Blood Transfusion Triggers

Time for new TRICCS?

Suzy O’Neill
Anaemia in ICU

- Anaemia is common in ICU

**Causes:**
- Acute: bleeding
- Chronic: blood taking, nutritional deficiencies, sepsis
- Post op
- Bone marrow failure
Anaemia and oxygen delivery

• Inadequate O2 delivery with severe anemia
  • *RBC transfusion improves O2 delivery*

• Critically ill patients more susceptible to adverse effects of oxygen depletion
  • impairs oxygen delivery to critical organs
  • cardiovascular system must compensate

• *RBC transfusion should improve outcomes*
**Oxygen Delivery (DO2)**

- DO2 = Hb X %SaO2 X CO

- Hb is normally fully saturated with O2

- Baseline extraction of O2 in resting tissue is 25%
Changes in cardiac output (A) oxygen extraction (B) oxygen delivery (C) and oxygen consumption (D) as hemoglobin decreases in humans and animals

Changes to maintain DO2

- Tissues increase extraction of O2
- Increase CO (HR, SV, decrease viscosity)
- Increase 2 3 DPG
Myocardial oxygen delivery

- Near maximal oxygen extraction at rest (65%)

- PaO2 coronary sinus 3KPa

- Local mechanisms attempt to increase coronary blood flow

- At risk: coronary stenosis, stiff left ventricle, tachycardia
Transfusion trigger

- Transfusion trigger is Hb/Hct at which the risks of decreased O2 carrying capacity exceed the risks of transfusion
Transfusion triggers in critical care

- Is a *restrictive* strategy better than a *liberal* strategy in surgical and critically ill patients?
TRICC Study: Transfusions in the ICU

- Multi-centre, prospective, randomized study
- > 24 h ICU stay expected
- Hb < 9.0 g/dL within 72 h
- Volume resuscitated or normovolaemic

- Restrictive: Maintain 7-9 g/dL (APACHE II: 20.8)
- Liberal: Maintain 10-12 g/dL (APACHE II: 21.3)
TRICC Study: Transfusions in the ICU

- MODS and cardiac complication rates significantly less with restrictive

- RBC transfusions reduced by 52%

- Reduced exposure to any RBCs by 33%
The TRICC Study

8.7% vs 16.1%

5.7% vs 13.0%

Herbert PC, et al. NEJM 1999
“A restrictive red blood cell transfusion strategy generally appears to be safe in most critically ill patients with cardiovascular disease... with the possible exception of patients with acute myocardial infarction and unstable angina.”
ABC Study-Transfusions in the ICU

- Prospective, observational study in 3534 patients in 176 western European ICUs
- 30% of patients with Hb <10 g/dL
- 37% percent of patients transfused in ICU
- If stay greater than 1 week 73% transfused
- Mean pre-transfusion Hb = 8.4 g/dL

- Transfused patients had higher mortality rates at every admitting Hb level when compared to non-transfused
- Dose-dependent relationship with number of units transfused and mortality
- 28 day mortality 22.7% in transfused versus 17.1 in non-transfused (p = 0.05)
CRIT Study

- Prospective, multi-center, observational cohort
- 4892 patients in 284 US ICUs
- 44% of patients transfused
- Mean pre-transfusion Hb was 8.6+/- 1.7 g/dL
- Number of RBC units transfused was an independent predictor of worse clinical outcome

CRIT Results

35% of Blood transfused in patients with Hb ≥ 9

The mean pre-transfusion Hb was 8.6 ± 1.7 g/dL

RBC transfusion was independently associated with higher mortality (OR 1.65 CI 1.35-2.03). OR 2.62 if 3-4 units transfused p < 0.0001
Blood transfusion and acute coronary syndrome

Figure 1. Kaplan-Meier Estimates of 30-Day Mortality Among Patients Who Did and Did Not Receive Blood Transfusion

Adjusted hazard ratio 3.94 (3.26-4.75)

