Transfusion in beating heart organ donors

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Outline

Evidence for transfusion thresholds

- Focus on risk for organ dysfunction/ischemic events

Beating heart organ donor population

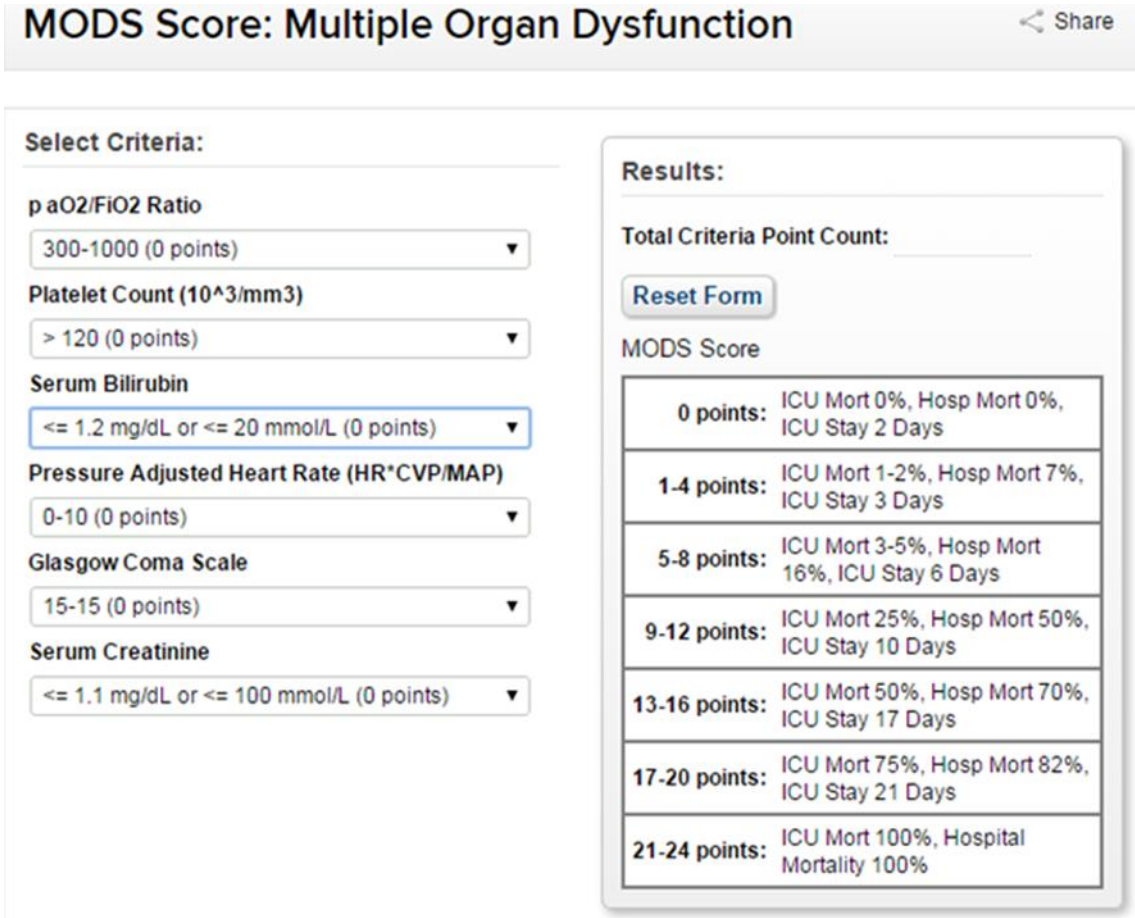
Transfusion practices in beating heart organ donors

Evidence for transfusion thresholds

RBC transfusion thresholds

Transfusion requirements in critical care (TRICC trial)

- 838 adults admitted to the ICU
- 7 g/dL vs 10 g/dL
- Lower in-hospital mortality rate in the restrictive strategy group, with trend toward lower 30-day mortality with restrictive strategy
- The multiple organ dysfunction score was significantly lower (p=0.03) in the restrictive strategy group



NEJM. 1999;340(6).
http://reference.medscape.com/calculator/mods-score-multiple-organ-dysfunction

