Transfusion en chirurgie cardiaque: hétérogénéité des pratiques
Comment y remédier?

Philippe Van der Linden MD, PhD
Conflict of Interest Disclosure

In the past 5 years, I have received honoraria or travel support for consulting or lecturing from the following companies:
Fresenius-Kabi GmbH
CSL Behring GmbH
Janssen-Cilag SA
Blood Transfusion in CABG Surgery

- Observational cohort study of 102,470 patients undergoing primary CABG under cardiopulmonary bypass in 2008 (798 sites < STS Adult Cardiac Surgery Database)

Hospital specific transfusion rate:
- RBC: 8-93%
- FFP: 0-98%
- Plts: 0-90%

Blood Transfusion in CABG Surgery

- Observational cohort study of 102,470 CABG patients (year 2008; 798 sites< STS Adult Cardiac Surgery Database)

- Multivariate analysis after adjustment for patient-level risks factors revealed that hospital transfusion rates varied by geographic location, hospital volume and academic status

- These 3 hospital characteristics combined explained only 11.1% of the variation in hospital risk-adjusted RBC usage

- Case mix explained 20.1% of the variation between hospitals in RBC usage

Independent Predictors of Chest Tube Drainage After Transfusion Cardiac Surgery

✓ Retrospective observational cohort study of patients undergoing cardiac surgery with CPB (1/2002-2/2008: N=2,575)

✓ Independent chest tube drainage predictors identified through multivariate analysis: individual operating surgeon, internal mammary artery grafting, CPB time, urgency of surgery, tricuspid valve surgery, redo surgery, LV impairment, male gender, low BMI and higher preop Hb
Independent Predictors of Chest Tube Drainage After Transfusion Cardiac Surgery

✓ Retrospective observational cohort study of patients undergoing cardiac surgery with CPB (1/2002-2/2008: N=2,575)

Effects of Perioperative Blood Transfusion and Blood Conservation in Cardiac Surgery Clinical Practice Guidelines upon Clinical Practices

✓ Survey of cardiac anesthesiologists and perfusionists' clinical practice to determine the role the STS and SCA Guidelines had in changing these practices.

✓ 1402 surveys from 1061 institutions (32% response rate).

✓ 78% of anesthesiologists & 67% of perfusionists reporting having read all, part, or a summary of the Guidelines.

Effects of Perioperative Blood Transfusion and Blood Conservation in Cardiac Surgery Clinical Practice Guidelines upon Clinical Practices

✓ 20% of respondents reported that an institutional discussion had taken place and 14% that an institutional monitoring group had been formed.

✓ 26% of respondents reported 1 or more practice changes in response to the Guidelines. The changes made were reported to be highly (9%) or somewhat (31%) effective in reducing overall transfusion rates.

✓ 4/38 Guideline recommendations were reported by >5% of respondents to have been changed in response to the Guidelines.

RBC Transfusion in Cardiac Surgery: Impact of a Novel Clinical Decision Support Tool

☑ Before and after study: implementation of a novel single-view clinical decision support tool within computerized provider order entry coupled with a provider feedback loop

RBC Transfusion in Cardiac Surgery: Impact of a Novel Clinical Decision Support Tool

✔ Before and after study: implementation of a novel single-view clinical decision support tool within computerized provider order entry coupled with a provider feedback loop

<table>
<thead>
<tr>
<th></th>
<th>Pre-intervention N=744</th>
<th>Post-intervention N=765</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Postop RBC transfusion (%)</td>
<td>50</td>
<td>41</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Postop RBC units</td>
<td>1.6 ± 2.9</td>
<td>1.25 ± 2.5</td>
<td>0.01</td>
</tr>
<tr>
<td>Pre-transfusion Hb level (g/dl)</td>
<td>8.1 ± 1.5</td>
<td>7.7 ± 1.4</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

✔ No difference in intra-operative transfusions

✔ No difference in ICU length of stay and in-hospital mortality

RBC Transfusion in Cardiac Surgery: Impact of a Novel Clinical Decision Support Tool

✓ Before and after study: implementation of a novel single-view clinical decision support tool within computerized provider order entry coupled with a provider feedback loop

Intraoperative Hemoglobin Management in Cardiac Surgery: Impact on RBC Transfusion

