Anemia and ACS

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No conflicts or disclosures
Anemia in ACS

Prognosis: causality or association?
Simple decision to transfuse?
Liberal or restrictive strategy?
Symptoms or Hb concentration?
Benefit or harm with transfusion?
Planning trials - what endpoints?
Transfusions per year:
85 million units worldwide
15 million units in USA
Wasting Health-care Money

2009 - $210 billion wasted on unnecessary services

2012 - AMA and JCAHO “National Summit on Overuse”

1. Blood transfusions
2. Coronary stents
3. Ear tubes
4. Antibiotics
5. Induction of birth in pregnant women

http://www.amednews.com/article/20130812/opinion/1308199714/
(accessed March 29, 2016)
Transfusions in Adults

*Restrictive* rather than *liberal* strategy is preferred

Hb concentration <7 to 8 g/dL

Treatment of symptoms

Patients' wishes
Mayo Clinic
Blood Transfusion Standardization Project

Introduced restrictive guidelines in 2013

2 years later....

Transfusions, outside of published guidelines, had fallen from 40% to 25%

Cost savings of >$11 million
Are coronary heart disease patients at greater risk with anemia?
Baseline anemia in ACS causes ischemia

% with Holter ST shift in first 48 hours

INTERACT trial – Rousseau M: Am J Cardiol: 2010
Anemia and 30-Day Surgical Outcome
A “Natural History” Study in 1958 patients

Mortality
Morbidity/mortality

Pre-op Hemoglobin g/dL

Carson JL: Lancet 1996
Anemia and 30-Day Surgical Mortality
A “Natural History” Study

Carson JL: Lancet, 1996

Preoperative hemoglobin (g/dL)

Adjusted odds ratio

- Cardiovascular disease
- No Cardiovascular disease

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Major bleeding occurs in 2-10% of ACS Patients
Strong association between bleeding or anemia with mortality in ACS patients
Bleeding equivalent to having an MI
Observations from ACUITY

- Myocardial infarction
- Major bleeding
- Blood transfusion

Hazard ratio for mortality (95% CI)

Mehran R: EHJ, 2009
Any major bleed in first month is associated with higher mortality

MI (days)
- 0-1
- 2-7
- 8-30
- ≥31

Major bleed (days)
- 0-1
- 2-7
- 8-30
- ≥31

Transfusion (days)
- 0-1
- 2-7
- 8-30
- ≥31

Hazard ratio for mortality (95% CI)

Observations from ACUITY

Mehran R: EHJ, 2009
Anemia in ACS patients undergoing PCI
Mayo Clinic

Death

0,0 0,2 0,4 0,6 0,8 1,0

Moderate/severe
Hb <11 g/dL

Mild
Hb 11-12/13 g/dL

No anemia

P<0.001

No. at risk

<table>
<thead>
<tr>
<th>Time (years)</th>
<th>None</th>
<th>Mild anemia</th>
<th>Moderate-severe</th>
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<tbody>
<tr>
<td>0</td>
<td>3,762</td>
<td>1,041</td>
<td>706</td>
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<tr>
<td>1</td>
<td>2,747</td>
<td>740</td>
<td>429</td>
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<tr>
<td>2</td>
<td>2,347</td>
<td>608</td>
<td>336</td>
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<tr>
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<td>4</td>
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<td>361</td>
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<td>5</td>
<td>891</td>
<td>225</td>
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Al-Hijji M (under review): 2016
Why might bleeding lead to higher mortality?

Physiologic stress
Cessation of antiplatelet and anticoagulant therapy ± other guideline-directed therapy
Hypotension – remote ischemic organs
Unmask occult malignancy
Transfusion risk?
Risk by association – not causality
Transfusions and Higher Mortality in ACS
Data from GUSTO IIb, PURSUIT, PARAGON B

Rao SV: JAMA, 2004

P<0.001

Proportion cumulative mortality

Day
Risks of RBC Transfusions

- 1 in 100 million
- 1 in 10 million
- 1 in 1 million
- 1 in 100,000
- 1 in 10,000
- 1 in 1,000
- 1 in 100
- 1 in 10
- 1 in 1

- Firearm homicide
- Motor vehicle fatalities
- Airplane fatalities
- Lightning fatalities
- Death from medical error
- Fall fatalities
- TACO
- Fever
- Life-threatening reaction
- Fatal hemolysis
- TRALI
- HBV
- HCV
- HIV

## Guidelines for RBC Transfusion in ACS
Limited to Observational Data Only

<table>
<thead>
<tr>
<th>Organization</th>
<th>Recommendation</th>
<th>Grade</th>
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<tbody>
<tr>
<td>ACC/AHA</td>
<td>Routine transfusion if Hb &gt;8g/dL</td>
<td>III</td>
</tr>
<tr>
<td>ESC</td>
<td>Transfuse if hemodynamically unstable or Hb ≤7 g/dL or hematocrit &lt;25%</td>
<td>IIb</td>
</tr>
<tr>
<td>AABB</td>
<td>None</td>
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<th>Quality of evidence</th>
<th>Strength of rec.</th>
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<td>Pre-existing CV disease and stable</td>
<td>Moderate</td>
<td>Weak</td>
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<td><em>Restrictive strategy recommended</em></td>
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<td>Hb ≤8 g/dL or symptoms*</td>
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*Chest pain, orthostatic hypotension or tachycardia unresponsive to fluid, CHF
## AABB Guidelines: Evidence from RCTs

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<td>Hb ≤8 g/dL or symptoms*</td>
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<tr>
<td><strong>ACS and hemodynamically stable</strong></td>
<td>Very low</td>
<td>?</td>
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<tr>
<td><em>Unable to argue for or against a liberal or restrictive transfusion strategy</em></td>
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*Chest pain, orthostatic hypotension or tachycardia unresponsive to fluid, CHF

MINT Trial – Transfusion Strategy in ACS

Hypothesis:
Liberal versus a restrictive transfusion strategy will reduce the primary endpoint of all-cause death and recurrent MI through 30 days

Liberal transfusion
Recommend if Hb <10 g/dL

Restrictive transfusion
Permitted if Hb <8 g/dL
Recommend if Hb <7 g/dL

3500 ACS patients
Summary of anemia and bleeding in ACS

Relatively common with prognostic implications
By association or causal?
Quality of data to guide management is poor
Transfusions: a precious and expensive resource
Restrictive transfusion but with clinical judgement
Symptoms or Hb threshold?
Focus on identification of high risk patients and prevention of bleeding