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Ten Year Retrospective Review of Transfusion Practices in Beating Heart Organ Donors

Running Title: Transfusion in beating heart organ donors

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Abstract

BACKGROUND: Recent studies suggest that restrictive transfusion strategies are equivocal or non-inferior to liberal strategies in various patient populations, however evidence for the optimal transfusion threshold or current transfusion practice in beating heart organ donors (BHODs) is lacking. A 10-year retrospective analysis of blood product utilization in BHODs was performed to determine current transfusion practice. **STUDY DESIGN AND METHODS:** An IRB-approved retrospective review of 439 BHODs from January 1, 2004 to October 1, 2014 was performed. For each donor, hemoglobin, platelet, PT/INR, and fibrinogen levels as well as all transfusion reaction reports were recorded from the time of declaration of brain death to organ procurement. **RESULTS:** Packed red blood cell transfusion occurred in 304 donors (69.2%), with a trough hemoglobin >8 g/dL in 63.2% and >10 g/dL in 15.8%; final hemoglobin was >10 g/dL in 44.1% of transfused donors. Platelet transfusion occurred in 165 donors (37.6%), with a trough platelet count >50 x 10^3/mcL in 113 (68.5%) and >100 x 10^3/mcL in 15 (9.1%). Plasma transfusion occurred in 217 donors (49.4%), with a peak INR of <1.5 in 75 donors (34.6%) and a peak INR of 1.6 to 2.0 in 112 donors (51.6%). Only 17.4% of donors who received cryoprecipitate had fibrinogen levels measured, and results were all >200 mg/dL. Transfusion reactions were underreported (p=0.0001). **CONCLUSIONS:** This study suggests potential suboptimal use of limited biologic resources in the BHODs, as well as significant under-reporting of suspected transfusion reactions. Additional studies are indicated to determine optimal transfusion thresholds in this population.

Key Words: organ donor, organ transplantation, brain death, transfusion threshold, transfusion guidelines

Introduction

Restrictive transfusion strategies using a hemoglobin transfusion trigger of 7.0 g/dL have been found to be associated with equivalent or lower rates of mortality compared to liberal transfusion strategies using a trigger of 9.0 g/dL or above in different patient populations.[1-3] Additionally, several studies have demonstrated similar or reduced rates of organ dysfunction and ischemic end-organ damage in restrictively transfused patients.[1,2,4] Despite this evidence, blood product overuse continues to occur in a variety patient populations and has lead the Joint Commission and the American Medical Association to select blood transfusion as one of the top five overused medical procedures in the United States.[5]

Organ transplantations in the US occur through the Organ Procurement and Transplantation Network (OPTN), which was created by the National Organ Transplant Act of 1984. The private nonprofit organization United Network for Organ Sharing (UNOS) operates the OPTN through a federal contract. UNOS is responsible for overseeing the regional organ procurement organizations (OPOs) which work with local hospitals to procure and allocate tissue and organs. [6]

The most common source of transplant organs in Western countries is from beating heart organ donors, where organs are harvested for donation after neurologic determination of death but prior to death by cardiorespiratory criteria.[6] The medical management of beating heart organ donors is complicated by a series of pathophysiologic changes that occur after brain death, including temperature dysregulation, hemodynamic instability, multiple endocrine dysfunction, and in some cases coagulopathy.[6] While specific guidelines are available for optimal management of beating heart organ donors, such as monitoring of core body temperature, use of pressors for hemodynamic support, insulin infusions with glucose monitoring, and hormonal therapy with vasopressin, methylprednisolone, and thyroid hormone replacement, data to support transfusion practice is lacking.[7]

Randomized controlled trials of optimal transfusion thresholds in beating heart organ donors have not been performed, and optimal transfusion thresholds for this population remain unknown. Some published recommendations suggest maintaining a hemoglobin level of greater than 10.0 g/dL in beating heart organ donors,[8] however these guidelines were developed prior to studies showing the benefit of restrictive transfusion practices in other populations, including critically ill patients, and may be "excessive".[9] Others suggest a target hemoglobin of 9-10 g/dL with a lowest acceptable limit of 7 g/dL, based on published findings from transfusion thresholds in critically ill adults, however significant variation in practice remains.[10,11] There are no defined transfusion guidelines for platelet count or PT/INR in this population.[10] This study was performed to evaluate current transfusion practices in beating heart organ donors.

Methods

An IRB approved retrospective analysis of all patients listed as beating heart organ donors between January 1, 2004 and October 1, 2014 was performed. At our institution, the first name of all beating heart organ donors is changed to "Donor" in the electronic medical record at the time of neurologic determination of death. A search of patients with first name "Donor" revealed a total of 439 patients during this time period. No patients were excluded from analysis.

