

Duration of Red-Cell Storage and Complications after Cardiac Surgery

NEJM, 2008; 358; 1229-1239.

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Background

The transfusion of red cells is common and widespread but the very act of transfusion may carry risks including death.

Researchers have been trying to figure out if part of the risk of blood transfusion is related to the age of the blood that is transfused. In this country, the FDA allows for storage of packed red cells for up to 42 days. Red cells undergo physical and chemical changes as they age.

Hypothesis

The transfusion of packed red cells over 2 weeks old after cardiac surgery carries a higher risk of serious complication and death than with red cells less than 2 weeks old.

Study Design

Study type: single center, retrospective analysis

Setting: Cleveland Clinic

Time period: 6/1998 – 1/2006

Inclusion Criteria:

Adults older than 18 years who underwent CABG, valve surgery, or both.

Those patients who received exclusively blood that had been stored for 14 days or less.

Those patients who received exclusively blood that had been stored for greater than 14 days.

Exclusion Criteria:

Those patients who received blood that was both newer and older than 14 days.

Randomization: none

N = 6002, were split into two groups

Received newer blood (N=2872): 8,802 total units.

Received older blood (N=3130): 10,782 total units.

Patient characteristics: See table 1. Median age was 70 for both groups of predominantly “white” patients. Patients getting newer blood received mostly type O blood while patients getting older blood received mostly type A blood. The median day of storage for newer blood was 11 while for older blood it was 20.

Outcomes: Two sets:

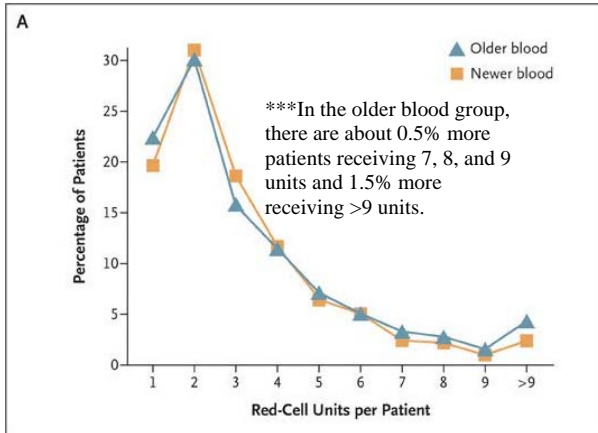
- First was a specific list of complications that entered into the adult cardiac surgery database as defined by the Society of Thoracic Surgeons, see table 2. Newer blood demonstrated fewer complications across the board.
- Second was long term survival after transfusion. Mortality was less at one year for those receiving newer blood, 7.4% vs. 11.0% (P<0.001).

The evidence

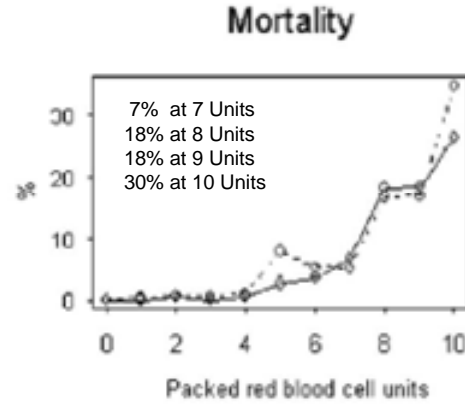
Adverse outcome	Patients receiving newer blood (N=2872)	Patients receiving older blood (N=3130)	P Value
In-hospital death	49 (1.7%)	88 (2.8%)	0.004
Composite Outcome	642 (22.4%)	810 (25.9%)	0.001
Death at one year	594 (7.4 %)	1101 (11.0%)	<0.001

Confounders:

- When you use means, the newer blood group received ~3 units/person while older blood group received 3.4 units/person. In general, there is a higher risk of mortality in just the number of units blood transfused. The study did not adjust for this important factor.



Koch CG, Liang L, Sessler DI, et al. Duration of red-cell storage and complications after cardiac surgery. *N Engl J Med* 2008; 358:1229-1239.



Koch CG, Duncan AI, Mihaljevic T, et al. Morbidity and mortality risk associated with red blood cell and blood component transfusion in isolated coronary artery bypass grafting. *Crit Care Med* 2006; 34:1608-1616. *Courtesy of Dr. Hess.*

- Were some surgical cases more complicated than others?
- Blood appears to be matched less often in the older blood group

Selection Bias:

- What happened to the patient who received 0 units of PRBCs?
- What about the ones who got mixed of old and new blood?

Measurement Bias:

By dichotomizing transfusion into simply older blood and newer blood, you lose information. Keeping this variable continuous (as a scale of 0-42 days) would have yielded more information.

Conclusion:

- The study asserts that transfusing red cells older than 2 weeks in this surgical population confers increased risk of post-op complication and worsened short/long-term mortality
- We argue that there are too many confounders/bias data (especially with the more numbers of PRBCs transfused in older group) toward fore-mentioned conclusion without appropriate statistical adjustment to correct for them.
- This is not a treatment study, rather epidemiological associations

Final Comment

- EBM is only helpful if we understand the evidence which may hinge on "outside" knowledge.