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Brief Report

Twenty-four-hour packed red blood cell requirement is the strongest independent prognostic marker of mortality in ED trauma patients

Albert Arslan, MD, Lindsey Flax, MD, Robert Fraser, MD, Marc Kanter, MD, Ronald Simon, MD, Nicholas D. Caputo, MD, MSc *

Department of Emergency Medicine, Lincoln Medical and Mental Health Center, Bronx, NY

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ABSTRACT

Background: Injury severity score, serum lactate, and shock index help the physician determine the severity of injuries present and have been shown to relate to mortality. We sought to determine if an increasing amount of packed red blood cells (PRBCs) given in the first 24 hours of admission is an independent predictor of mortality and how it compares to other validated markers.

Methods: A 6-year retrospective, observational study of adult trauma patients was conducted at a level 1 trauma center. Charts were reviewed for demographic data, amount of PRBC received in the first 24 hours, injury severity score, shock index, and lactate levels. Subgroups were used to determine if each variable was an independent predictor of mortality. Correlation coefficients and linear regression were used to determine the strength of correlation between each variable and mortality.

Results: One hundred fifty-seven patients met criteria over a 6-year period. The average age was 28 years, 93% were male, and 86% had penetrating injuries. The average injury severity score, serum lactate, and shock index were 18, 6.1, and 0.9, respectively. The average amount of blood given was 6.7 U.

Conclusion: Twenty-four-hour PRBC requirement is both a novel independent predictor of and has the greatest correlation to mortality in adult trauma patients when compared to injury severity score, shock index, and serum lactate.

1. Background

Hemorrhagic shock is one of the leading causes of death in trauma patients, accounting for 30% to 40% of all fatalities [1,2]. This is due to hypovolemic shock leading to an imbalance of oxygen delivery to cellular consumption to meet the demands of metabolic activity [3]. This is further complicated by coagulopathy due to the loss of platelets and coagulation factors [4]. Approach to the actively bleeding trauma patient is to control catastrophic bleeding to prevent further hemodynamic decompensation to prevent shock [5]. Resuscitation efforts involve normalization of physiologic equilibrium as measured by hemodynamic measures (ie, vital signs) and biochemical markers (ie, serum lactate, base excess) by volume replacement with blood products including packed red blood cells (PRBCs), platelets, and coagulation factors [6–8].

Research has emphasized the use of hemodynamic and serum biomarkers to help guide management and resuscitative efforts [9–11]. These measures, along with anatomic systems, have been used to develop several different clinical prediction scoring systems such as the injury severity score (ISS), shock index (SI), trauma severity score, and assessment of blood consumption (ABC) score for predicting massive transfusion [12–14]. All of these measures and scoring systems of severity of shock and predicted patient mortality have a common root: they are an indirect marker for whole blood loss/deficit. Research in the area of trauma prognostics has concentrated on the ratio of red blood cells to plasma and platelets and less on absolute measure of resuscitation needed to restore physiologic equilibrium in severely injured trauma patients, PRBC requirement [15]. One study has shown that trauma patients who require blood products have worse outcomes than those who do not [16].

We sought to determine that within those subgroup of patients who require transfusion does an increasing amount of PRBCs given in the first 24 hours of admission correlate to a higher rate of mortality and could this be an independent predictor of mortality. Finally, if so, how it compares to other validated markers of predicted mortality.

2. Methods

A 6-year (January 2008 to December 2014) retrospective, observational study was conducted at a urban, level 1 trauma center. In this retrospective analysis, patients were stratified by amount of PRBCs

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* Corresponding author at: Department of Emergency Medicine, Lincoln Medical and Mental Health Center, 234 East 149th Street, Bronx, NY 10451. Tel.: +1 718 579 6010; fax: +1 718 579 4224.

E-mail address: Nicholas.caputo@nychhc.org (N.D. Caputo).

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required for resuscitation in the following manner: (1) 1 to less than 4 U, (2) greater than 4 to less than 8 U, (3) greater than 8 to less than 12 U, and (4) greater than 12 U. These groupings were based on the natural distribution of the population from the lowest amount given (1 U PRBC) to the maximum (35 U PRBC) given. Then determining from this at which values were the means of the most commonly given amounts of PRBC groups given statistically different from each. This ensured that the group stratifications were truly different from each other, so that any comparison of proposed markers would not be skewed by overlap (ie, a patient in the grouping 1 to <4 that received 2 or 3 U PRBC truly received a different amount than a patient in the >4 to <8 grouping that received 5 or 6 U PRBC). Inclusion criteria were as follows: age older than 18 years, presentation for trauma (blunt or penetrating) requiring a tier 1 trauma activation (the hospital bases its tiered response on the American College of Surgeons, Committee on Trauma activation criteria recommendations [17]), and need for blood product administration initiated in the emergency department (ED) and up through the first 24 hours of admission. The hospital has a formal policy for initiation of blood products for trauma patients based on the Advanced Trauma Life Support recommendations and a formal massive transfusion protocol, which uses the ABC score for the activation of massive transfusion [18]. The ABC score uses hemodynamic (ie, systolic blood pressure and heart rate) as well as mechanistic (ie, penetrating injury) and diagnostic (ie, Focused Assesment with Sonography for Trauma examination) criteria as a means for starting transfusion. These criteria help determine the presence of the main indication for transfusion in trauma, the presence of shock despite damage control, and fluid resuscitation.