For each donor the peak, trough, initial, and final levels for hemoglobin, platelet count, PT/INR, and fibrinogen were recorded during the time between neurologic determination of death and organ harvest. Additionally, records for all blood product transfusions and reports of suspected transfusion reactions during this time period were collected. When pooled platelet products of 5-6 were transfused, they were tabulated as a single unit. Data included in the medical record prior to the time of neurologic determination of death was excluded from review.

All data were collected by one physician, and were validated through random review of 10% of the sample by a second independent physician. Statistical analysis was performed with GraphPad (La Jolla, California). The unpaired Student's t-test and chi square test were used, and $P < 0.05$ was considered statistically significant. For chi square analysis, the rate of suspected transfusion reactions was estimated at 1% of blood product transfusions.[12]

Results

Packed red blood cells. During the study period, 304 donors (69.2%) were transfused a total of 894 units of packed red blood cells. For donors who received PRBC transfusion, the median number of units transfused was 2 (Fig. 1). The trough hemoglobin level was greater than 7 g/dL in 86.5%, greater than 8 g/dL in 63.2%, and greater than 10 g/dL in 15.8% of donors who received transfusion (Fig. 2). The final hemoglobin value was greater than 10 g/dL in 134 transfused donors (44.1%) (Fig. 3). The hemoglobin level was measured only once for 47 donors (15.5%). One patient who received transfusion had no hemoglobin measurement. Of the donors who did not receive PRBC transfusion, 114 (88.9%) had a lowest documented hemoglobin level that was greater than 9.0 g/dL. (Fig 1.)

Statistical analysis showed that donors with a trough hemoglobin of 10.1 g/dL or greater were significantly less likely to receive PRBC transfusion (P=0.0004). Comparison of the transfused and non-transfused groups for trough hemoglobin levels between 7.1 and 8.0 g/dL, 8.1 to 9 g/dL, and 9.1 to 10.0 g/dL demonstrated no statistically significant difference (P=0.08, 0.47, and 0.76, respectively).

Platelets. For platelet transfusions, 165 donors (37.6%) received a total of 316 platelet units, with a median of 2 units per donor (Fig. 1). Of donors who received platelet transfusions, 113 (68.5%) had trough platelet counts of greater than 50 x 10^3/mcL and 15 (9.1%) had a trough platelet count of greater than 100 x 10^3/mcL (Fig. 4). 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.

While there was no statistically significant difference between transfused and non-transfused groups when the trough platelet count was ≤ 50 x 10^3/mcL or ≥ 101 x 10^3/mcL (P= 0.42 and 0.07, respectively), there was a statistically significant difference between transfused and non-transfused groups when trough platelet count was between 51 x 10^3/mcL and 100 x 10^3/mcL.

Plasma. Plasma transfusions were given to 217 donors (49.4%). A total of 845 units of plasma were administered, with a median of 3 units per donor (Fig. 1). Of donors who received plasma transfusion, 75 (34.6%) had a peak INR of ≤ 1.5 and 112 (51.6%) had a peak INR of 1.6 to 2.0 (Fig. 5). There was a statistically significant difference between transfused and non-transfused groups when peak INR was ≤ 1.5 and between 1.6 and 2.0 (P=0.0001 and 0.047, respectively). When peak INR was ≥ 2.1, there was no statistically significance between transfused and non-transfused groups (P=0.45).

Cryoprecipitate. A total of 23 donors (5.2%) received cryoprecipitate transfusion. Of these donors, 19 (82.6%) did not have any fibrinogen levels measured. For the remaining 4 patients that did have fibrinogen levels measured, the lowest level documented for any patient was 239 mg/dL.

Transfusion reactions. Three suspected transfusion reactions were reported to the transfusion service out of a total 2055 blood product administrations. Two reactions were determined by the transfusion service to be mild allergic reactions (1 related to PRBCs, 1 to plasma) and 1 reaction was determined to be related to the donor's underlying medical condition.

Chi square analysis found that suspected transfusion reactions were reported significantly less often than expected (P=0.0001).

Discussion

To date, there are no randomized controlled trials to determine the optimal transfusion threshold in beating heart organ donors, and publications evaluating current transfusion practices in this population

are lacking. This study, to our knowledge, is the first to evaluate transfusion practices in beating heart organ donors.

Although studies to evaluate the optimal transfusion threshold for beating heart organ donors have not been performed, studies in a variety of other patient populations, including adult and pediatric intensive care unit and surgical patients, have found that restrictive transfusion strategies are equal or non-inferior to liberal transfusion strategies in preventing organ dysfunction and end-organ ischemia in other populations.[1,2,4] The primary purpose of transfusion in beating heart organ donors is to maintain optimal perfusion and oxygen delivery to preserve organ function until the time of organ procurement. This study demonstrates that in this population of beating heart organ donors, blood transfusion occurred at much higher thresholds than the optimal thresholds for other patient populations, suggesting the possibility of suboptimal blood product use. Excessive transfusion not only uses a limited biologic resource that must be reserved for patients most in need, but may also have potential adverse effects on organ function in the beating heart organ donor population.[1] It is unknown if hypertransfusion after neurologic determination of death may subsequently impact organ function in the organ recipient. Further studies are needed to evaluate this possibility, and would require the cooperation of OPOs and UNOS to track and monitor outcomes in organ recipients over time.