- Retrospective, before and after study: implementation of measures aiming at reducing hemodilution volume:
  - Decrease in intravenous fluid volume
  - Reduction of CPB circuit size
  - Use of retrograde autologous priming

- Total IV fluids reduced by 974 ml (672-1276): p<0.001
- Mean on-pump increase in Hct > 2%

Intraoperative Hemoglobin Management in Cardiac Surgery: Impact on RBC Transfusion

✓ Retrospective, before and after study: implementation of measures aiming at reducing hemodilution volume:
  • Decrease in intravenous fluid volume
  • Reduction of CPB circuit size
  • Use of retrograde autologous priming

✓ Variability in transfusion rate among anesthesiologists

Comparison of 2 Doses of Tranexamic Acid in Patients Undergoing Cardiac Surgery

- Multicenter double-blinded randomized study
- Patients stratified according to transfusion risk
  - Low-dose group: 10 mg/kg + 1 mg/kg.h (N=284)
  - High-dose group: 30 mg/kg + 16 mg/kg.h (N=285)

<table>
<thead>
<tr>
<th>Transfusion during the first week; all patients</th>
<th>Low Dose n = 284</th>
<th>High Dose n = 285</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood transfusion (yes)</td>
<td>180 (63.4)</td>
<td>170 (59.6)</td>
<td>0.3†</td>
</tr>
<tr>
<td>Packed erythrocyte transfusion (yes)</td>
<td>167 (58.8)</td>
<td>160 (56.1)</td>
<td>0.4†</td>
</tr>
<tr>
<td>FFP transfusion (yes)</td>
<td>74 (26.1)</td>
<td>53 (18.6)</td>
<td>0.03†</td>
</tr>
<tr>
<td>PC transfusion (yes)</td>
<td>64 (22.5)</td>
<td>43 (15.1)</td>
<td>0.02†</td>
</tr>
<tr>
<td>Fibrinogen (yes)</td>
<td>8 (2.8)</td>
<td>1 (0.4)</td>
<td>0.02†</td>
</tr>
<tr>
<td>Blood products (number of units)</td>
<td>4.10±0.39</td>
<td>2.49±0.38</td>
<td>0.02*</td>
</tr>
<tr>
<td>Packed erythrocytes (number of units)</td>
<td>2.14±0.18</td>
<td>1.57±0.18</td>
<td>0.07*</td>
</tr>
<tr>
<td>FFP (number of units)</td>
<td>1.07±0.14</td>
<td>0.49±0.14</td>
<td>0.02*</td>
</tr>
<tr>
<td>PC (number of units)</td>
<td>1.13±0.15</td>
<td>0.50±0.15</td>
<td>0.02*</td>
</tr>
<tr>
<td>Transfusion during the first week; patients transfused</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Packed erythrocytes (number of units)</td>
<td>3.61±0.24</td>
<td>2.81±0.25</td>
<td>0.08*</td>
</tr>
<tr>
<td>FFP (number of units)</td>
<td>4.99±0.38</td>
<td>2.90±0.45</td>
<td>0.04*</td>
</tr>
<tr>
<td>PC (number of units)</td>
<td>5.45±0.42</td>
<td>4.34±0.53</td>
<td>0.3*</td>
</tr>
</tbody>
</table>

Comparison of 2 Doses of Tranexamic Acid in Patients Undergoing Cardiac Surgery

- Multicenter double-blinded randomized study
- Patients stratified according to transfusion risk
  - Low-dose group: 10 mg/kg + 1 mg/kg.h (N=284)
  - High-dose group: 30 mg/kg + 16 mg/kg.h (N=285)

<table>
<thead>
<tr>
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<th>Low Dose n = 284</th>
<th>High Dose n = 285</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood loss during day 1 (ml)</td>
<td>820±50.7</td>
<td>590±50.4</td>
<td>0.01*</td>
</tr>
<tr>
<td>Return to surgery for hemostasis</td>
<td>17 (6.0)</td>
<td>7 (2.5)</td>
<td>0.03†</td>
</tr>
<tr>
<td>Mortality from day 0 to day 7</td>
<td>9 (3.2)</td>
<td>4 (1.4)</td>
<td>0.2†</td>
</tr>
<tr>
<td>Mortality from day 0 to day 28</td>
<td>14 (4.9)</td>
<td>8 (2.8)</td>
<td>0.2†</td>
</tr>
</tbody>
</table>

