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The effects of red cell transfusion donor age on nosocomial infection among trauma patients

Tyler J. Loftus [a], Ryan M. Thomas [b], Travis W. Murphy [c], Linda L. Nguyen [d], Frederick A. Moore [a], Scott C. Brakenridge [a], Philip A. Efron [a], Alicia M. Mohr [a, *]

[a] University of Florida Health Department of Surgery and Sepsis and Critical Illness Research Center, Gainesville, FL, USA
[b] Malcom Randall Veterans Affairs Medical Center Department of Surgery, Gainesville, FL, USA
[c] University of Florida Health Department of Emergency Medicine, Gainesville, FL, USA
[d] University of Florida Health College of Medicine, Gainesville, FL, USA

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ABSTRACT

Background: We hypothesized that packed red blood cell (PRBC) transfusions from older donors would be associated with fewer nosocomial infections among trauma patients.
Methods: We performed a four-year retrospective analysis of 264 consecutive adult trauma patients who received ≥1 PRBC transfusion during admission. The capacity of donor age to predict nosocomial infection was assessed by logistic regression.
Results: Thirty-three percent of all patients developed a nosocomial infection. Donor age was significantly higher among patients with nosocomial infection (40.3 vs. 37.6 years, $p = 0.035$), and the incidence of infection was directly proportional to donor age. The association between donor age and infection was strongest among recipients age ≥60 years, and was significant on multivariate regression for this cohort (OR 1.07 (95% CI 1.01–1.13), $p = 0.024$).
Conclusions: Among trauma patients receiving PRBC transfusions, blood from older donors may be associated with increased risk for nosocomial infection.

1. Introduction

Blood loss and anemia are common among patients with traumatic injuries. Severely anemic trauma patients often receive packed red blood cell (PRBC) transfusions to restore hemoglobin levels and oxygen delivery capacity. Unfortunately, PRBC transfusion is also associated with immunomodulation and infectious complications.[1–6] Previous studies have investigated the impact of PRBC storage duration and pre-storage leukoreduction on transfusion-related immunomodulation and post-transfusion morbidity and mortality, leading to the adoption of blood bank policies favoring short PRBC storage duration and universal pre-storage leukoreduction.[1,7,8] However, the effects of blood donor age on post-transfusion morbidity and mortality remain unclear. Multicenter studies investigating relationships between donor age and mortality for diffuse patient populations have reported conflicting results,[9,10] and the effects of blood donor age on nosocomial infection have not been previously reported.

Several pre-clinical studies suggest that the age of a blood donor may affect the immunomodulatory effects of transfused blood. Animal studies have demonstrated that transfusion of aged mice with blood from young mouse donors has significant vascular, muscular, and neurologic effects.[11–13] With advanced age, hematopoietic stem cells lose their full proliferative capacity, and their microenvironment is gradually replaced by fat.[14] Total myeloid cell output is maintained throughout the aging process, whereas lymphocyte production decreases over time.[15,16] These phenomena may be inconsequential for donated blood that is subjected to pre-storage leukoreduction, which removes nearly all white blood cells, minimizing their physiologic impact and immunosuppressive potential.

* Corresponding author. University of Florida, Department of Surgery, 1600 SW Archer Road, Box 100108, Gainesville, FL, 32610, United States.
E-mail addresses: Tyler.Loftus@surgery.ufl.edu (T.J. Loftus), Ryan.Thomas@surgery.ufl.edu (R.M. Thomas), Travis.Murphy@surgery.ufl.edu (T.W. Murphy), Linda.Nguyen@ufl.edu (L.L. Nguyen), Frederick.Moore@surgery.ufl.edu (F.A. Moore), Scott.Brakenridge@surgery.ufl.edu (S.C. Brakenridge), Philip.Efron@surgery.ufl.edu (P.A. Efron), Alicia.Mohr@surgery.ufl.edu (A.M. Mohr).

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However, allogenic red blood cells themselves may suppress T-cell receptor expression by an arginase-dependent mechanism, and aging has been associated with decreased erythrocyte arginase production.[17–20] Therefore, it is plausible that PRBCs donated from older subjects may be less immunosuppressive than blood from young donors, leading to fewer infections.

The purpose of this study was to assess the effects of PRBC donor age on nosocomial infections among trauma patients, and therefore whether blood donor age should be considered in blood bank policies regarding allocation of PRBC products. We hypothesized that blood from elderly donors would be associated with fewer infectious complications.

2. Methods

We performed a retrospective analysis of 264 consecutive adult trauma patients who received one or more PRBC transfusions at our level one trauma center from 6/1/2011–10/1/2015. Subjects were identified by searching our institutional research database for adult patients (age ≥ 18 years) who received at least one PRBC transfusion. Patients were excluded if they had burn injuries, were transferred from an outside facility, underwent massive transfusion (≥10U PRBC within 24 h), had unmeasured blood loss unrelated to their injury (e.g. postoperative or gastrointestinal bleeding), or death within 48 h.