Rao SV et al. JAMA. 2004;292:1555-1562
Early Goal-directed Therapy in sepsis

- Severe sepsis and septic shock patients (n=263)
  - SIRS and SBP < 90mm Hg or lactate > 4mmol/L
  - Prospective, randomized controlled trial
  - Goal-directed therapy vs. control (standard of care)
- **Goal-directed therapy** performed in ER prior to ICU
  - Placement of CVP line, CVP goal 8-12, $\text{ScVO}_2$ > 70%
  - Guidelines for vasopressor, dobutamine, blood tx
  - Maintained for at least 6 hours

Rivers E et al. NEJM 345(19) November 8, 2001:1368-77
Supplemental oxygen ± endotracheal intubation and mechanical ventilation

Central venous and arterial catheterization

Sedation, paralysis (if intubated), or both

CVP
- <8 mm Hg: Crystalloid
- 8–12 mm Hg: Crystalloid or Colloid

MAP
- <65 mm Hg: Vasoactive agents
- >90 mm Hg: Inotropic agents

ScvO₂
- <70%: Transfusion of red cells until hematocrit ≥30%
- ≥70%: Inotropic agents

Goals achieved

Hospital admission
Early Goal-directed Therapy in Severe Sepsis

- Early Goal-directed Therapy resulted in:
  - Reduced in-hospital mortality, 30.5% vs 46.5% (p=0.0009)
  - Higher ScVO$_2$, lower lactate, lower base deficit
  - Early goal-directed therapy provides significant benefits in outcome in patients with severe sepsis and septic shock.

Rivers E et al. NEJM 345(19) November 8, 2001:1368-77
<table>
<thead>
<tr>
<th>Category</th>
<th>Reference</th>
<th>Year</th>
<th>Clinical effect</th>
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<tbody>
<tr>
<td>Infection</td>
<td>Taylor et al[^9]</td>
<td>2002</td>
<td>Increased nosocomial infection</td>
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<td></td>
<td>Claridge et al[^9]</td>
<td>2002</td>
<td>Increased overall infection</td>
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<td></td>
<td>Hill et al[^9]</td>
<td>2003</td>
<td>Increased postoperative infection</td>
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<td></td>
<td>El-Masri et al[^12]</td>
<td>2005</td>
<td>Increased infection</td>
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<td></td>
<td>Banbury et al[^8]</td>
<td>2006</td>
<td>Increased bloodstream infection</td>
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<tr>
<td>Cardiac disease</td>
<td>Hebert et al[^19]</td>
<td>2001</td>
<td>Increased organ dysfunction</td>
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<td></td>
<td>Wu et al[^15]</td>
<td>2001</td>
<td>Decreased mortality</td>
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<td></td>
<td>Rao et al[^16]</td>
<td>2004</td>
<td>Increased mortality, myocardial infarction</td>
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<td></td>
<td>Yang et al[^17]</td>
<td>2005</td>
<td>Increased mortality, combined mortality/reinfarction</td>
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<td>Cardiac surgery</td>
<td>Engoren et al[^20]</td>
<td>2002</td>
<td>Increased mortality</td>
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<td>Koch et al[^20]</td>
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<td>Increased renal failure, ventilator dependence, infection, cardiac complications, neurological events</td>
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<td>Pulmonary</td>
<td>Schonhofer et al[^21]</td>
<td>1999</td>
<td>Successful weaning</td>
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<td></td>
<td>Hebert et al[^21]</td>
<td>2001</td>
<td>No difference in weaning</td>
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<td></td>
<td>Vamvakas and Carven[^22]</td>
<td>2002</td>
<td>Prolonged ventilation</td>
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<td></td>
<td>Croce et al[^23]</td>
<td>2005</td>
<td>Increased acute respiratory distress syndrome, death</td>
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<td></td>
<td>Gong et al[^23]</td>
<td>2005</td>
<td>Increased acute respiratory distress syndrome, death due to acute respiratory distress syndrome</td>
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<td>Trauma</td>
<td>Malone et al[^24]</td>
<td>2003</td>
<td>Increased mortality, length of stay</td>
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<td></td>
<td>Dunne et al[^24]</td>
<td>2004</td>
<td>Increased rates of systemic inflammatory response syndrome, death</td>
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<td></td>
<td>Robinson et al[^24]</td>
<td>2005</td>
<td>Increased mortality, length of stay</td>
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<td>Palmieri et al[^24]</td>
<td>2006</td>
<td>Increased infection, mortality</td>
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<tr>
<td></td>
<td>Dunne et al[^24]</td>
<td>2006</td>
<td>Increased infection, admission to intensive care unit</td>
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Efficacy of red blood cell transfusion in the critically ill: A systematic review of the literature*