Transfusion Algorithm Based on Point-of-care Coagulation Assays in Cardiac Surgery

✓ Retrospective, before and after study: institution of a practical POC-based transfusion algorithm

From Karkouti K et al. Anesthesiology 122:560-70, 2015.
Transfusion Algorithm Based on Point-of-care Coagulation Assays in Cardiac Surgery

☑ Retrospective, before and after study: institution of a practical POC-based transfusion algorithm

<table>
<thead>
<tr>
<th>Effectiveness measures</th>
<th>Prealgorithm (N = 1,311)</th>
<th>Postalgorithm (N = 1,170)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Erythrocyte transfusions (up to POD-7)</td>
<td>1,311</td>
<td>1,170</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Median number of units (IQR)</td>
<td>676</td>
<td>476</td>
<td>0.09</td>
</tr>
<tr>
<td>Platelet transfusions (up to POD-7)</td>
<td>1,311</td>
<td>1,170</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Median number of units (IQR)</td>
<td>448</td>
<td>266</td>
<td>0.83</td>
</tr>
<tr>
<td>Plasma transfusions (up to POD-7)</td>
<td>1,311</td>
<td>1,170</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Median number of units (IQR)</td>
<td>449</td>
<td>167</td>
<td>0.35</td>
</tr>
<tr>
<td>Cryoprecipitate or fibrinogen concentrate transfusions (up to POD-7)</td>
<td>1,311</td>
<td>1,170</td>
<td>0.5</td>
</tr>
<tr>
<td>Prothrombin complex concentrate</td>
<td>1,311</td>
<td>1,170</td>
<td>0.5</td>
</tr>
<tr>
<td>Large-volume (≥4 units) erythrocyte transfusions (POD-0)</td>
<td>1,311</td>
<td>1,170</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Recombinant factor VIIIa (up to POD-1)</td>
<td>1,311</td>
<td>1,170</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

☑ No difference in outcome measures, except a lower incidence of surgical re-exploration in the postalgorithm group

From Karkouti K et al. Anesthesiology 122:560-70, 2015.
Transfusion Algorithm Based on Point-of-care Coagulation Assays in Cardiac Surgery

- Retrospective, before and after study: institution of a practical POC-based transfusion algorithm

- Results for subgroup analyses were consistent

<table>
<thead>
<tr>
<th></th>
<th>Erythrocyte Transfusions, OR (95% CI)</th>
<th>Platelet Transfusions, OR (95% CI)</th>
<th>Plasma Transfusions, OR (95% CI)</th>
<th>Large-volume Erythrocyte Transfusions, OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All patients</td>
<td>0.50 (0.32–0.77)</td>
<td>0.22 (0.13–0.37)</td>
<td>0.20 (0.12–0.34)</td>
<td>0.23 (0.11–0.48)</td>
</tr>
<tr>
<td>High bleeding risk—yes</td>
<td>0.46 (0.23–0.95)</td>
<td>0.17 (0.08–0.34)</td>
<td>0.14 (0.08–0.27)</td>
<td>0.25 (0.12–0.50)</td>
</tr>
<tr>
<td>High bleeding risk—no</td>
<td>0.51 (0.30–0.86)</td>
<td>0.30 (0.15–0.60)</td>
<td>0.34 (0.18–0.78)</td>
<td>0.25 (0.02–0.34)</td>
</tr>
<tr>
<td>Anemia—yes</td>
<td>0.27 (0.11–0.67)</td>
<td>0.14 (0.05–0.37)</td>
<td>0.13 (0.04–0.37)</td>
<td>0.17 (0.06–0.49)</td>
</tr>
<tr>
<td>Anemia—no</td>
<td>0.57 (0.34–0.95)</td>
<td>0.26 (0.15–0.47)</td>
<td>0.21 (0.11–0.92)</td>
<td>0.27 (0.07–0.98)</td>
</tr>
<tr>
<td>Cell saver—yes</td>
<td>0.48 (0.27–0.86)</td>
<td>0.15 (0.07–0.29)</td>
<td>0.20 (0.10–0.40)</td>
<td>0.28 (0.12–0.66)</td>
</tr>
<tr>
<td>Cell saver—no</td>
<td>0.58 (0.31–1.10)</td>
<td>0.45 (0.32–0.94)</td>
<td>0.16 (0.06–0.41)</td>
<td>0.17 (0.04–0.81)</td>
</tr>
<tr>
<td>Desmopressin—yes</td>
<td>0.43 (0.18–1.00)</td>
<td>0.14 (0.06–0.31)</td>
<td>0.12 (0.05–0.27)</td>
<td>0.51 (0.19–1.37)</td>
</tr>
<tr>
<td>Desmopressin—no</td>
<td>0.60 (0.37–0.96)</td>
<td>0.35 (0.18–0.67)</td>
<td>0.29 (0.13–0.63)</td>
<td>0.08 (0.02–0.36)</td>
</tr>
<tr>
<td>±6 months*</td>
<td>0.60 (0.32–1.14)</td>
<td>0.29 (0.14–0.62)</td>
<td>0.25 (0.12–0.53)</td>
<td>0.31 (0.12–0.81)</td>
</tr>
</tbody>
</table>