RBC transfusion thresholds

Transfusion strategies for patients in pediatric intensive care units

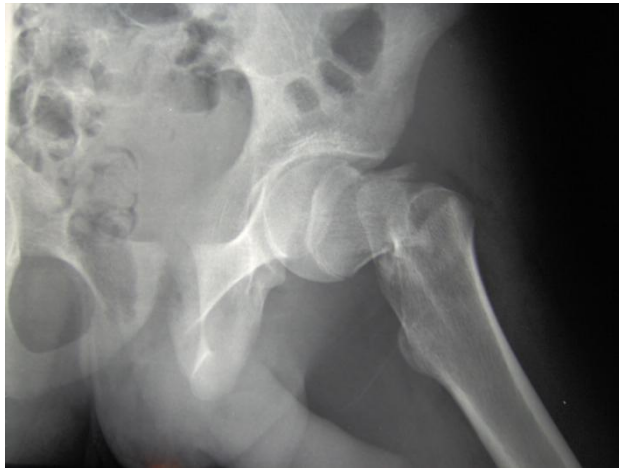
- 637 pediatric ICU patients
- 7 g/dL vs. 9.5 g/dL
- No significant difference between the two groups in mortality, serious adverse events, length of hospital stay
- No significant difference between groups in organ dysfunction (PELOD-2)

NEJM. 2007;356(16).

Evidence for RBC transfusion thresholds

Transfusion trigger trial for functional outcomes in cardiovascular patients undergoing surgical hip fracture repair (FOCUS trial)

- 2016 adults with cardiovascular disease and hip fracture surgery
- Excluded active bleeding, cancer, or acute MI within past 30 days
- 8 g/dL vs 10 g/dL
- No significant difference between groups in rates of in-hospital acute myocardial infarction, unstable angina, serious adverse events, or death



NEJM. 2011;365(26).

Evidence for RBC transfusion thresholds

Transfusion strategies for acute upper gastrointestinal bleeding

- 889 adults with acute upper GI bleed
- Excluded patients who were exsanguinating/massive transfusions
- 7 g/dL vs 9 g/dL
- 45-day mortality, rate of re-bleeding, overall rate of complications, and length of stay were all significantly less in the restrictive group

Table 3. Study Outcomes.*

Outcome	Restrictive Strategy (N=444)	Liberal Strategy (N=445)	Hazard Ratio with Restrictive Strategy (95% CI)	P Value
Death from any cause within 45 days — no. (%)	23 (5)	41 (9)	0.55 (0.33–0.92)	0.02
Adverse events — no. (%)†				
Any‡	179 (40)	214 (48)	0.73 (0.56–0.95)	0.02
Transfusion reactions	14 (3)	38 (9)	0.35 (0.19–0.65)	0.001
Fever	12 (3)	16 (4)	0.74 (0.35–1.59)	0.56
Transfusion-associated circulatory overload	2 (<1)	16 (4)	0.06 (0.01–0.45)	0.001
Allergic reactions	1 (<1)	6 (1)	0.16 (0.02–1.37)	0.12
Cardiac complications§	49 (11)	70 (16)	0.64 (0.43–0.97)	0.04
Acute coronary syndrome¶	8 (2)	13 (3)	0.61 (0.25–0.49)	0.27
Pulmonary edema	12 (3)	21 (5)	0.56 (0.27–1.12)	0.07
Pulmonary complications	48 (11)	53 (12)	0.89 (0.59–1.36)	0.67
Acute kidney injury	78 (18)	97 (22)	0.78 (0.56–1.08)	0.13
Stroke or transient ischemic attack	3 (1)	6 (1)	0.49 (0.12–2.01)	0.33
Bacterial infections	119 (27)	135 (30)	0.87 (0.63–1.21)	0.41

NEJM. 2013;368(1).

Evidence for RBC transfusion thresholds

Transfusion requirements in septic shock (TRISS trial)

- 1005 adults with septic shock
- Excluded patients with acute MI or life-threatening bleeding
- 7 g/dL vs 9 g/dL
- No difference in mortality, rate of ischemic events, or use of life support between the two groups

NEJM. 2014;371(15).

RBC transfusion thresholds

Liberal or restrictive transfusion after cardiac surgery

- 2003 nonemergent cardiac surgery patients
- 7.5 g/dL vs 9.0 g/dL
- All-cause mortality at 90 days was higher in the restrictive group (4.2% vs 2.6%, p=0.045)
- No statistically significant difference between groups in ischemic events, including myocardial infarction and acute kidney injury

NEJM. 2015;372(11).

Platelet transfusion thresholds

Clinical Setting 3: Adult Patients Having Major Elective Nonneuraxial Surgery

Recommendations

Recommendation 4: The AABB suggests prophylactic platelet transfusion for patients having major elective nonneuraxial surgery with a platelet count less than 50×10^9 cells/L.

Ann Int Med. 2015;162(3).