Transfusion reactions in beating heart organ donors were reported significantly less often than expected based on the total number of products transfused. The reasons for this are unknown, but may be related to the inability of the donor to report transfusion reaction-related symptoms. Additionally, the fluctuations in vital signs that occur after neurologic determination of death (hemodynamic instability, loss of temperature regulation, and myocardial dysfunction)[6] may make it difficult to determine if fluctuations are related to transfusion or if they are caused by brain death. The OPO medical staff

responsible for the medical management of beating heart organ donors may also be less familiar with the recognition of suspected transfusion reactions.

This study had several limitations. Midway through the study period, our institution began assigning new medical record numbers to beating heart organ donors effective at the time of neurologic determination of death; this practice prevented us from accessing any patient data from prior to that time period. Because data were collected only during the period from neurologic determination of death until time of organ harvest, the impact of laboratory studies or transfusions that occurred prior to that time is not known. Additionally, all beating heart organ donors during this 10 year time period were evaluated as a single group so the potential of changing transfusion practices during this time cannot be evaluated, although evidence for the benefit of restrictive transfusion practices in other populations was available for five years prior to the start of this study.[1] The study did not evaluate the transfusion practices of individual clinicians over this time period, so it is possible that transfusion practices varied between individuals which may have influenced the overall data. Finally, the data was collected from a single institution, and our experience may not reflect transfusion practices at other hospitals.

Given the current lack of studies to evaluate the optimal transfusion thresholds in beating heart organ donors, further studies are needed to determine these thresholds. This may be challenging, since the organs of a single donor may be transplanted in multiple recipients. This study establishes baseline transfusion data for this rare but critical population, and additional studies are needed to confirm these data for other locations.

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Legends of the figures

Fig. 1. Total number of units transfused, by blood product. Boxes represent the 25^{th}—75^{th} percentiles, with lines extending from the minimum to maximum number of units transfused per individual.

Fig. 2. Packed red blood cell transfusions and trough hemoglobin levels.

Fig. 3. Packed red blood cell transfusions and final hemoglobin levels.

Fig. 4. Platelet transfusions and trough platelet counts.

Fig. 5. Plasma transfusions and peak INR.

Fig. 1.

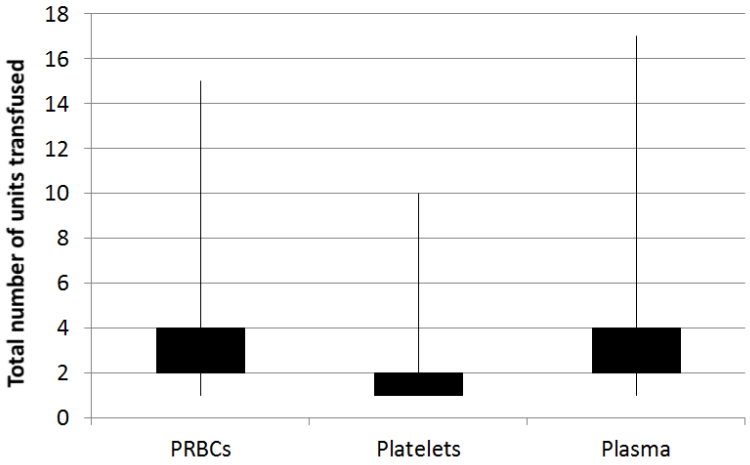

Total number of units transfused
18
16
14
12
10
8
6
4
2
0
PRBCs
Platelets
Plasma

Fig. 2.

