Transfusions in Acute Care – Too Little?

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Low Transfusion Triggers

- Based primarily on the landmark TRICC study

**The New England Journal of Medicine**

A MULTICENTER, RANDOMIZED, CONTROLLED CLINICAL TRIAL OF TRANSFUSION REQUIREMENTS IN CRITICAL CARE

Paul C. Hebert, M.D., George Wells, Ph.D., Morris A. Blajchman, M.D., John Marshall, M.D., Claudio Martin, M.D., Giuseppe Pagliarello, M.D., Martin Tweeddale, M.D., Ph.D., Irwin Schweitzer, M.Sc., Elizabeth Yetisir, M.Sc., and the Transfusion Requirements in Critical Care Investigators for the Canadian Critical Care Trials Group*
TRICC Trial Design

- Euvolemic, non-bleeding patients with Hb $\leq 9.0$ g/dL within 72 hours of admission to ICU
- Randomized to
  - Restrictive strategy:
    - RBC if Hb < 7.0 g/dL, to maintain at 7.0 - 9.0 g/dL
  - Liberal strategy:
    - RBC if Hb < 10.0 g/dL, to maintain at 10.0 - 12.0 g/dL
TRICC Trial Conclusion

- In most critically ill patients, the red-cell transfusion trigger should be 70 g/L
  - With the possible exception of patients with active coronary ischemic syndromes
Assume That TRICC Findings are Fully Valid

- Ignore potentially important design limitations
  - Unblinded
  - Allowed for multiple transfusions in euvolemic patients
  - Used fixed transfusion triggers
    - Practice misalignment among:
      - Patients with mild disease randomized to liberal arm (unnecessarily exposed to risks of treatment)
      - Patients with severe disease randomized to restrictive arm (unnecessarily exposed to risks of anemia)

To Whom Do the Results Apply?
To Whom Do the Results Apply?

6451 Assessed

3206 Found eligible

3245 Excluded
- Chronic anemia (n=800)
- Active blood loss (n=786)
- Anticipated length of stay, <24 hr (n=818)
- Enrollment in other studies (n=423)
- Moribund (n=162)
- DNR order (n=133)
- Other reasons (n=123)

2039 Screened for consent

1167 Not screened
- Previous transfusion (n=297)
- Time limitations (n=256)
- No next of kin (n=174)
- Language barrier (n=36)
- Other reasons (n=404)

838 Consented

1201 Refused
- Physician refusal (n=598)
- Patient or family refusal (n=603)

420 Assigned to liberal transfusion strategy

418 Assigned to restrictive transfusion strategy
Who are The Other 90%?

- Not euvoletic
- Actively bleeding
- Chronic anemia
- Cardiac surgery
- Physician refusal
  - Those in whom Hb 70 g/L deemed unsafe?
  - “Other reasons”
What about The Other 90%?
What about The Other 90%?
What about The Other 90%?

- Does the ‘one-size-fits-all’ approach to anemia make sense?
- Can they all tolerate a Hb of 70 g/L?
Anemia Tolerance: One Size Does Not Fit All

- Normal Hb varies by gender, race, etc.

Anemia Tolerance: One Size Does Not Fit All

- Anemia’s prognostic value also varies by gender, race, etc.

Anemia Tolerance in CVS

Adjusted OR = 1.1 (0.8 – 1.6) P = 0.4

Karkouti et al. Transfusion 2008;48:666-672
Anemia Tolerance in CVS

Adjusted OR = 1.5 (1.1 – 2.1) P = 0.007

Karkouti et al. Transfusion 2008;48:666-672
ACS – Anemia and Mortality in STEMI

Sabatine et al. Circulation 2005; 111:2042
ACS – Anemia and Mortality in STEMI

RBC $\alpha$ ↓ Death if Hb < 12
OR 0.42 (0.20 – 0.89)

Sabatine et al. Circulation 2005; 111:2042
ACS – Anemia and Mortality in NSTEMI

### Unadjusted OR & 95% CI for CVD/MI/RI by 30 d

<table>
<thead>
<tr>
<th>Hgb (g/dl)</th>
<th>n</th>
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<td>&gt;17</td>
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RBC α ↑Death
OR 1.5 (1.1 – 2.1)

Sabatine et al. Circulation 2005; 111:2042
CVS – Intraoperative Anemia and AKI

Nadir Hct

Acute Renal Failure (%)

- <21%: N=75/2377
- 21-25%: N=37/4555
- >25%: N=22/2148

Anemia and Coagulopathy

Valeri et al. Transfusion 2001;41:977-83
Anemia and Coagulopathy

Valeri et al. Transfusion 2001;41:977-83
What about ‘The Other 90%?’