Plasma transfusion thresholds

Table 1
Fresh Frozen Plasma Transfusion Guidelines

Author	Year	Laboratory Criteria	Dose (mL/kg)
National Institutes of Health[1]	1985	None given	None given
Hong Kong Government Blood Banking Advisory Committee[2]	1990	PT/INR >1.5 times normal	10-15
British Committee for Standards in Haematology[3]	1992	PT/PTT >1.5 times normal; PT >1.8 times normal with liver disease	12-15
Committee Report[4]	1994	PT/PTT >1.5 times normal	15
College of American Pathologists[5]	1994	PT >1.5 times midpoint of normal; PTT >1.5 times upper normal; factor level <25%	2 U (6-7 mL/kg)
American Society of Anesthesiologists[6]	1994	PT/INR >1.5 times normal; factor level <30%	10-15
American College of Obstetrics and Gynecology[7]	1994	PT/PTT >1.5 times normal	2 U (6-7 mL/kg)
Canadian Medical Association Expert Working Group[8]	1997	Significantly increased coagulation time; PT >2.0 with liver disease	10-15
Japanese Ministry of Health and Welfare[9]	1999	PT/PTT >1.5 times normal; factor level <30%	8-12
North Ireland Clinical Resources Efficiency Support Team[10]	2001	PT/PTT >1.5 times normal	12-15
Australia National Health and Medical Research Council[11]	2001	Abnormal coagulation	5-20
American Red Cross[12]	2002	PT/PTT >1.5 times normal	None given
South African National Blood Service[13]	2003	Disturbed coagulation	15-20
British Committee for Standards in Haematology[14]	2004	Multiple factor deficiencies	10-15
New York State Council on Human Blood and Transfusion Services[15]	2004	PT/PTT >1.5 times normal	10-20

INR, international normalized ratio; PT, prothrombin time; PTT, partial thromboplastin time.

$INR=(\text{patient PT}/\text{mean normal PT})^{ISI}$

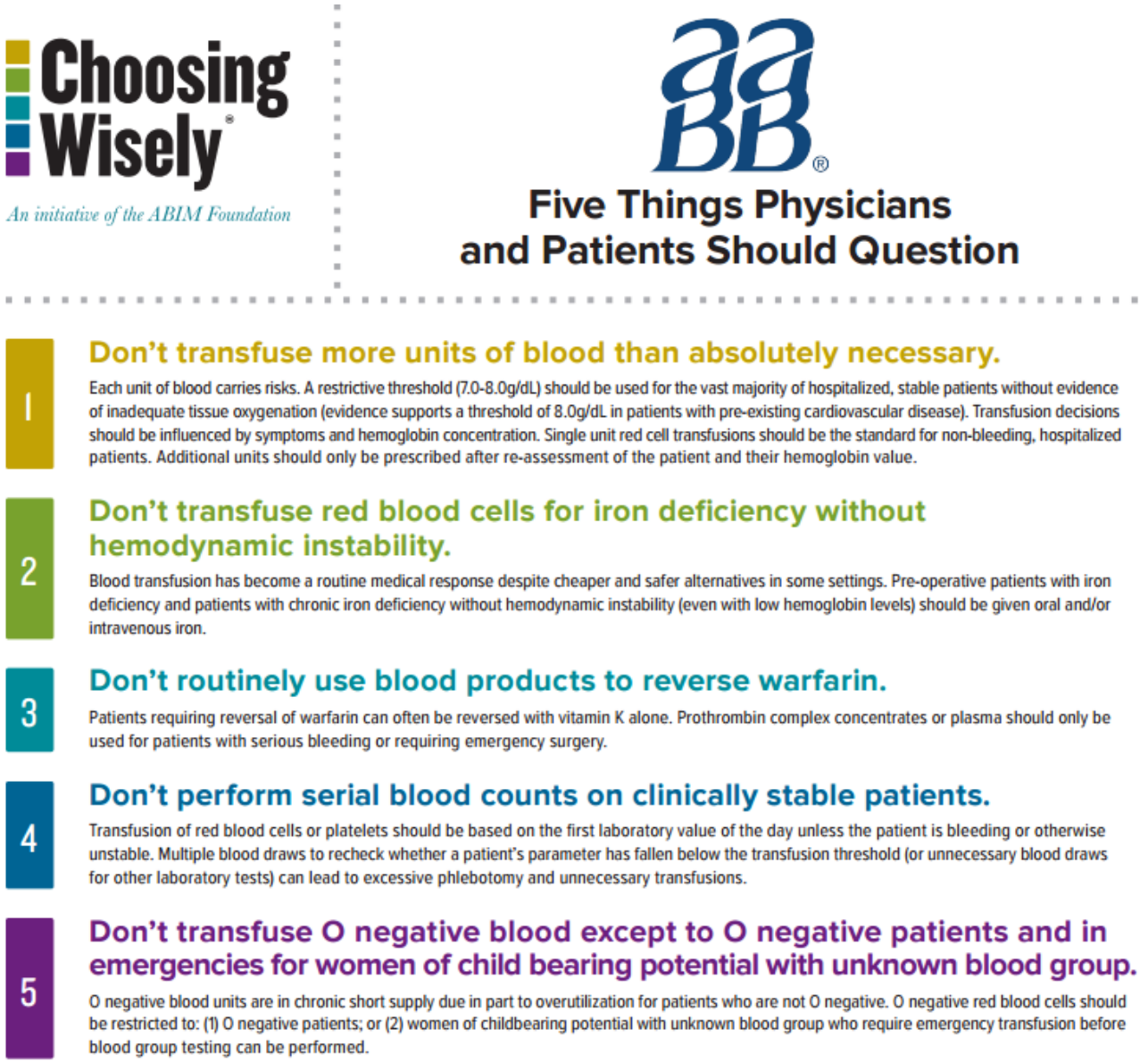
Am J Clin Pathol 2006;126(1).

