Variables Predicting Trauma Patient Survival Following Massive Transfusion

Introduction: The literature contains little information regarding demographic or transfusion-related factors associated with survival following massive blood transfusion in trauma patients. The objective of this study was to describe patient, transfusion, and laboratory variables contributing to survival in this population during the first and second days after arrival at the hospital. A secondary objective was to identify costs associated with massive blood transfusion.

Methods: A 7-year, retrospective review of 13,005 consecutive trauma patient records yielded a sample of 46 who were transfused with ≥50 units of blood products in the first post-injury day. Descriptive statistics were computed to describe the sample, transfusion data, and laboratory values. Logistic regression was used to predict survival using selected patient characteristics, laboratory data, and transfusion characteristics for both the first and second days.

Results: Overall survival among this group who received massive transfusion was 63%. No significant differences were found between survivors and nonsurvivors in age, sex, type of trauma, or amount of any of the blood components administered on Day 1. Nonsurvivors had higher Injury Severity Scores and shorter ICU and hospital lengths of stay. Controlling for other variables, only arterial base deficit levels made a significant unique contribution to predicting survival. The volume of blood transfused on Day 2 did not contribute to survival prediction. The average cost of blood transfusion was more than $49,000 per survivor and $51,000 per nonsurvivor.

Conclusion: Defining medical futility based solely on the volume of blood products transfused currently is unjustified. The search for other early indicators of survival in the trauma population must continue.
Emergency and critical care nurses involved in trauma resuscitation are familiar with that small subset of patients who urgently require massive blood transfusion (MBT) for severe, exsanguinating injuries. This high-acuity population consumes huge quantities of blood products in what often seems an ultimately futile effort. Although there have been promising advances in the development of synthetic substitutes, homologous donor blood remains an essential resource for trauma patients. Nonetheless, the supply of packed red blood cells (PRBCs) and other blood components is limited, and demand for this life-saving commodity can quickly exceed reserves. A scarcity of available blood products in communities throughout the United States is frequent and often chronic.1,2 Moreover, grim survival statistics following prolonged hypovolemic shock and massive blood transfusion have been well documented in the trauma literature.3

Issues of high cost, limited availability, and questionable efficacy have driven efforts to identify a massive blood transfusion futility point.7 Despite the use of huge volumes of donor blood in the major trauma population, the health care literature contains: (1) no consistent definition of massive blood transfusion; (2) no data about the impact of ongoing transfusion beyond the initial 24-hour resuscitation period; and (3) little information regarding patient or transfusion-related factors associated with survival. Therefore, it remains unclear whether or when to continue or stop aggressive transfusion.

**Background**

A review of the literature does not reveal a standardized definition of how many units of blood, administered within what time frame, constitutes MBT, nor is there consistency regarding which blood components are counted.4 Various reports reflect the administration of only red cell products (PRBCs and whole blood).5,8-14 Some reports also include “white” blood products (ie, fresh frozen plasma, cryoprecipitate, and platelets).6,7,15,16 In addition, transfusion studies to date have involved heterogeneous populations. Early samples consisted of all patients receiving massive quantities of blood, including those with obstetrical hemorrhage, ruptured aortic aneurysms, and gastrointestinal bleeding.8,9 Other series have encompassed trauma patients in general,3,6,7,11,12,14-16 and some have limited subjects to blunt trauma victims.5,10,13

Whereas 10 or more units of PRBCs in the first 24 hours appears to be a common definition of massive transfusion,15,16 other definitions found in the literature include 6 or more units of PRBCs transfused during the first 12 hours,11 more than 20 units of blood during a single hospitalization,10 more than 50 units of blood products in the first 24 hours,7 50 or more units of PRBCs or whole blood in the first 48 hours,6 50-plus units administered during the first “one to two days,”14 transfusion exceeding “one blood volume in 2 hours,”17 “two blood volumes” given during the first 24 hours,8 and “four blood volumes in the initial posttraumatic 12 hours.”15

Also, older series report the number of whole blood units transfused,5,8,9 whereas recent literature refers to units of PRBCs. This difference reflects changes in blood banking practices over time. Although component therapy is now considered expedient,18-20 this modification in transfusion practices is significant because packed cells contain virtually no clotting factors, making comparisons between earlier and current studies difficult at best. Even recent reports frequently fail to enumerate anything other than PRBC use.11-14 Consequently, studies that exclude white products potentially understate the resource consumption of MBT. Nonreporting of these data is particularly important in hypotensive, hypothermic, acidotic trauma patients in whom there is a significant incidence of coagulopathy and a generally high rate of white component use.

A recent report by Vaslef and colleagues7 examined numerous patient characteristics and transfusion-related factors in trauma patients who received massive transfusions (≥50 units of blood products). The authors identified only one independent risk factor associated with mortality: a base deficit greater than 12 mmol/L at any time during the initial 24-hour period. The presence of this finding increased the risk of death more than fivefold. These researchers also noted the average total transfusion cost per patient in their series was in excess of $11,000, although they did not specify how this figure was derived.
Velmahos et al.\textsuperscript{12} posed the question, “Is there an upper limit, a point at which further transfusion efforts become futile?” These investigators performed a 4-year, retrospective analysis of trauma patients who received between 20 and 68 units of PRBCs or whole blood during preoperative and intraoperative resuscitation. Of the 141 subjects included in the study, 43 (30\%) survived. No difference was found between the amount of blood given to survivors and nonsurvivors, and there were viable patients at even the highest transfusion volumes.

