What have we learned about Blood Transfusions?

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Disclosures

• No conflicts of interest related to this presentation.

• I have been a member of the Northern New England Cardiovascular Disease Study Group since 1996.

• The perfusion registry was started in 1995 by NNE perfusionists Gordon Defoe, Richard Forest, Craig Warren, Charlie Krumholz, Catherine Morse and John Perroni.

• With direction and support from Gerald T. Oconnor, Cathy Ross and Elaine Olmstead.
The Northern New England Cardiovascular Disease Study Group exists to develop and exchange information concerning the treatment of cardiovascular disease. It is a regional, voluntary, multi-disciplinary group of clinicians, hospital administrators, and health care research personnel who seek to improve continuously the quality, safety, effectiveness, and cost of medical interventions in cardiovascular disease.
Development and Validation of Registries

- **CABG/Valve registry**: est. July 1987 (N= 91,893)
- **PCI registry**: est. Jan. 1990 (N=131,551)
- **Cardiac anesthesia**: est. May 1996 (N= 38,362)
- **Perfusion**: est. June 1995 (N= 58,371)

*Case count and discharge status validated-May 2014*
*Long-term mortality outcomes: July 1987-June 2010*
## NNE Perfusion Registry

**Myocardial Protection**

**Prime Volume Management**

**Fluid Management**

**Temperature Management**

**Hemodilution Transfusion**

**Filtration**

**Glycemic Management**

**Cerebral Monitoring**

### NNECDSG PERFUSION REGISTRY

<table>
<thead>
<tr>
<th>Procedure Initiated:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type of surgery:</td>
</tr>
<tr>
<td>Indication:</td>
</tr>
<tr>
<td>Date of adm:</td>
</tr>
<tr>
<td>Date of surgery:</td>
</tr>
</tbody>
</table>

### Cardioplegia Methods

<table>
<thead>
<tr>
<th>Aortic cross clamp:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Indication doze:</td>
</tr>
<tr>
<td>Infusion time:</td>
</tr>
<tr>
<td>Proximal technique:</td>
</tr>
<tr>
<td><em>Hot shot</em> used:</td>
</tr>
</tbody>
</table>

### Fluid Volumes and Blood Products

<table>
<thead>
<tr>
<th>Blood product:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Estimated number of ml:</td>
</tr>
<tr>
<td>Volume of PRBC:</td>
</tr>
</tbody>
</table>

### Details of Perfusion

<table>
<thead>
<tr>
<th>Hematonic value:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lowest perfusion:</td>
</tr>
<tr>
<td>Highest perfusion:</td>
</tr>
<tr>
<td>Infusion rate:</td>
</tr>
</tbody>
</table>

### Use of Dose (mg/kg)

<table>
<thead>
<tr>
<th>Dose:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Typical dose:</td>
</tr>
<tr>
<td>Maximum dose:</td>
</tr>
</tbody>
</table>

### Use of Blood Products

<table>
<thead>
<tr>
<th>Blood product:</th>
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</thead>
<tbody>
<tr>
<td>Volume of PRBC:</td>
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</table>

### Cerebral Monitoring

<table>
<thead>
<tr>
<th>Monitoring:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Central monitoring:</td>
</tr>
</tbody>
</table>

(Definitions attached) Version 14.0

- Confidential for QA Purposes Only
Bethel Inn
1998
Lowest Hematocrit on Bypass and Adverse Outcomes Associated With Coronary Artery Bypass Grafting

Gordon R. DeFoe, CCP, Cathy S. Ross, MS, Elaine M. Olmstead, BS, Stephen D. Surgenor, MD, Mary P. Fillinger, MD, Robert C. Groom, CCP, Richard J. Forest, CCP, John W. Pieroni, CCP, Craig S. Warren, CCP, Mary E. Bogosian, RN, Charles F. Krumholz, CCP, Cantwell Clark, MD, Robert A. Cloough, MD, Paul W. Weldner, MD, Stephen J. Lahey, MD, Bruce J. Leavitt, MD, Charles A. S. Marrin, MB, BS, David C. Charlesworth, MD, Peter Marshall, MD, and Gerald T. O’Connor, PhD, for the Northern New England Cardiovascular Disease Study Group

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6,980 consecutive CABG patients at six medical centers.

(Ann Thorac Surg 2001;71:769–76)
The Risks of Anemia

### Lowest hematocrit on CPB and in-hospital outcomes

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Lowest Hct on CPB (%)</th>
<th>p value**</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt;19</td>
<td>19-20</td>
</tr>
<tr>
<td>N (Total = 6,980)</td>
<td>994</td>
<td>1,507</td>
</tr>
<tr>
<td>In-hospital mortality (%)</td>
<td>3.9</td>
<td>3.3</td>
</tr>
<tr>
<td>Intra- or post-op IABP (%)</td>
<td>6.1</td>
<td>5.8</td>
</tr>
<tr>
<td>Return to bypass pump (%)</td>
<td>7.5</td>
<td>5.4</td>
</tr>
<tr>
<td>Intra- or post-op stroke (%)</td>
<td>2.2</td>
<td>0.9</td>
</tr>
<tr>
<td>Return to O.R. for post-op bleeding (%)</td>
<td>3.4</td>
<td>2.5</td>
</tr>
</tbody>
</table>

