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Massive Blood Transfusions and Outcomes in Trauma Patients; An Intention to Treat Analysis

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ABSTRACT

Objective: To determine if there exists an upper limit for amount of blood transfused in trauma patients before it reaches a point of futility.
Methods: A prospective cohort study was conducted on 131 patients who received massive blood transfusion (MBT), defined as 10 U or higher of PRBCs received in the initial 24 hours. Data collected from a Level II trauma center registry were used to analyze reports of adult patients from July 2014 to 2017. Cohorts were divided by amount of blood received - 0 to 9 U, 10-19 U, 20 to 29 U, 30-39 U, 40 U or higher - odds ratio for mortality and p-values for mean Injury Severity Score and overall hospital length of stay were calculated for each group.
Results: Odds ratios for massive blood transfusion groups from 10 units to 39 units each contained the null value, while our 40 units and above group did not (OR 12.52, 95% CI 1.3-117.7).
Conclusion: Although this study is limited by its sample size, these results suggests that 40 units of PRBCs may be a threshold at which survival rates begin to decrease significantly.

Keywords: Massive transfusion; Blood transfusion; Trauma; Blood loss.

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Introduction

The question of whether or not there is an upper limit for amount of blood that a patient should receive following trauma before it reaches a point of futility has been posed in previous literature, but it is yet to be adequately answered. With each unit of packed red blood cells (PRBCs) costing upwards of $200 and a limited supply of blood products depending on the facility, it is important to use these resources only when appropriate. While clinicians may rely on their clinical judgment or various scoring systems to determine the need to begin transfusion of blood products, there currently exist no upper limit for amount of blood transfused before it is considered an inappropriate use of resources

and beyond which transfusion should be terminated [1]. Knowing if there were an upper limit of futility would allow trauma centers to use their resources more efficiently. The Pragmatic, Randomized Optimal Platelet and Plasma Ratios (PROPPR) trial defines massive blood transfusion as "greater than or equal to 10 units of PRBCs within 24 hours" [2]. Our study sought to determine if there exists an upper limit for amount of PRBCs patients should receive before a point of futility is reached.

Materials and Methods

Study Population

This study was approved by the Touro University-California Institutional Review Board. Natividad Medical Center (NMC) has a Level II Trauma Center that serves Monterey County in Central California. We abstracted data and obtained our endpoints of interest from a de-identified dataset from our trauma registry, which is maintained by dedicated trauma registrars. Our study analyzed demographics and individual trauma criteria collected from patients admitted to NMC's trauma service from July 1, 2014 to July 1, 2017. Injury Severity Score (ISS), overall hospital length of stay (LOS) and mortality were our measured endpoints. Endpoints were followed for the duration that the patient was being evaluated at our facility.

Study Protocol

There were 3,861 cases in the trauma registry queried in total. Patients were included if they were 18 years or older and if they had blood transfusion information available. Nearly all of the patients excluded from the study did not have blood transfusion information available. The remaining 131 patients included victims of various types of trauma who received between 0 and 87 units of PRBCs in the initial 24 hours and were divided by amount of blood received (0-9 units, 10-19 units, 20-29 units, 30-39 units, 40 units and above). Table 1 displays an in-depth breakdown of patient demographics including age, gender and mechanism of injury. Need for blood at our facility is determined by clinical judgement by either the trauma surgeon or emergency physician, using vital signs on presentation, injury severity and diagnostic studies. Imaging results and laboratory results, such as arterial blood gas, were not readily available for analysis in this study.

Statistical Analysis

All data was compiled and analyzed using a Microsoft Excel database. All graphs and tables were made using either Microsoft Excel or IBM SPSS. Mortality was calculated as a percentage for each group and odds ratios were calculated by generating an outcome frequency table. Mean ISS and hospital LOS were calculated, and Student's T-tests were performed to obtain p-values.

Results

Of the 131 patients included in our study, the mortality rate was 27% (36 expired). Patients were between the ages of 18 and 89 and made up of 32% women and 68% men. We categorized these patients into five groups: patients who received 0 to 9 units PRBCs (n=95), patients who received 10-19 units PRBCs (n=19), patients who received 20-29 units (n=8), patients who received 30-39 units (n=4), and patients who received 40 units and above PRBCs (n=5). Mortality rates for these groups were 24%, 21%, 38%, 50% and 80%, respectively.

Table 2 demonstrates the distribution of survivors and expired patients categorized by the amount of blood received. Odds ratios for the groups receiving massive blood transfusion (greater than 10 U) are seen below. Odds ratios with 95% confidence interval for mortality contained the null value for our 0-9 units, 10-19 units, 20-29 units and 30-39 units. Odds ratio for our 40 units and above group however was 12.52 and did not contain the null, indicating a statistically significant difference from our control.

P-values for ISS were less than 0.05 for our 20-29 units and our 40 units and above groups, indicating that our higher ISSs seen in these groups were statistically significant. *P*-values for groups 10-19 units and 30-39 however greater than 0.05. When analyzing hospital length of stay, there were no

Table 1. Baseline characteristics and ISS with *p* values for patients included in study, stratified by number of units of packed red blood cells received within the first 24 hours of treatment. Mean values include standard deviation.