From Karkouti K et al. Anesthesiology 122:560-70, 2015.
Incidence & Importance of Anemia in Patients Undergoing Cardiac Surgery in UK

- National service audit (2010-2012): 12/35 UK cardiac surgery centers provided data
- 20% of the patients (4754/23,800) did not have preop Hb
- Incidence of anemia (WHO definition): 31% (23 to 45%)
- Regional variation remained an independent effect

- Independent association of anemia with transfusion, mortality, and hospital stay

A 10g/L ↓ in Hb was associated with a 43% ↑ in the risk of transfusion and a 16% ↑ in the risk of death (both p<0.001)

Patient Blood Management

✓ Defined as “the appropriate use of blood and blood components with a goal of minimized their use”.

✓ Encompasses an evidence-based medical and surgical approach that is multidisciplinary (transfusion medicine specialists, surgeons, anesthesiologists, and critical care specialists) and multiprofessional (physicians, nurses, pump technologists, and pharmacists).

Patient Blood Management Program

- Preop RBC mass
- Periop blood loss
- Reduce the Transfusion Trigger
Effect of a standardized multidisciplinary approach of blood conservation program on allogeneic transfusion exposure?
Perioperative Blood Conservation Strategy

Preop RBC mass
Standardized preop treatment (antiplatelets, iron...)

Periop blood loss
Standardized blood conservation programs

Reduce the Transfusion Trigger
Standardized transfusion trigger
Standardized Blood Transfusion Strategy

✓ Control group: September 97 - August 98
   N = 321 (group 1)

✓ Treated group: September 98 - August 99
   N = 315 (group 2)

✓ Data analyzed using analysis of variance, Student's t test, $\chi^2$, and Fisher's exact test where applicable

✓ Data expressed as percentage of the total or mean ± SD
Standardized Blood Transfusion Strategy

Acute normovolemic hemodilution (%)

<table>
<thead>
<tr>
<th>Group</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>72.8</td>
</tr>
<tr>
<td>2</td>
<td>89.2</td>
</tr>
</tbody>
</table>

$p=0.001$

Acute normovolemic hemodilution (mL)

<table>
<thead>
<tr>
<th>Group</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1500</td>
</tr>
<tr>
<td>2</td>
<td>2000</td>
</tr>
</tbody>
</table>

$p=0.001$
Standardized Blood Transfusion Strategy

Patients (%)

Group 1

- Aprotinin: 48.6%
- Others: 25.9%

Group 2

- Aprotinin: 51.4%
- Others: 28.1%
Standardized Blood Transfusion Strategy

Allogeneic blood transfusion (%)

<table>
<thead>
<tr>
<th>Group</th>
<th>Allogeneic Blood Transfusion (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1</td>
<td>33</td>
</tr>
<tr>
<td>Group 2</td>
<td>18.1</td>
</tr>
</tbody>
</table>

p<0.001

Allogeneic blood (U)

