td>0</td>
<td>1.00</td>
<td>…</td>
<td>1.00</td>
<td>…</td>
</tr>
<tr>
<td>1</td>
<td>1.46</td>
<td>0.92–2.11</td>
<td>1.63</td>
<td>1.02–2.48</td>
</tr>
<tr>
<td>2</td>
<td>2.36</td>
<td>1.42–3.30</td>
<td>2.30</td>
<td>1.32–3.50</td>
</tr>
<tr>
<td>3 or 4</td>
<td>3.82</td>
<td>2.22–5.47</td>
<td>4.49</td>
<td>2.78–6.22</td>
</tr>
<tr>
<td>5–9</td>
<td>10.75</td>
<td>5.83–15.9</td>
<td>11.79</td>
<td>6.80–16.7</td>
</tr>
<tr>
<td>&gt;9</td>
<td>45.44</td>
<td>22.6–73.6</td>
<td>46.39</td>
<td>24.5–75.4</td>
</tr>
</tbody>
</table>

*Effect estimates were estimated from adjusted models, including the interaction of units of RBCs and hematocrit stratum as described in the text, and pooled over hematocrit strata using stratum-specific coefficients weighted by the number of patients (see Appendix D in the online-only Data Supplement). This method of estimation explains the apparent contradiction between odds ratios reported in the Table for any transfusion vs none, compared with the estimates from the prespecified analysis reported earlier.

Hemoglobin levels: the right trigger?

Liberal or Restrictive Transfusion after Cardiac Surgery

Gavin J. Murphy, F.R.C.S., Katie Pike, M.Sc., Chris A. Rogers, Ph.D., Sarah Wordsworth, Ph.D., Elizabeth A. Stokes, M.Sc., Gianni D. Angelini, F.R.C.S., and Barnaby C. Reeves, D.Phil., for the TITRe2 Investigators*

**Restrictive** transfusion threshold: 7.5 g/dl hemoglobin

**Liberal** transfusion threshold: 9 g/dl hemoglobin

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Restrictive Transfusion Threshold (N=1000)</th>
<th>Liberal Transfusion Threshold (N=1003)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Other procedure</td>
<td>36 (3.6)</td>
<td>26 (2.6)</td>
</tr>
<tr>
<td>Tranexamic acid used — no./total no. (%)</td>
<td>806/999 (80.7)</td>
<td>809/1002 (80.7)</td>
</tr>
<tr>
<td>Aprotinin used — no./total no. (%)</td>
<td>39/942 (4.1)</td>
<td>32/952 (3.4)</td>
</tr>
<tr>
<td>Blood-recovery system used — no./total no. (%)</td>
<td>481/999 (48.1)</td>
<td>503/1003 (50.1)</td>
</tr>
</tbody>
</table>

*Table 1. (Continued.)*

Murphy et al. NEJM 2015.
Hemoglobin levels: the right trigger?

![Graph showing hemoglobin levels over days since randomization for two groups: Liberal-threshold group and Restrictive-threshold group.]

**No. at Risk**

<table>
<thead>
<tr>
<th>Group</th>
<th>No. at Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liberal-threshold group</td>
<td>994 967 894 773 732 501 405 338 245 204 170 998</td>
</tr>
<tr>
<td>Restrictive-threshold group</td>
<td>998 971 894 758 713 502 401 303 226 175 147 1003</td>
</tr>
</tbody>
</table>

*Murphy et al. NEJM 2015.*
Hemoglobin levels: the right trigger?