- Does the ‘one-size-fits-all’ approach to anemia make sense?
- Can they all tolerate a Hb of 70 g/L?
What about ‘The Other 90%?’

- Does the ‘one-size-fits-all’ approach to anemia make sense?
- Can they all tolerate a Hb of 70 g/L?

No
What about ‘The Other 90%?’

- Does the ‘one-size-fits-all’ approach to anemia make sense?
- Can they all tolerate a Hb of 70 g/L?
- When is 70 not 70?

No
When is 70 not 70?

- 0 to 10 day old blood
- 25 to 35 day old blood
- 1 hour PT
- 24 hours PT
- 0 to 10 day old blood
- 25 to 35 day old blood

Luten et al. Transfusion 2008;48:1478 - 1485
What then, should the transfusion trigger be?
What then, should the transfusion trigger be?

- Non-bleeding, euvolemic patient
- The only indication for RBC transfusion is to increase oxygen delivery to tissues in the setting of tissue hypoxemia*
  - Varies from patient to patient
  - Varies from organ to organ
  - Varies from setting to setting
  - Difficult to recognize
  - May occur at Hb > 70 g/L

*Consensus Conference. Perioperative red blood cell transfusion. JAMA 1988;260:2700
What then, should the transfusion trigger be?

- Bleeding patient
  - More complex?
    - Volume status: fluctuating and rarely euvoletic
    - Amount of blood lost
    - Expectations for ongoing blood loss
    - Number of red-cells transfused

- Or is it all very simple?
  - Trigger Hb 100 g/L as part of goal-directed therapy
  - E.g., Rivers et al. NEJM 2001; 345:1368-77
Transfusion Triggers: Current Algorithms

ASA Algorithm for RBC Transfusion

- Monitor for blood loss
- Monitor for inadequate perfusion and oxygenation of vital organs
- Monitor hemoglobin
  - Hb > 100 g/L → transfusion is usually unnecessary
  - Hb < 60 g/L → transfusion is usually necessary
  - Hb 60 – 100 g/L → transfusion depends on 1 and 2
What about other blood products?

ASA Algorithm for Cryoprecipitate

- Fibrinogen > 150 mg/dl  →  transfusion rarely indicated
- Fibrinogen < 80-100 mg/dl  →  transfusion usually indicated
Clotting factor levels and the risk of diffuse microvascular bleeding in the massively transfused patient

D. Ciavarella, R. L. Reed, R. B. Counts, L. Baron, E. Pavlin, D. M. Heimbach and C. J. Carrico

Summary. Clotting factor activities and coagulation screening tests in 36 massively transfused patients were measured after every 12 units of blood and whenever diffuse microvascular bleeding (MVB) developed. Moderate deficiencies in clotting factors were common, but they were not associated with MVB. MVB was associated with severe abnormalities of coagulation, i.e. a fibrinogen level <0·5 g/l or clotting factor levels <20%.

FFP or cryoprecipitate is recommended whenever the fibrinogen is less than 0·8 g/l
In order to establish the frequency and clinical complications of DIC during remission induction of untreated adults with acute lymphoblastic leukemia, we retrospectively reviewed the records of 125 consecutive patients treated with vincristine, doxorubicin, and dexamethasone but without L-asparaginase.

Two thromboses and four hemorrhages in six of the 16 patients with fibrinogen levels < 100 mg/dl but with only one hemorrhage among 23 patients (4%) with fibrinogen levels > 100 mg/dl ($P < 0.01$).
Conclusions

- Don’t consider established transfusion practice or guidelines as *established*
  - Likely based on limited, faulty, or inapplicable data

- The transfusion decision is, by necessity, complex
  - Cannot be based on simplistic ‘triggers’
Thank You