Charts were reviewed for demographic data (age, sex, injury type, initial hematocrit), amount of PRBC received in the first 24 hours, ISS, SI, and lactate levels. Subgroups were used to determine if each variable was an independent predictor of mortality by analysis of variance. Data are presented as mean (± SD). Subgroups were used to determine if each variable was an independent predictor of mortality by analysis of variance, and correlation coefficients and linear regression were used to determine the strength of correlation between each variable and mortality. Finally, we corrected for the ratio of factor replacement and its impact on mortality and the prediction of mortality by each variable using a multivariate linear regression with PRBC as a continuous variable. All statistics were performed in Statplus statistical package software (Analysoft, UK).

3. Results

Over the 6-year period, there were 12 186 presentations for trauma. Of these, 1828 (15%) met criteria for tier 1 trauma activation. Of these, 157 (8.5%) of patients had blood products (ie, either PRBCs alone or in combination with fresh frozen plasma [FFP] and single-donor platelets [SDP]) initiated and administered in the ED. The average age of the overall cohort was 28 (±1.8). Most patients were male (93%) and had penetrating injuries (86%). The average injury severity score, serum lactate, and SI were 8, 6.1, and 0.9, respectively. The average initial hematocrit was 35.8 ± 3.9. The average amount of blood given was 6.7 U. Table 1 shows how each subgroup compared with regard to demographics.

Each group differed significantly from each other with regard to every variable, as more blood products were required to resuscitate. As 24-hour blood product requirements increased across the groups, presenting systolic blood pressure dropped, presenting heart rate increased, ISS increased, SI increased, and initial lactates increased. Clearance of lactate also diminished as blood product requirement increased. Table 2 also demonstrates that 24-hour blood product requirement is an independent predictor of mortality which also increased significantly across the subgroups.

Figure demonstrates that 24-hour blood product requirement correlates most strongly with mortality when compared to all other independent predictors of mortality ($r^2 = 0.97$). When correcting for mortality adjusted for coagulation replacement with a ratio of 1 to 1 to 1 using multivariate regression, the correlation was $r^2 = 0.85$ for PRBC, although still the strongest predictor as correlations adjusted for the other variables also decreased (lactate $r^2 = 0.81$, ISS $r^2 = 0.84$, SI $r^2 = 0.67$). Mortality was also lower in patients who received coagulation replacement (FFP and SDP) to PRBC replacement in a 1:1:1 fashion compared to those who did not (31.5% vs 57.1%; $P = .052$).

Table 1
Subgroup analysis of patient demographics

	Units of PRBC				
	1 to< 4	>4 to< 8	>8 to< 12	>12	*P*
Age	29 ± 11.5	28.6 ± 11.2	25.9 ± 5.3	28.5 ± 13.7	.9
% male	92.3	93	91	94	.5
% penetrating	84	90	94	77	.08
Initial Hct	36.2 ± 5.5	35 ± 4.9	35.9 ± 6.7	35.4 ± 4.5	.1
Initial INR	0.9 ± 0.6	1.1 ± 0.8	0.8 ± 0.6	1.2 ± 0.9	.7
Initial PT (s)	11.35 ± 4.5	11.0 ± 5.2	11.1 ± 4	12.1 ± 1.3	.5
Initial aPTT (s)	30 ± 7.3	28 ± 8.2	31 ± 7.6	34 ± 10.2	.8
Initial PLT (10^9/L)	253 ± 67	282 ± 59	264 ± 49	288 ± 67	.3

Abbreviations: Hct, hematocrit; INR, international normalized ratio; PT, prothrombin time; aPTT, activated partial thromboplastin time; PLT, platelet.

4. Discussion

Uncontrolled hemorrhage in trauma leads to an imbalance in oxygen delivery to cellular demand, which ultimately impacts on metabolic function. The goal of damage control resuscitation is to control bleeding and restore physiologic equilibrium as soon as possible to prevent irreversible damage and death [18]. A large part of damage control resuscitation is replacement of volume loss with blood products. Several studies have shown the importance of replacement with not only PRBCs but also in combination of specific ratios with FFP and platelets, to prevent coagulopathy (a major cause of mortality in trauma) [19,20]. Research has demonstrated the utility of anatomic, physiologic, and hemodynamic measures such as ISS, serum lactate, and SI in determining the extent to which the patient has suffered loss and can help guide resuscitative efforts. Although our study confirms that these measures are abnormal in trauma patients requiring blood products, there are limitations to them. One would expect that, in a trauma patient requiring transfusion, ISS would be higher than 18 (the average ISS in our population). This may be due to the fact that most patients requiring transfusion in our study had penetrating injuries, which inherently have lower ISS. Despite this limitation, our findings further demonstrate that as blood requirement increases, these measures become more abnormal and risk of fatal outcome becomes greater.

Table 2
Subgroup analysis of variance that demonstrates the difference of each independent variable and their respective mortality rates

	Units of PRBC				
	1 to <4	>4 to <8	>8 to <12	>12	*P*
Mortality (%)	5.4	8.7	19	28.6	.02
Group average units PRBC req.	2.9	6.6	10.7	19	<.001
% Received FFP	12.7	29	85	96	.002
Average amount of units FFP	2.3	5.4	6.8	9.58	.049
% Received SDP	5.45	10.7	55	76	<.001
Average amount of units SDP	0.5	1.7	3.4	4.2	.05
ISS	12.7	18.2	21.1	30	.002
Initial lactate	5	6.5	7.4	8.4	.04
Second lactate	2.3	3.6	4.3	6.7	<.001
Third lactate	1.7	3	3	4.6	<.001
SI	0.8	1.08	1.2	1.3	.001
Systolic blood pressure	127	109	104	98	.001
Heart rate	96	117	121	128	<.001

Abbreviation: req., requirements.