* adjusted for: age, sex, BSA, comorbidity, prior CABG surgery, pre-op LVEDP, pre-op EF, left main stenosis and priority at surgery

** p of trend
Lowest Hematocrit on Bypass and Adverse Outcomes Associated with CABG

Defoe G, Ann Thorac Surg 2001;71;769

Conclusion: “Female Patients and patients with smaller Body surface area may be more hemodiluted than larger patients. Minimizing intraoperative anemia may result in improved outcomes for this patient subgroup.”
Transfusion and mortality by nadir Hct

Lowest Hct on CPB

- <=20: 2.3%
- 21-22: 1.3%
- 23-24: 1.4%
- >=25: 0.8%

Not transfused: 5.2%, Transfused: 6.5%
Preop HCT
(tranfused and non transfused)

The lower the preop HCT the worse the survival. Patients with HCT <36 have very poor short term mortality.
Preop HCT
(non transfused)

Survival by preop HCT – no RBCs

Again, the lower the preop HCT the worse the long term survival.
# Preoperative Anemia

**TABLE 1. Investigations examining effect of preoperative anemia on postoperative outcomes**

<table>
<thead>
<tr>
<th>Investigation</th>
<th>Design</th>
<th>n</th>
<th>Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zindrou et al&lt;sup&gt;6&lt;/sup&gt;</td>
<td>Observational</td>
<td>2059</td>
<td>Increased mortality</td>
</tr>
<tr>
<td>Hung et al&lt;sup&gt;3&lt;/sup&gt;</td>
<td>Observational</td>
<td>2688</td>
<td>Increased transfusion requirement, ICU stay, and mortality</td>
</tr>
<tr>
<td>van Straten et al&lt;sup&gt;5&lt;/sup&gt;</td>
<td>Observational</td>
<td>10,626</td>
<td>Increased mortality</td>
</tr>
<tr>
<td>Ranucci et al&lt;sup&gt;7&lt;/sup&gt;</td>
<td>Observational</td>
<td>3003</td>
<td>Prolonged ventilation, renal insufficiency, stroke, reoperations</td>
</tr>
<tr>
<td>Karkouti et al&lt;sup&gt;9&lt;/sup&gt;</td>
<td>Observational</td>
<td>3500</td>
<td>Increased in-hospital death, stroke, or acute kidney injury</td>
</tr>
<tr>
<td>Kulier et al&lt;sup&gt;4&lt;/sup&gt;</td>
<td>Observational</td>
<td>5065</td>
<td>Neurologic, renal, and GI complications</td>
</tr>
<tr>
<td>De Santo et al&lt;sup&gt;8&lt;/sup&gt;</td>
<td>Observational</td>
<td>1214</td>
<td>Postoperative renal insufficiency</td>
</tr>
<tr>
<td>Kazmierski et al&lt;sup&gt;10&lt;/sup&gt;</td>
<td>Observational</td>
<td>563</td>
<td>Postoperative delirium</td>
</tr>
</tbody>
</table>

*ICU*, Intensive care unit; *GI*, gastrointestinal.
RBC use increases in-hospital mortality for men and women even after risk adjustment
Long-term survival by gender and RBC transfusion

Unadjusted long-term survival is worse with blood for both.

HR = 1.81, CI = 1.68-1.95
log rank p value <0.001

HR = 1.45, CI = 1.29-1.63
log rank p value <0.001
KMs censored at 6 months

After 6 months, mortality decline is less among women than men.
Survival for men after RBCs continues to decline over time.
There is very little long-term survival disadvantage for women who get RBCs.
Among patients who survive to 6 months

For patients who live at least 6 months, there is continuing mortality risk for men and none for women.
Association of Gender and Lowest Hematocrit on Cardiopulmonary Bypass With Acute Kidney Injury and Operative Mortality in Patients Undergoing Cardiac Surgery

Rajendra H. Mehta, MD, MS, Serenella Castelvecchio, MD, Andrea Ballotta, MD, Alessandro Frigiola, MD, Eduardo Bossone, MD, and Marco Ranucci, MD
Duke Clinical Institute and Duke Medical Center, Durham, North Carolina; and IRCCS Policlínico San Donato, Milan, Italy

Background. Nadir hematocrit on cardiopulmonary bypass (CPB) is a known risk factor for worse outcomes after cardiac surgery. Whether women, because of lower nadir hematocrit on CPB, are more prone to worse outcomes than men after cardiac surgery remains unknown.

Methods. We evaluated 13,734 patients (31.3% women) undergoing cardiac surgery (6/1/2001 to 6/30/2011) to study the association of hematocrit on CPB and gender with postoperative acute kidney injury (AKI) stage 2-3 (increase in creatinine at least twice the baseline), and operative mortality.