<table>
<thead>
<tr>
<th>Group</th>
<th>Allogeneic Blood (U)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1</td>
<td>3</td>
</tr>
<tr>
<td>Group 2</td>
<td>1</td>
</tr>
</tbody>
</table>

p<0.001

Group 1: 340 units in 108 patients; Group 2: 161 units in 57 patients
Standardized Blood Transfusion Strategy

Group 1: 145 units in 28 patients; Group 2: 54 units in 15 patients
Perioperative Hemoglobin Level

Hemoglobin (g/dL)

* p<0.05, ** p<0.01 vs previous measurement

Group 1: N=321
Group 2: N=315
Standardized Blood Transfusion Strategy

In-hospital mortality (%)

- **Group 1**: 4.7%
- **Group 2**: 3.8%

Length of stay (days)

- **ICU**
  - Group 1: 1.5 days
  - Group 2: 1.4 days
- **Hospital**
  - Group 1: 7.5 days
  - Group 2: 7.0 days

Legend:
- **Group 1**
- **Group 2**
Developing a Blood Conservation Strategy

- Reliable data base

- Choice of alternative techniques
  - Surgical procedure and technique
  - Patients limitations
  - Health Care environment
  - Immediate and long term costs

- Continuous monitoring

- Multidisciplinary approach: anesthesiologists, surgeons, blood bankers...

Blood Use in Elective Cardiac Surgery: The 2 Austrian Benchmark Studies

- Prospective observational multicenter studies
- April 04–February 05 (N=777) / July 09–August 10 (N=714)
- Less women, longer surgery and higher use of platelets inhibitors in the 2nd study

<table>
<thead>
<tr>
<th></th>
<th>1st benchmark</th>
<th>2nd benchmark</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preop anemia (%)</td>
<td>24</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Preop Hb (%)</td>
<td>108 ± 12</td>
<td>106 ± 12</td>
<td>0.001</td>
</tr>
<tr>
<td>Lowest postop Hb (%)</td>
<td>79 ± 9</td>
<td>76 ± 10</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>POD5 Hb (%)</td>
<td>84 ±10</td>
<td>81 ± 11</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Blood Use in Elective Cardiac Surgery: The 2 Austrian Benchmark Studies

✓ Prospective observational multicenter studies
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<th>2nd benchmark</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lost RBC volume (%)</td>
<td>45</td>
<td>43</td>
<td>0.515</td>
</tr>
<tr>
<td>Transfusion rate (%)</td>
<td>55</td>
<td>57</td>
<td>0.465</td>
</tr>
<tr>
<td>Median units transfused (IQR)</td>
<td>2 (2)</td>
<td>2 (2)</td>
<td>0.878</td>
</tr>
<tr>
<td>One unit transfusion (%)</td>
<td>11.7</td>
<td>11.3</td>
<td>0.914</td>
</tr>
</tbody>
</table>

Blood Use in Elective Cardiac Surgery: The 2 Austrian Benchmark Studies

✓ Prospective observational multicenter studies
✓ April 04–February 05 (N=777) / July 09–August 10 (N=714)

Benchmark: Definition

« Benchmark is a structured continuous collaborative process in which comparisons for selected indicators are used to identify factors that, when implemented will improve transfusion practices »

The NATA Benchmark Project

√ Step 1: Evaluation of transfusion practices in different interested centers across Europe and Canada

√ Step 2: Implementation of measures of improvement in these different centers according to their own results

√ Step 3: Re-evaluation of the practices – development of “NATA centers of excellence“

√ Step 4: Enlargement of the project to additional centers under the coordination of these centers of excellence
The NATA Benchmark Project

✓ Aim: Providing the basis for educational strategies to implement optimal PBM in participating centers

✓ Prospective observational study with online data collection (10 European centers and one Canadian)

✓ Incidence of transfusion and volume of RBC transfused significantly different between centers

✓ The relative importance of factors explaining RBC transfusion differs across institutions, some being patient related whereas others are related to the healthcare process

The NATA Benchmark Project

Developing a Patient Blood Management Program

✓ Reliable database

✓ Choice of strategies
  • Surgical procedures and techniques
  • Patients’ limitations
  • Health care environment
  • Immediate and long term costs

✓ Multidisciplinary approach

✓ Continuous monitoring