Cryoprecipitate transfusion thresholds

Primarily used to treat fibrinogen deficiency, recommended when fibrinogen is less than 100 mg/dL

Overuse

The Joint Commission and American Medical Association have identified blood transfusion as one of the top 5 overused medical treatments



Proceedings from the National Summit on Overuse. 2012. http://www.choosingwisely.org/doctor-patient-lists/american-association-of-blood-banks

Beating heart organ donors

Beating heart organ donors

Organ donation after brain stem death, but prior to death by cardiorespiratory criteria

Allows for organs to be harvested under optimal conditions for organ viability

Common source of transplant organs in Western countries, consent to procure organs and tissue is granted by families in more than 70% of cases when requested

Organ harvesting generally occurs as soon as possible after declaration of brain death, usually within 1-2 days

The purpose of transfusion in beating heart organ donors is to maintain organ viability

Following diagnosis of brain stem death, section 43 of the Human Tissue Act 2004 allows *interventions to optimize organ quality prior to donation, but only for the least invasive and minimum steps necessary*.

Surgery. 2014;32(7).
Crit Care Clin. 2014;30(4).

Beating heart organ donors

The Uniform Anatomic Gift Act of 1968 grants individuals 18 years and older the power to donate their organs and tissue

The National Organ Transplant Act of 1984 developed a national organ transplant system (Organ Procurement and Transplantation Network--OPTN)

In 1986 the United Network for Organ Sharing (UNOS), a private nonprofit organization, was awarded a contract to operate the OPTN

UNOS Data Collection

http://www.unos.org/donation/index.php?topic=data_collection#dcf

UNOS Data Collection

Number of transfusions during this (terminal) hospitalization: *

- NONE
- 1 - 5
- 6 - 10
- GREATER THAN 10
- UNKNOWN

Initial hypotheses

Evidence for transfusion thresholds equally applies to beating heart organ donors

Blood product overuse occurs with beating heart organ donors, as it does in living patients

Transfusion reactions are under-reported in beating heart organ donors

Methods

IRB approved retrospective analysis of all beating heart organ donors between January 1, 2004 and October 1, 2014

At the time brain death is declared, the first name of all beating heart organ donors is changed to “Donor” in the electronic medical record

A search of patients with first name “Donor” revealed a total of 439 patients during this time period

No exclusions

Data Collection

For each donor

- Peak, trough, initial, and final hemoglobin
- Peak, trough, initial and final platelet count
- Peak, trough, initial and final PT/INR
- Fibrinogen level
- Total number of PRBC, platelet, plasma, and cryoprecipitate transfusions
  - When pooled platelet products of 5-6 were transfused, they were tabulated as a single unit.
- Reported transfusion reactions

Statistical analysis

All data was collected by one physician for consistency

Validation through random review of 10% of the sample by a second independent physician

Statistical analysis was performed with GraphPad (La Jolla, California)

- Unpaired Student's t-test and chi square test
- $p < 0.05$ was considered statistically significant

Results

Packed red blood cells

304 donors (69.2%) were transfused a total of 894 units of packed red blood cells