Results. Women were older (68 ± 12 vs 65 ± 12 years, \( p < 0.001 \)), with more comorbidities. Baseline (37.4% ± 4.4% vs 39.8% ± 4.6\%, \( p < 0.001 \)) and nadir (24.5% ± 3.5% vs 27.4% ± 3.6\%, \( p < 0.001 \)) hematocrit were lower, whereas the hematocrit drop on CPB (baseline and nadir) was greater in women (12.9% ± 4.3% vs 12.4% ± 4.2\%, \( p < 0.001 \)). Observed AKI stage 2-3 and mortality rates were significantly higher in women than in men (5.8% vs 4.9\%, \( p = 0.025 \) and 4.3% vs 3.4\%, \( p = 0.009 \), respectively). While nadir hematocrit was inversely related to AKI stage 2-3 and death in both genders, the subgroup of patients with severe hemodilution (nadir hematocrit ≤ 22\%) demonstrated a nonsignificant higher rate of AKI stage 2-3 in men (9.2%) vs 7.8\%) and a significant higher mortality in men (11% vs 7.6\%) compared with women.

Conclusions. Both men and women undergoing cardiac surgery on CPB were prone to the deleterious effects of hemodilution on renal functions and death. Yet, despite greater hemodilution, women had a lower relative risk of AKI and death than men at lower nadir hematocrit values on CPB suggesting better tolerance to hemodilution in women.


Women have been shown to have a higher risk for acute kidney injury (AKI) and operative mortality after cardiac surgery [1–4]. Additionally, the nadir hematocrit (HCT) on cardiopulmonary bypass (CPB) is a known risk factor for AKI and operative mortality in patients undergoing cardiac surgery [5–7]. Women also have lower preoperative values of HCT, and due to their lower body surface area are more prone to severe hemodilution on CPB during cardiac surgery [5–7]. Given the relationship between nadir HCT on CPB with the risk of AKI and death, and the greater likelihood of hemodilution on CPB in women undergoing cardiac surgery, one could hypothesize that the risk of AKI and mortality may be higher in women because of lower values of nadir HCT on CPB in women compared with men. However, the relationship between gender and lowest HCT on CPB with AKI and mortality has not been previously studied.

The present study was designed to assess if the association of hemodilution (nadir HCT) on CPB with AKI and mortality differed between women and men undergoing cardiac surgery.

Material and Methods

Study Design

This was an observational, retrospective, single-center study. The local ethics committee (ASL Milano 2, Melegnano, Italy) approved the experimental design and waived the need for an informed consent of the patients who, however, consented to the use of their data for scientific purposes at the time of hospital admission.

Patient Population

We evaluated data on consecutive patients age 18 years or greater undergoing on-pump cardiac surgery at IRCCS Policlínico San Donato, Milan, Italy between June 1, 2001 and June 30, 2011. We excluded patients requiring surgery for congenital heart disease, or undergoing off-pump procedure, and patients on chronic dialysis.
Information Drives Change
Rates of transfused RBCs have declined by half since 2001
Several centers reduced RBC transfusions; others did not.
Very little change over time
Minimizing Use of transfused RBCs

Elective + urgent patients receiving transfused RBCs
(last 150 cases for each center)

Center

PRH  CMMC  DHMC  FAHC  MMC  CMC  EMMC  CH  All

No RBCs  72  80  78  61  88  87  88  50  75
1 unit   8  6  5  11  8  6  5  8  7
2 units  6  6  5  15  4  6  4  18  18
>=3 units 4  8  6  14  2  6  5  8  7

CONFIDENTIAL INFORMATION – FOR QUALITY ASSURANCE USE ONLY  Data through June 2013
Minimizing Use of transfused RBCs

Use of transfused RBC’s by sex

Elective and urgent patients among last 150 isolated CABG cases

CONFIDENTIAL INFORMATION – FOR QUALITY ASSURANCE USE ONLY  Data through June 2013
Intraop RBC use among elective & urgent MEN

Intraop RBC use among elective & urgent WOMEN
Minimizing Use of transfused RBCs
Timing of Transfusion- isolated CABG

When are transfused RBCs given (elective & urgent patients)?
(last 150 cases for each center)
Women are more likely to receive blood intraoperatively while men more often get blood postoperatively.
Anemia
Where do we go from here?

Anemia FOR DUMMIES®
Get the advice you need to keep you and your body healthy

“A thorough, accurate, and highly informative guide.” — Los Angeles Times
Summary

- Anemia is bad
- Transfusion is worse
- Sex is very interesting
  - Girls are different than boys
- It takes a village
- Much to learn
Atul Gwande
“Become a Positive Deviant.”

1. Ask Questions
2. Don’t complain- have dialog about interesting problems
3. Count Something
4. Write Something
5. Change

Better- Gwande Metropolitan Books
Three Hypothetical Scenarios:
Small Circuit + RAP + Fluid Restriction

- Customized circuit (prime = 1000cc) + RAP + fluid restriction (approx. 600cc)
- Customized circuit (prime = 1000 cc) + RAP
- Old circuit (prime = 1300 cc)

Assume pre-op Hct = 35
Blood volume = 65ml X body wt in Kg

Kg Body Weight

Estimated Hct On Bypass

Graph showing estimated Hct on bypass with body weight in kg.