Paul E. Marik, MD, FACCP, FCCM, FCCP; Howard L. Corwin, MD, FACCP, FCCM, FCCP

- Meta-analysis of observational studies
- 45 studies - 272,596 patients
- Multivariate analysis correcting for age and illness severity

Outcome measures:
- Mortality
- Infection
- Multi-organ dysfunction
- ARDS

Crit Care Med 2008;36(9):2667-74
Results

Association between blood transfusion and the risk of death (OR & 95% CI). Pooled OR 1.7 (95% CI 1.4-1.9)

Crit Care Med 2008;36(9):2667-74

Association between blood transfusion and the risk of infectious complications (OR & 95% CI). Pooled OR 1.8 (95% CI 1.5-2.2)
Results

Association between blood transfusion and the risk of ARDS (OR & 95% CI).

Pooled OR 2.5 (95% CI 1.6-3.3)

Crit Care Med 2008;36(9):2667-74
So what does this all mean?

- If Hb < 6-7 g/dL transfusion is usually necessary
- If Hb between 7 and 10 g/dl transfusion may not be necessary
- ? In MI, ACS, UA
- In septic shock if central venous O2 saturation < 70% (EGDT)
- Hb > 10 g/dL transfusion not indicated
• RBCs should be administered as single units for most operative and inpatient indications (transfuse and reassess strategy) except for ongoing blood loss with hemodynamic instability.

• Tx decisions are clinical judgments that should be based on the overall clinical assessment of the individual patient. Transfusion decisions should not be based on laboratory parameters alone.
Why is blood transfusion NOT associated with improved outcome?
Stored RBCs

- Decreased RBC deformability
- Decreased 2,3, DPG
- Metabolic acidosis
- Altered oxygen carrying capacity
- Increased red cell death with increased age of blood (~30% dead)
- No improvement in oxygen utilization at the tissue level
Age of Blood

Day 1

Day 21

Day 35

Scanning electron micrographs of red blood cells isolated from stored blood on Day 1, Day 21, and Day 35. During storage, the shape of RBCs changed gradually from normal discoid to echinocytes (dented or shriveled red cells). Reproduced with permission from: Hovav et al. *Transfusion*. 1999;39:277-281.
Poor Efficacy of Blood Tx

- RBCs stored > 15 days lose deformability and ATP
- Altered capillary lumen size (decreased cross-sectional diameter) in critically ill patients
- Increased “stickiness” (adherence) of RBCs to altered endothelium in the microcirculation of critically ill pts.
Duration of Red-Cell Storage and Complications after Cardiac Surgery

Colleen Gorman Koch, M.D., Liang Li, Ph.D., Daniel I. Sessler, M.D., Priscilla Figueroa, M.D., Gerald A. Hoeltge, M.D., Tomislav Mihaljevic, M.D., and Eugene H. Blackstone, M.D.

New Blood, Old Blood, or No Blood?

John W. Adamson, M.D.
Transfusion ditty

1, 2, 3, 4, 5, have some blood to stay alive
6, 7, 8, 9, 10, you may wish to think again.
   6 is for the fit and young
Those both sound in heart and lung.
   Older with a good heart rate?
   You may wish to stick at 8.
   Acute MI or frail, well then
   No one knows but some say 10.