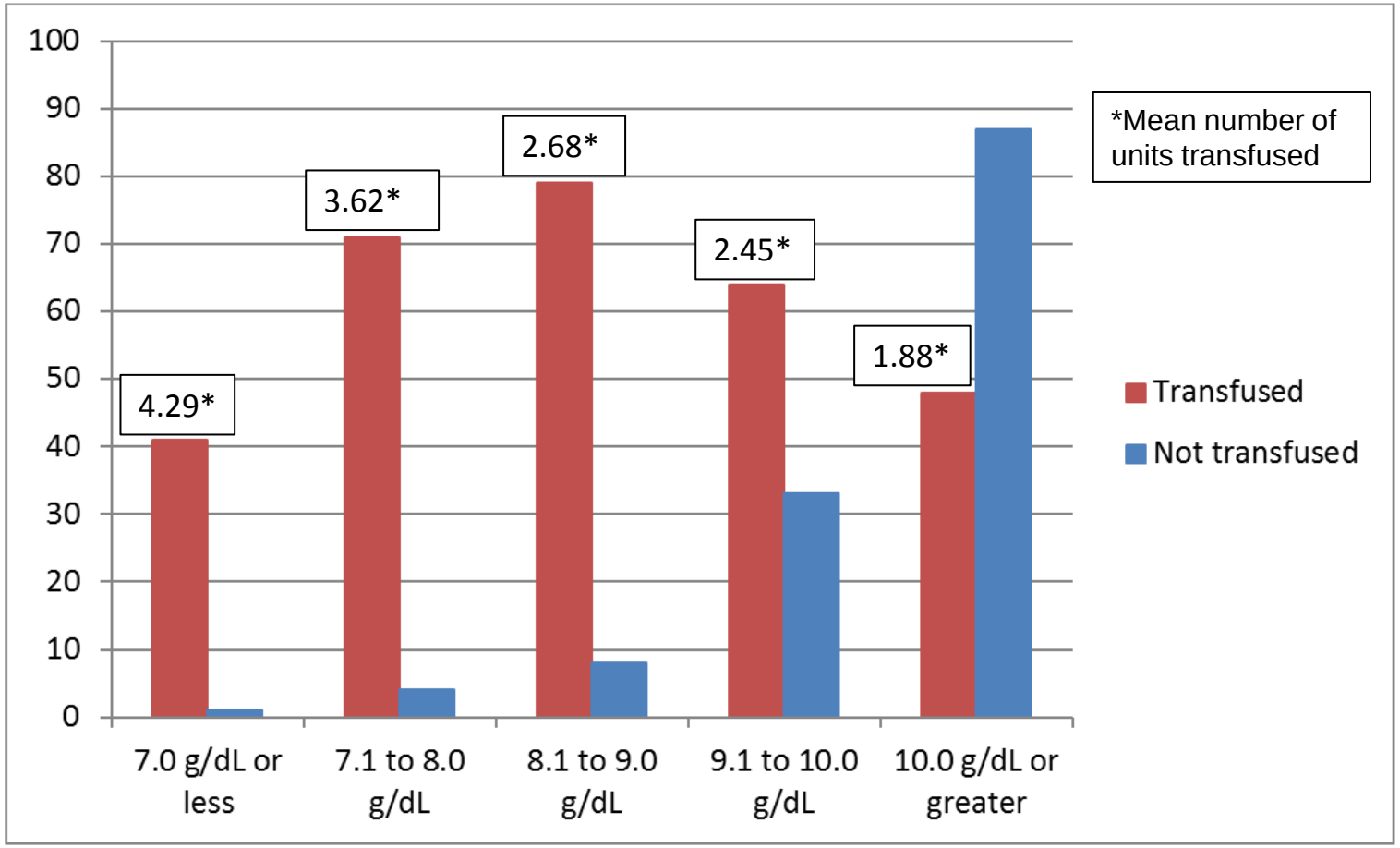
- Average number of units transfused was 2.94 (range 1 to 15 units).
- The hemoglobin level was measured only once for 47 donors (15.5%) and one patient had no hemoglobin measurement

Of the donors who did not receive PRBC transfusion, 114 (88.9%) had a trough hemoglobin level greater than 9.0 g/dL.