Massive transfusion is only one component of trauma resuscitation, making it difficult to separate the effect of type and volume of blood products transfused from patient characteristics and multiple other therapeutic interventions. Patient factors such as age, Injury Severity Score (ISS), and mechanism of injury have been reported to influence overall trauma patient outcome.\textsuperscript{21-23} Additional important variables in any trauma resuscitation scenario include time from injury to trauma center arrival, extent of prehospital care, and in-hospital interventions.

Moreover, rapid advances in trauma care have made identifying the relative effect of MBT difficult to assess. Survival in the 1970s among patients receiving more than 25 units of blood in less than 24 hours was reportedly as low as 7\%,\textsuperscript{4} whereas a 2002 study documented a 43\% survival among patients receiving 50 or more units.\textsuperscript{7} These data imply that, even if an MBT futility point were identified, the number could be a moving target as overall trauma care continues to improve. Aggressive patient rewarming measures, early correction of coagulopathies, reversal of acidosis, increased use of “damage control” surgery, and improved blood banking techniques are all factors that have been associated with enhanced survivability in the MBT population, independent of transfusion volume.\textsuperscript{6,8,12,13}

**Objectives**

The purpose of this study was to identify variables predicting survival in trauma patients following massive blood transfusion. Specifically, this article describes characteristics of trauma patients who received MBT and explores how these characteristics predict survival. A secondary aim was to determine costs associated with massive transfusion.

**Methods**

This descriptive, retrospective study was conducted at an academic, level I trauma center in the Pacific Northwest. Before data collection, Institutional Review Board approval and permission to access the databases were granted. The facility’s trauma registry documented 13,005 patients admitted in the 7-year period between January 1, 1994, and December 31, 2001. From this number, 50 patients were identified who received 50 or more units of blood products during Day 1 of hospital admission. This definition of massive transfusion was selected to: (1) identify persons who had very high transfusion requirements during the initial resuscitation period, and (2) facilitate comparison with the study by Vaslef and colleagues.\textsuperscript{7} The sample was further reduced to eliminate patients with long intervals (≥12 hours) between injury and tertiary care facility arrival, yielding a final sample size of 46.

Additional variables obtained from the trauma registry included age, sex, mechanism of injury (blunt vs penetrating), length of hospital stay, survival status, and ISS.\textsuperscript{23} The blood bank database was queried to determine the precise amounts and types of blood products transfused in 3 time frames: Day 1, Day 2, and remainder of hospital stay.

Defining a patient’s initial postinjury day was not at all straightforward. Ideally, the Day 1 clock would start ticking at the time of injury. Unfortunately, these data were not available in the trauma registry; only time of hospital arrival was recorded. Identifying actual time of transfusion also was difficult. When blood was infused in mass quantities, medical record review proved inadequate to determine exact times. The only consistently reliable documentation regarding transfusion time was the date the blood was released from the blood bank. Because of this inability to pinpoint transfusion time, for the purposes of this study, “Day 1” had to be defined by calendar dates instead of a 24-hour clock. With the incidence of trauma peaking in the evening, employing a midnight cut-off time would artificially shorten Day 1 for the majority of patients in the sample. Therefore, for any patient who arrived before 4 pm, Day 1 ended at midnight (potential range 8 to 24 hours), whereas Day 1 for patients arriving after 4 pm lasted until the following midnight (potential range
24 to 32 hours). In this study, the average length of Day 1 was 23.3 hours (SD ± 6.1). Day 1 lasted 8 to 16 hours for 20% of subjects, 16 to 24 hours for 30% of subjects, and 24 to 32 hours for 50% of subjects. Analysis showed that the length of time ascribed to Day 1 did not influence survival status.

Our institution’s blood bank defines a “unit” as a blood product derived from a single donor for transfusion into a patient. Because cryoprecipitate and most platelet products are pooled from multiple donors, a single bag of these blood products is counted as 5, 8, or 10 units rather than one. This methodology is consistent with the recent study by Vaslef and colleagues, but few previously published series contain a description of how units were counted. The most extreme results for hemoglobin, platelet count, base deficit, prothrombin time international normalized ratio (PT-INR), fibrinogen level, and activated partial thromboplastin time (aPTT) for each of the 3 time periods were obtained from the electronic medical record.

DATA ANALYSIS
Descriptive statistics were computed to describe the sample, transfusion data, and laboratory values. To identify characteristics of survivors and non-survivors, t tests were used. Logistic regression was used to predict survival using selected patient characteristics, transfusion characteristics, and laboratory data. Cost data were computed from charge information supplied by the blood bank.