Table 3. Outcomes.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Restricted Transfusion Threshold (N = 1000)</th>
<th>Liberal Transfusion Threshold (N = 1003)</th>
<th>Estimated Treatment Effect</th>
<th>Odds Ratio or Hazard Ratio (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serious infection or ischemic event: primary outcome</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall</td>
<td>331/944 (35.1)</td>
<td>317/962 (33.0)</td>
<td>1.11 (0.91–1.34)*</td>
<td>0.30</td>
<td></td>
</tr>
<tr>
<td>Infectious event†</td>
<td>238/936 (25.4)</td>
<td>240/954 (25.2)</td>
<td>1.02 (0.83–1.26)*</td>
<td>0.83</td>
<td></td>
</tr>
<tr>
<td>Sepsis</td>
<td>210/982 (21.4)</td>
<td>214/983 (21.8)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wound infection</td>
<td>55/921 (6.0)</td>
<td>46/936 (4.9)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ischemic event</td>
<td>156/991 (15.7)</td>
<td>139/991 (14.0)</td>
<td>1.16 (0.90–1.49)*</td>
<td>0.26</td>
<td></td>
</tr>
<tr>
<td>Permanent stroke</td>
<td>15/989 (1.5)</td>
<td>17/985 (1.7)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>3/987 (0.3)</td>
<td>4/981 (0.4)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gut infarction</td>
<td>6/987 (0.6)</td>
<td>1/982 (0.1)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acute kidney injury</td>
<td>140/989 (14.2)</td>
<td>122/989 (12.3)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stage 1</td>
<td>49/989 (5.0)</td>
<td>40/989 (4.0)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stage 2</td>
<td>39/989 (3.9)</td>
<td>35/989 (3.5)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stage 3</td>
<td>50/989 (5.1)</td>
<td>46/989 (4.7)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Mortality: 2.6% vs. 1.9%

Murphy et al. NEJM 2015.
Complications in cardiac surgery

- Pulmonary infections / edema
- Blood transfusions
- Acute kidney injury
- Systemic inflammatory response
- Myocardial infarction
- Cerebrovascular events
<table>
<thead>
<tr>
<th>Stage</th>
<th>Serum creatinine</th>
<th>Urine output</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1.5–1.9 times baseline OR ≥0.3 mg/dl (≥26.5 μmol/l) increase</td>
<td>&lt;0.5 ml/kg/h for 6–12 hours</td>
</tr>
<tr>
<td>2</td>
<td>2.0–2.9 times baseline</td>
<td>&lt;0.5 ml/kg/h for ≥12 hours</td>
</tr>
<tr>
<td>3</td>
<td>3.0 times baseline OR Increase in serum creatinine to ≥4.0 mg/dl (≥353.6 μmol/l) OR Initiation of renal replacement therapy OR In patients &lt;18 years, decrease in eGFR to &lt;35 ml/min per 1.73 m²</td>
<td>&lt;0.3 ml/kg/h for ≥24 hours OR Anuria for ≥12 hours</td>
</tr>
</tbody>
</table>

4-5%  
3.5-3.9%  
4.7-5.1%

KDIGO AKI staging 2015; Murphy et al. NEJM 2015.
Pathophysiology of AKI

Surgical injury:
- Inflammation
- Oxidative/Nitric stress
- Vascular trauma
- Cholesterol emboli
- Hemolysis

- Decreased cardiac output
- Decreased renal perfusion pressure

Right heart failure
Tricuspid regurgitation
Elevated venous pressure

Renal congestion

Oliguria

Fluid overload

AKI

Anemia

Lung edema

Bleeding
Positive pressure ventilation
Anesthesia
Volume losses

Acute tubular necrosis and AKI

Ischemia Nephrotoxins

(1) Vasoconstriction
Renin-angiotensin
endothelin
↓ PG12
↓ NO

(2) Obstruction by casts
↑ Intratubular pressure
↓ Tubular fluid flow

(3) Tubular backleak

(4) Interstitial inflammation

(5) ? Direct glomerular effect

↓ GFR

↓ Tubular damage
(proximal tubules and ascending thick limb)

Oliguria
AKI: Non-modifiable and modifiable factors

**Patient factors**
- Age
- Diabetes mellitus
- Anemia
- Preop renal dysfunction

**ECC factors**
- CPB duration
- Hypotension/hypovolemia
- Low hematocrit
Fig. 4. Adjusted odds ratios for acute kidney injury, cardiac complications, and myocardial injury by time spent with a mean arterial pressure <55 mmHg.
Original Article

Costs and outcomes of acute kidney injury (AKI) following cardiac surgery

Joseph F. Dasta¹, Sandra L. Kane-Gill², Amy J. Durtschi³, Dev S. Pathak⁴ and John A. Kellum⁵