PRBC transfusion

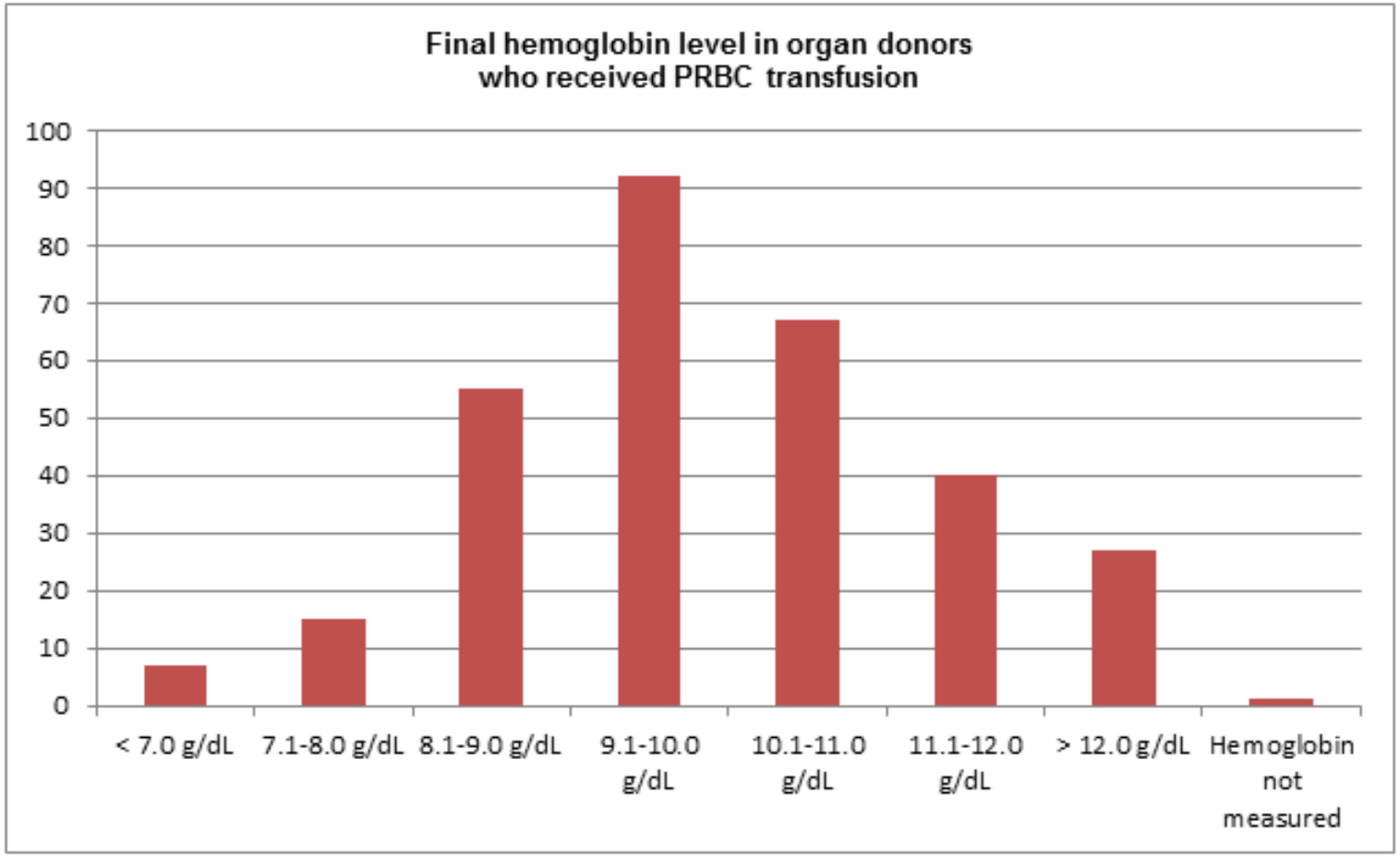
Trough hemoglobin was greater than 8 g/dL in 63.2% of donors who were transfused

48 donors (15.8%) were transfused when trough hemoglobin was greater than 10 g/dL



PRBC Transfusion

134 donors (44.1%) who were transfused had a final hemoglobin value of greater than 10 g/dL



Subgroup analysis:
Indication for RBC transfusion (1/1/13-10/1/14)

INDICATION FOR TRANSFUSION	**ORDERS**
Organ donor/donor management	60 (44.8%)
Active bleeding (or hemolysis) or anticipated bleeding (ex. surgery or procedure)	30 (22.4%)
Symptomatic anemia	22 (16.4%)
Acute blood loss with hemodynamic instability	8 (6.0%)
Low H/H	7 (5.2%)
Pre-op transfusion for anticipated blood loss	5 (3.7%)
Severe hemolytic anemia	1 (0.7%)
GSW	1 (0.7%)
TOTAL	**134 RBC orders** **73 unique donors**