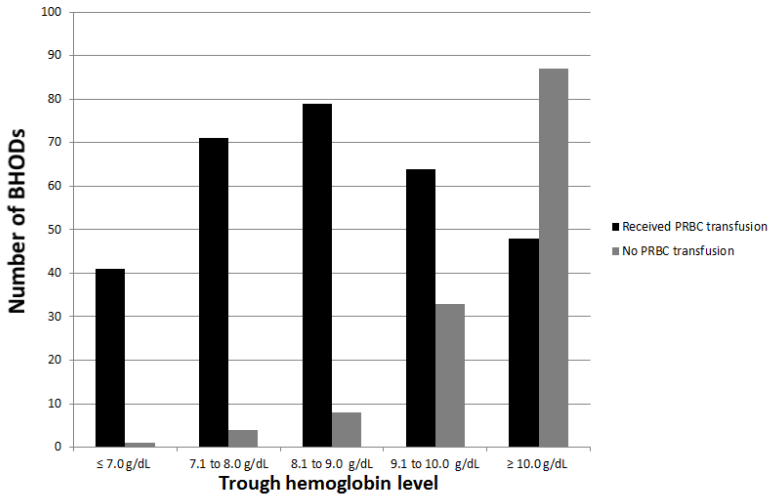

100
90
80
70
60
50
40
30
20
10
0
Number of BHODs
≤ 7.0 g/dL
7.1 to 8.0 g/dL
8.1 to 9.0 g/dL
9.1 to 10.0 g/dL
≥ 10.0 g/dL
Trough hemoglobin level
Received PRBC transfusion
No PRBC transfusion

Fig. 3.

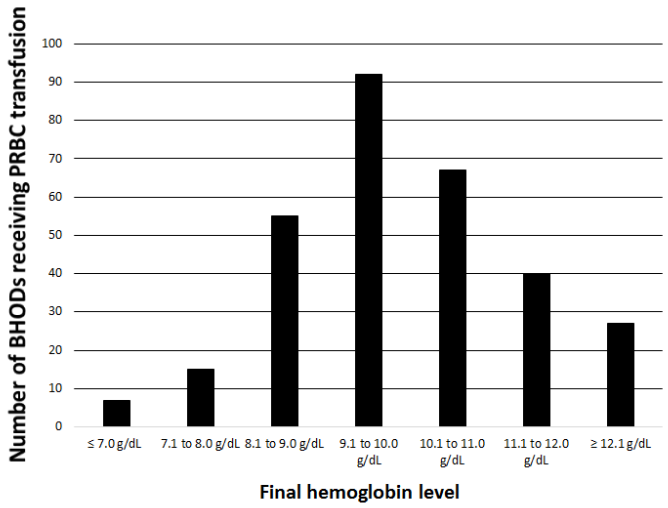

Number of BHODs receiving PRBC transfusion
100
90
80
70
60
50
40
30
20
10
0
≤ 7.0 g/dL
7.1 to 8.0 g/dL
8.1 to 9.0 g/dL
9.1 to 10.0 g/dL
10.1 to 11.0 g/dL
11.1 to 12.0 g/dL
≥ 12.1 g/dL
Final hemoglobin level

Fig. 4.

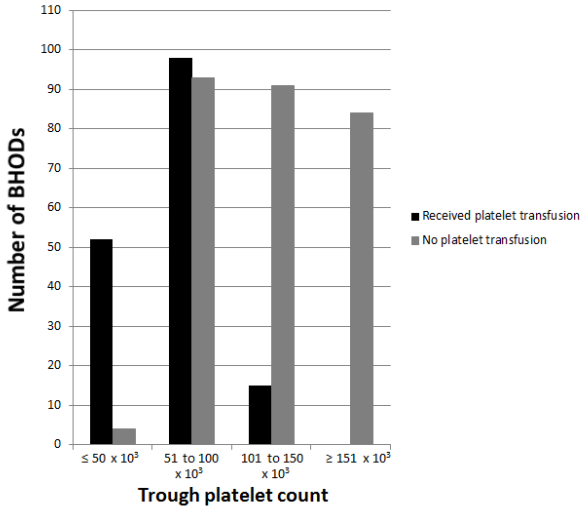
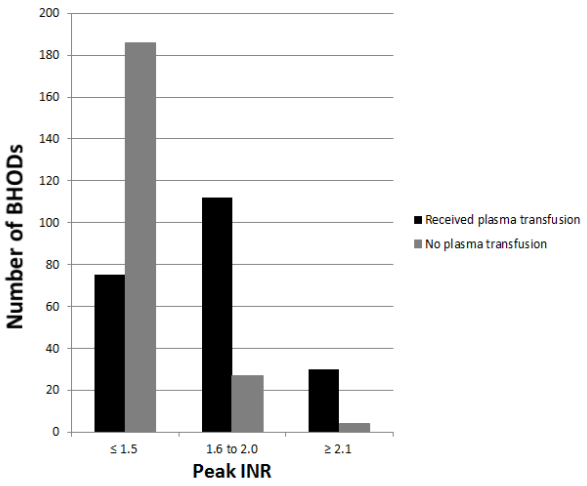

110
100
90
80
70
60
50
40
30
20
10
0
Number of BHODs
≤ 50 x 10³
51 to 100 x 10³
101 to 150 x 10³
≥ 151 x 10³
Trough platelet count
Received platelet transfusion
No platelet transfusion

Fig. 5.


200
180
160
140
120
100
80
60
40
20
0
Number of BHODs
≤ 1.5
1.6 to 2.0
≥ 2.1
Peak INR
Received plasma transfusion
No plasma transfusion