¹College of Pharmacy, The Ohio State University, Columbus, OH 43210, USA, ²School of Pharmacy, University of Pittsburgh, Pittsburgh, PA 15261, USA, ³Abbott Laboratories, Department of Clinical Affairs, Chicago, IL, USA, ⁴College of Pharmacy, The Ohio State University, Columbus, OH 43210, USA and ⁵The CRISMA (Clinical Research, Investigation, and Systems Modeling of Acute Illness) Laboratory, Department of Critical Care Medicine, University of Pittsburgh, Pittsburgh, PA, USA
AKI: increased mortality and costs

Table 4. Resource usage and outcomes of three RIFLE categories in patients with AKI after coronary artery bypass graft surgery

<table>
<thead>
<tr>
<th></th>
<th>RIFLE-R</th>
<th>RIFLE-I</th>
<th>RIFLE-F</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incidence (%)</td>
<td>53.5</td>
<td>27.1</td>
<td>19.4</td>
<td>&lt;0.003</td>
</tr>
<tr>
<td>Mortality (%)</td>
<td>5.1</td>
<td>12.9</td>
<td>26.0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>RRT (%)</td>
<td>0</td>
<td>2.9</td>
<td>14.0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Total postoperative costs</td>
<td>29,697 (20,041–52,351)</td>
<td>38,924 (25,092–70,424)</td>
<td>52,618 (35,250–91,954)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ICU costs</td>
<td>21,775 (13,444–41,427)</td>
<td>28,872 (17,961–63,322)</td>
<td>49,328 (21,454–83,687)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ICU costs (% of total costs)</td>
<td>73.3</td>
<td>74.2</td>
<td>93.7</td>
<td></td>
</tr>
<tr>
<td>Total postoperative LOS (days)</td>
<td>9 (6–17)</td>
<td>11 (7–19)</td>
<td>16 (12–25)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ICU LOS days</td>
<td>2.29 (1.34–5.2)</td>
<td>3.45 (1.9–7.7)</td>
<td>5.42 (2.8–12.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ICU LOS (% of total LOS)</td>
<td>25.4</td>
<td>31.3</td>
<td>33.8</td>
<td></td>
</tr>
<tr>
<td>ICU room</td>
<td>3400 (1197–7901)</td>
<td>5312 (2633–13,360)</td>
<td>9054 (4392–25,607)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ICU supplies</td>
<td>439 (97–1411)</td>
<td>1041 (207–2023)</td>
<td>1930 (578–4465)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Laboratory</td>
<td>2865 (1651–5516)</td>
<td>3483 (1788–6478)</td>
<td>4512 (2994–10,817)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Pharmacy</td>
<td>2198 (1180–3932)</td>
<td>2426 (1515–6106)</td>
<td>5054 (2878–9995)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Ventilatory</td>
<td>304 (152–679)</td>
<td>370 (257–1451)</td>
<td>903 (457–2717)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Dialysis</td>
<td>N/A</td>
<td>901 (587–1367)</td>
<td>2413 (841–4534)</td>
<td>0.06</td>
</tr>
</tbody>
</table>

- Increased mortality following AKI
- Renal replacement therapy
- Prolonged length of stay

Key messages

Allogeneic blood transfusion and outcome comprises a difficult association

Hemoglobin levels seem not to be the ultimate trigger for allogeneic blood transfusions
Key messages

The pathophysiology of postoperative AKI is multifactorial, with hypoperfusion and ischemia as main causes.

AKI is associated with unfavorable postoperative outcome.
New concepts to improve outcome

- New transfusion triggers
- Prevent hemodilution
- $\text{DO}_2/\text{VO}_2$

- Blood pressure
- Reduce inflammation
- Modern ECC
- $\text{DO}_2/\text{VO}_2$

Optimized oxygen carrying capacity of blood

Maintenance microvascular perfusion

Preoperative optimization of patients to prevent AKI

Patient blood management: reduce blood transfusion

- Treatment anemia
- Normal glucose control

- Surgical hemostasis
- Higher nadir Ht
- Prevent hemodilution