Platelet transfusion

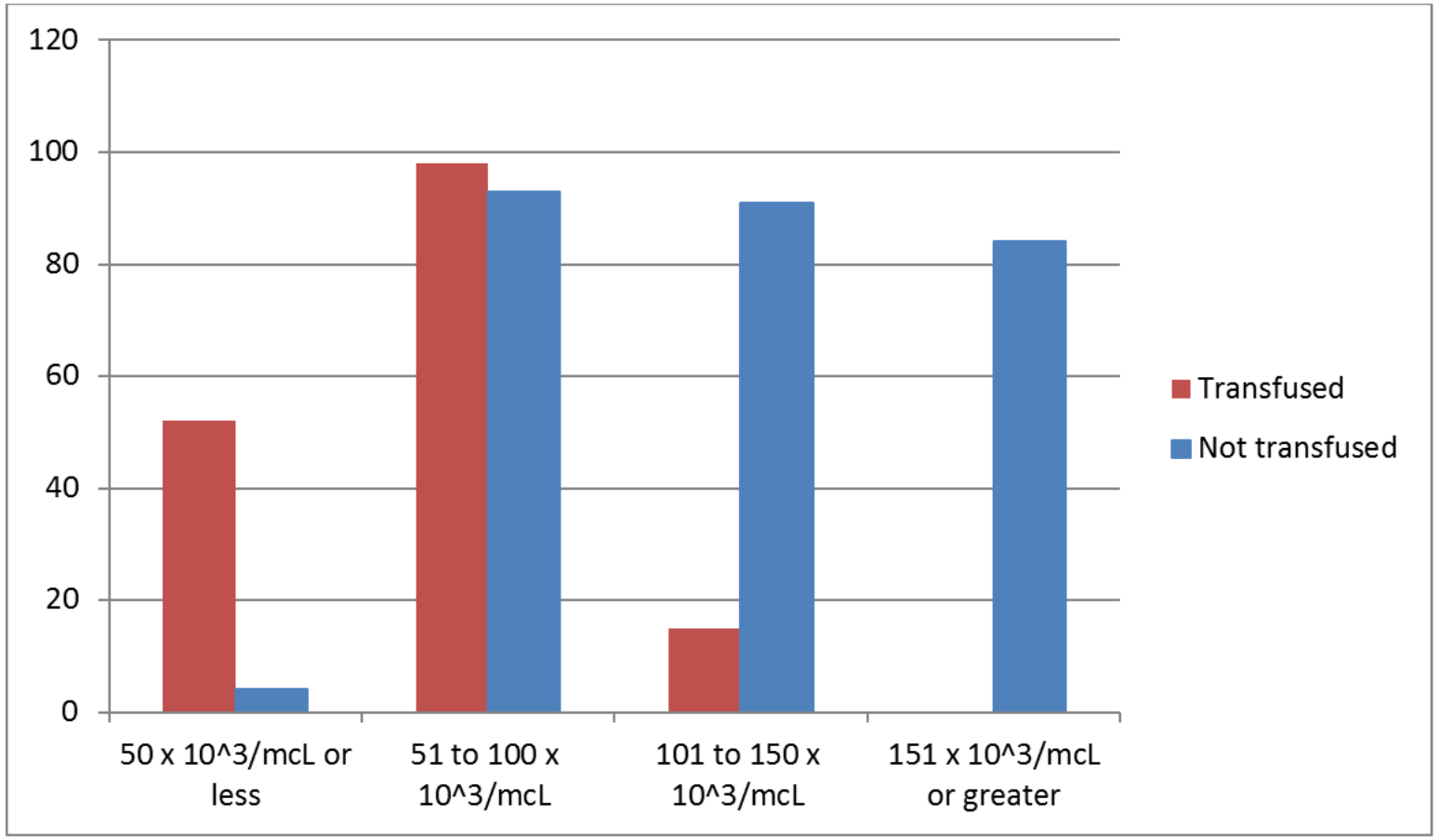
165 donors (37.6%) received a total of 316 platelet units, with an average of 1.91 units per donor (range 1-10 units)

Platelet transfusion

15 donors (9.1%) had a trough platelet count of greater than 100 x 10^3/mcL

197 (62%) platelet transfusions occurred in donors with a trough platelet count greater than 50 x 10^3/mcL

Of the donors who had a trough platelet count between 51 x 10^3/mcL and 100 x 10^3/mcL, 98 received platelet transfusion and 91 did not