Universal pre-storage leukoreduction was performed at our institution for the duration of the study period. Storage duration and donor age were determined for each PRBC unit transfused to each patient in the study population. These variables were collected in cooperation with LifeSouth Community Blood Centers, the private institution that supplied our blood products during the study period. All other data was collected from our institutional research database and by retrospective review of the electronic medical record. Hemorrhagic shock was defined as systolic blood pressure <90 mmHg or lactic acid ≥4 mmol/L on admission. Nosocomial infections were assessed from 48 h after admission to 30 days after discharge. Six percent of all patients had no post-discharge follow-up, and another six percent had follow-up within 30 days but not beyond 30 days. Urinary tract infection (UTI) was defined as a urine culture with $\geq 10^5$ pathogenic colony forming units/mL. Pneumonia was defined as a quantitative bronchoalveolar lavage culture with $\geq 10^4$ pathogenic colony forming units/mL or a clinical diagnosis of pneumonia for a non-intubated patient. Bloodstream infection was defined as ≥ 2/4 bottles positive for likely contaminants (*Staphylococcus epidermidis*, *Propionibacterium acnes*, *Bacillus* species, and *Corynebacterium* species) or ≥ 1/4 bottles positive for all other organisms. Deep and organ/space surgical site infection (SSI) was defined according to CDC criteria.[21] Superficial SSIs were not considered due to variability in culture availability and reporting practices.

Statistical analysis was performed with SPSS v23 (IBM, Armonk, NY). Characteristics of the study population were reported as mean (95% confidence interval) or n (%). The difference in blood donor age between patients with and without nosocomial infection was assessed by one-way analysis of variance. Correlations were assessed by Pearson's r. The effects of donor age on nosocomial infection were analyzed by Fisher's Exact test and illustrated in a figure created in GraphPad Prism (v6.05, GraphPad Software, La Jolla, CA). Predictors of nosocomial infection were identified on univariate and multivariate logistic regression. Factors were selected for inclusion in the multivariate model if they were predictive of nosocomial infection on univariate analysis and were not collinear to other variables in the model ($|r| < 0.20$ and $p > 0.05$). Confidence intervals were set at 95% and significance was set at $\alpha = 0.05$.

3. Results

Patient characteristics, management, and outcome parameters are listed in Table 1. The predominant phenotype was a middle aged patient who sustained moderate-severe blunt injury (age 48 years, 89% blunt trauma, Injury Severity Score 25). On average, patients underwent three operations and received five units of PRBCs. The average PRBC storage duration was 21 days; average PRBC donor age was 38 years. One in three patients developed a nosocomial infection, and 9% had multiple infections. Patients with a nosocomial infection had significantly longer ICU length of stay (15.0 (12.7–17.7) vs. 7.4 (6.3–8.6) days, $p < 0.001$). Inpatient and 180-day mortality were 8% and 11%, respectively. One in ten patients had an unplanned readmission within 30 days, and approximately half of these were related to infectious complications.

Univariate and multivariate predictors of nosocomial infection are listed in Table 2. Mean and maximum blood donor age were each associated with nosocomial infection. Maximum blood donor age was collinear with the total number of PRBCs transfused ($r = 0.55$, $p < 0.001$), whereas mean donor age was not ($r = 0.10$, $p = 0.105$); mean donor age was selected for further analysis. The incidence of nosocomial infection increased proportional to blood donor age (Fig. 1). Mean donor age was significantly higher among patients who developed a nosocomial infection compared to those that did not (40.3 (38.4–42.2) years vs. 37.6 (36.1–39.1) years, $p = 0.035$). This association was strongest among older transfusion recipients (Fig. 2).

Table 1
Patient characteristics, management, and outcomes. PRBC: packed red blood cell, #systolic blood pressure <90 mmHg or lactic acid ≥4 mmol/L. Data are presented as mean (95% confidence interval) or n (%).

Characteristics, management, and outcomes	n = 264
Age (years)	48 (46–51)
Male	169 (64%)
Charlson comorbidity index	0.6 (0.5–0.8)
Penetrating trauma	29 (11%)
Injury Severity Score	25 (23–26)
On admission	
Heart rate	100 (98–103)
Systolic blood pressure (mmHg)	124 (120–128)
pH	7.29 (7.27–7.30)
Lactic acid (mmol/L)	2.9 (2.7–3.2)
Hemoglobin (g/dL)	11.2 (10.9–11.4)
Hemorrhagic shock#	59 (22%)
Number of operations during admission	3.1 (2.8–3.4)
Total PRBC transfusions during admission	5.3 (4.9–5.8)
Received a PRBC transfusion within 24 h	154 (58%)
PRBC transfusions within 24 h	2.4 (2.1–2.7)
Received a PRBC transfusion after 24 h	217 (82%)
PRBC transfusions after 24 h	3.0 (2.7–3.3)
PRBC storage duration (days)	21 (20–22)
PRBC donor age (years)	38 (37–40)
Patients who had a nosocomial infection	86 (33%)
Urinary tract infection	41 (16%)
Pneumonia	47 (18%)
Bloodstream infection	16 (6%)
Deep or organ/space SSI	10 (4%)
Hospital length of stay (days)	18 (17–20)
Intensive care unit length of stay (days)	10 (9–12)
Inpatient mortality	20 (8%)
Unplanned readmission within 30 days	26 (10%)
Readmission with infection	12 (5%)
Mortality within 180 days	28 (11%)