		0-9 U	10-19 U	20-29 U	30-39 U	≥40 U
Demo -graphics	Mean Age	40 (SD 20)	33 (SD 13)	30 (SD 21)	46 (SD 17)	18 (SD 13)
	Sex					
	- % Male	73 (77%)	11 (58%)	5 (60%)	3 (75%)	3 (60%)
	- % Female	22 (23%)	8 (42%)	3 (40%)	1 (25%)	2 (40%)
	Mechanism of Injury					
	- Assault	35 (37%)	6 (32%)	3 (38%)	2 (50%)	3 (60%)
	- MVC	33 (35%)	11 (58%)	5 (63%)	2 (50%)	2 (40%)
	- Fall	12 (13%)	1 (5%)	0 (0%)	0 (0%)	0 (0%)
	- Other	15 (16%)	1 (5%)	0 (0%)	0 (0%)	0 (0%)
Injury Severity Score	Mean	19 (SD 13)	26 (SD 12)	37 (SD 20)	24 (SD 11)	36 (SD 13)
	p value	--	0.056	0.001	0.508	0.005

Table 2. Table demonstrating odds ratios for mortality and *p* value for hospital length of stay, stratified by number of units of packed red blood cells received within the first 24 hours of treatment. Mean values include standard deviation.

		0-9 U	10-19 U	20-29 U	30-39 U	≥40 U
Mortality	Expired	23	4	3	2	4
	Survived	72	15	5	2	1
	%	24%	21%	38%	50%	80%
	OR	--	0.83	1.88	3.13	12.52
	95% CI	--	0.25 to 2.77	0.42 to 8.47	0.41 to 23.49	1.33 to 117.7
Hospital LOS	Mean	10.1 (SD 12.1)	9.3 (SD 5.5)	9.0 (SD 8.0)	6.8 (SD 6.0)	4.6 (SD 6.2)
	p value	--	0.793	0.806	0.588	0.321

groups with *p*-values less than 0.05, indicating no statistically significant difference in LOS from control group.

Discussion

It was our hope that this study would shed new light on an old topic and determine if there exists an upper limit for which amount of blood given may be considered a point of futility. Decreased tissue perfusion and lactic acidosis due to hemorrhagic shock are preventable consequences of trauma, so determining when to begin blood transfusion remains an important question in the setting of trauma with massive blood loss [3-6]. Many facilities, such as ours, determine need to transfuse based on clinical presentation by the treating trauma surgeon or emergency physician without using a formal scoring system [7]. The Shiraz Trauma Transfusion Score is an example of a useful scoring system that quantifies need for blood products without solely relying on clinical judgement [8]. This study focuses less on the indications for beginning blood transfusion and more so on if an upper limit exists for massive transfusion.

Targeted resuscitation strategies for optimizing cardiac function as well as numerous prior studies have not been able to justify an upper limit for amount of PRBCs that should be transfused in a trauma patient before it reaches a point of futility [9-12]. A 1998 study published by the University of Southern California concluded that discontinuation of short-term care could not be justified based on transfusion of up to 68 units - in other words, an upper limit could not be determined [13]. While our study did take into account ISS as a means for eliminating possible spurious associations, this study looked at a total of 56 data elements in an attempt to define risk factors for mortality, including ISS. A similar study published in 2002 by Duke University showed a 43% survival rate for 7,734 trauma patients receiving 50 U of blood and higher [14].

Survival rates have been steadily improving for patients receiving massive blood transfusions, from 10% in the 1970s to around 40% in the 1990s. A 1999 article discusses the improved survival rates seen in trauma patients receiving massive transfusions, citing improved rewarming techniques, increased popularity in damage control laparotomies, evolving transfusion practices in regards to ratios to clotting factors, and maximizing blood banking practices [15-20]. Additionally, anecdotal evidence exists of patients surviving after receiving over 100 U of blood.

While it is clear that there is a correlation between the amount of PRBCs transfusion and mortality rate, current research cannot determine an upper limit for massive transfusion. Further studies are warranted to determine number needed to treat for trauma patients receiving massive blood transfusions on the order of 40U of PRBCs or greater. Several limitations of our study merit discussion. Our low sample size limits the power of our results. Additionally, while we did calculate mean ISS to evaluate for confounding, we recognize that this is an imperfect parameter for measuring need for blood. Due to low sample size, we were unable to perform subgroup analysis with multivariate logistic regression analysis to provide risk factors and determinants of outcomes in our patient population. It is difficult to draw definitive conclusions from a single-center study such as this, but these results lay the groundwork for larger future studies.

Current practices and literature agree that there does not exist an upper limit of futility for giving blood transfusions. Our study suggests that patients who receive massive blood transfusions from 10 units up to 39 units of PRBCs in the initial 24 hours have no increased risk of death compared to trauma patients who received less than 10 units. Patients who receive 40 units and above however are 13-times more likely to die compared to those receiving less than 10 units. Although this study is limited by its sample size, our results suggests that 40 units of pRBCs may be a threshold at which survival rates begin to decrease significantly.

Conflicts of Interest: None declared.

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