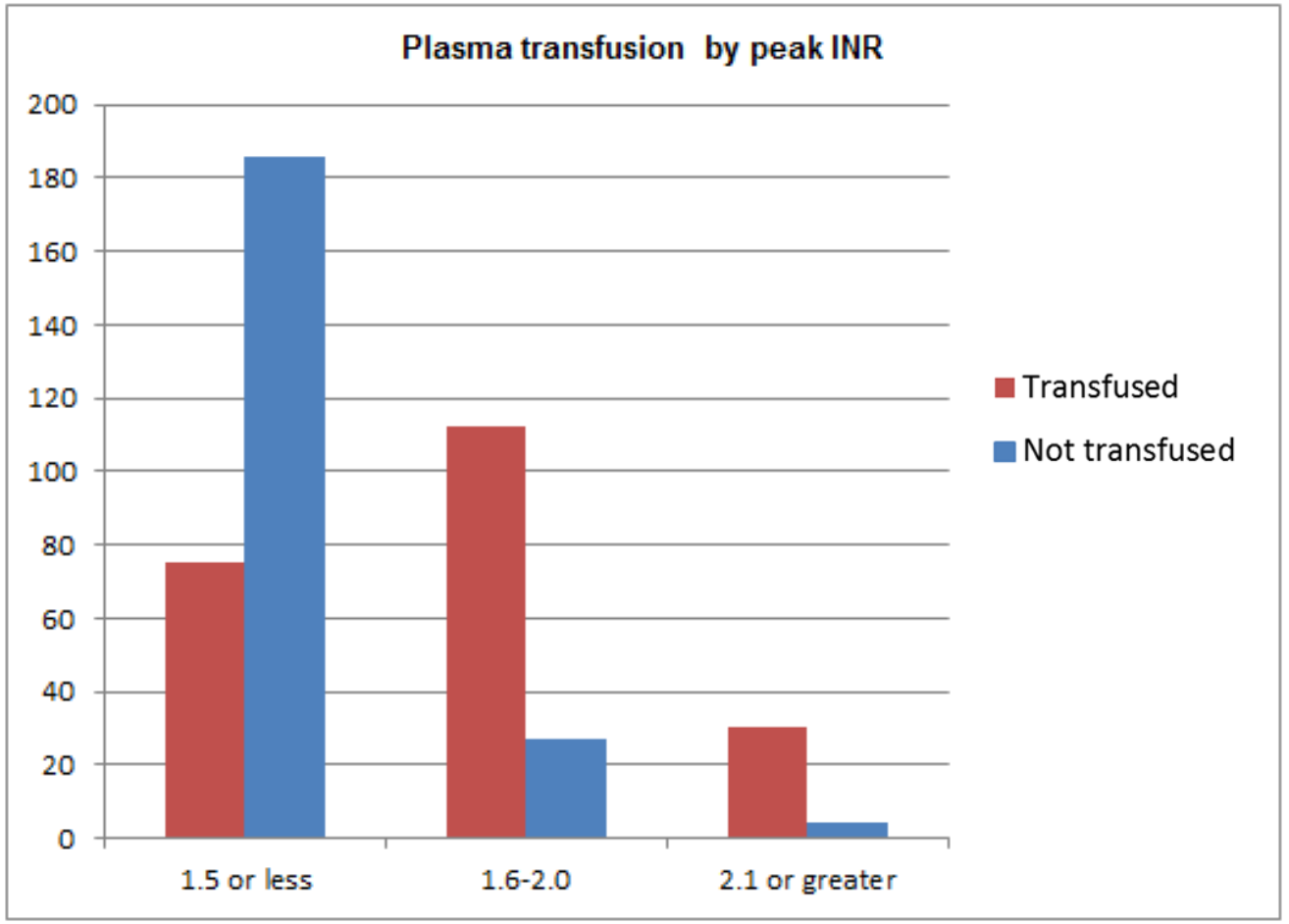
Plasma transfusion

217 donors (49.4%) received a total of 845 units of plasma, with an average of 3.89 units per donor (range 1-17 units)

Plasma transfusion

75 donors who received plasma transfusion (34.6%) had a peak INR of less than 1.5 and 112 (51.6%) had a peak INR of 1.6 to 2.0.

688 (81%) plasma units were transfused to donors with peak INR less than 2.0



Cryoprecipitate

A total of 23 patients (5.2%) received cryoprecipitate transfusion

- 19 (82.6%) did not have any fibrinogen levels
- Of the 4 patients that did have fibrinogen levels, the lowest level was 239 mg/dL

Transfusion reactions

Three potential transfusion reactions were reported to the transfusion service out of a total 2055 PRBC, platelet, and plasma units transfused (0.15%)

- 2 mild allergic reactions
- 1 reaction related to the donor's underlying medical condition

Mild allergic transfusion reactions are reported to occur in at least 1% of blood product transfusions

Allergic transfusion reactions were reported significantly less often than expected (p=0.0001)…why?

- Beating heart organ donors can't report symptoms?
- Vital sign fluctuations in beating heart organ donors make transfusion reactions more difficult to detect?
- The immune system of beating heart organ donors is altered such that certain types of transfusion reactions are less likely to occur?

Conclusions

Conclusions

Many large studies in various patient populations support restrictive transfusion strategies, which show equivalent or superior outcomes in organ dysfunction and ischemic events when compared to liberal transfusion strategies

While the optimal transfusion thresholds for beating heart organ donors are currently unknown, our study found that this population was transfused PRBCs, platelets, plasma and cryoprecipitate beyond the current best practice transfusion guidelines for other populations

- Highlights potential suboptimal use of limited biologic resource
- Potential for harm to donor organs
- Use beyond “minimum necessary”—ethical implications?

Transfusion reactions were underreported in this population

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