Results

DESCRIPTIVE DATA
The sample was 63% male. Of the total sample, 67% experienced blunt trauma and 33% had a penetrating injury. Overall, 63% (n = 29) of the sample survived. A total of 4875 units of blood products were administered (mean = 106 units per patient), with 78% transfused on Day 1, 6% on Day 2, and 16% during the remainder of the hospital stay. Average patient age was 36 years (SD ± 17.1), and the mean ISS was 39.4 (SD ± 14.4). There were no significant differences between survivors and non-survivors in age, sex, type of trauma, or amount of any of the blood components administered on Day 1. Nonsurvivors had higher ISSs (45.1 vs 36.1; t = 2.12; P < .04), shorter ICU and hospital lengths of stay, and significantly greater arterial base deficits than did survivors. Differences in other monitored laboratory values were not significant. For those who lived beyond Day 1 (n = 40), there were no differences between survivors and nonsurvivors in the amount of any blood components administered.

The sample was divided into 3 groups by volume of blood products transfused on Day 1: 50 to 74 units, 75 to 99 units, and more than 99 units. Within each group, there were no significant differences in terms of patient characteristics (age, ISS, trauma mechanism, or sex), amount of various blood components transfused (PRBCs, fresh frozen plasma, platelets, or cryoprecipitate), or survival. Patients who received the lowest volumes of blood had significantly less disruption in base deficit values compared with the 2 higher volume groups (−11.4 versus −16.5 and −17.7, respectively; F[2,43] = 3.19; P = .05). Patients transfused the most blood had significantly higher aPTT times: 74.2 seconds (50 to 74 units), 58.2 seconds (75 to 99 units), and 104.1 seconds (>99 units) (F[2,43] = 3.56; P = .04). There were no differences in PT-INR, fibrinogen, hemoglobin, or platelet results among survivors and nonsurvivors within each of the 3 volume groups. The sample was redivided into 3 age groups: 18 to 30 years, 31 to 54 years, and 55 years or greater. There were no statistically significant differences within the 3 groups in terms of survival, patient characteristics, individual component volumes transfused, or any laboratory data.

PREDICTING SURVIVAL
To predict overall survival, the authors initially planned to use all variables that differed significantly between survivors and nonsurvivors: ISS, Day 1 arterial base deficit, ICU length of stay, and hospital length of stay. However, both lengths of stay variables actually reflect survival, as opposed to predicting it. Thus, only ISS and Day 1 arterial base deficit were entered into logistic regression. This conservative model correctly predicted survival 70% of the time ($\chi^2 = 12.2, P = .002$). Base deficit was the only variable to make a significant unique contribution to survival. For those patients who lived beyond Day 1 (n = 40), there were no differences between survivors and
nonsurvivors in the type or amount of blood products administered on Day 2.

COSTS
Cost data were calculated based on current patient charges per unit of blood, as reported by our blood bank. These numbers reflect only charges directly associated with the blood products themselves and do not include any nursing-related expenses, nor do they account for changes over time. Altogether, the price of blood for these 46 patients was estimated at nearly $2.3 million. Average charges for all blood products were $49,113 per survivor and $51,388 for nonsurvivors. There were no significant differences between survivors and nonsurvivors in costs for any of the individual blood products (Table 1). Actual cost information is difficult to obtain, and we acknowledge the limitations of this methodology. Nevertheless, even these incomplete data reflect a substantial per-patient expenditure for blood products.

Discussion
No simple relationship exists between survival and volume of blood transfused. The amount of blood products administered on both Day 1 and Day 2 are not predictive of survival. Surprisingly, in this series, 60% of patients in the highest transfusion group (≥100 units, n = 10) survived. Also of interest was that other variables traditionally associated with survival such as patient age and a blunt injury mechanism did not prove to be significant individual predictors of survival among these subjects. Mortality increased with advancing age, yet even the oldest patients (≥55 years) who received massive transfusions (n = 8) had a 50% survival rate. Few individual variables were noted to be significantly different by survival status, and only base deficit uniquely predicted survival. The base deficit finding is consistent with numerous studies that have documented a well-established relationship between an increasing (more negative) base deficit and the need for early transfusion, the presence of intra-abdominal injury, and mortality.

The cost for blood products among the massively transfused patients in this study approached $2.3 million, and there were no significant differences in cost by survival status. While several authors allude to the high price of banked blood, only Vaslef and colleagues attempted to quantify these expenses. However, because the method of calculating costs was not specified, their estimate of $11,000 per patient cannot be directly compared with the $49,000 average cost per patient in this study.

LIMITATIONS
Massive transfusion of trauma patients is a memorable but infrequent occurrence. The trauma database, as initially examined, contained more than 13,000 patients, but the

### Table 1

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<th>Survivor (n = 29)</th>
<th>Nonsurvivor (n = 17)</th>
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<tr>
<td></td>
<td>Mean</td>
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<td>Total estimated cost by survival status</td>
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*Estimated transfusion costs were approximately $50,000 per patient. There were no significant differences in blood product cost between survivors and nonsurvivors (P = .05). Total blood costs for these 46 patients approached $2.3 million.

FFP, Fresh frozen plasma; PRBCs, packed red blood cells.
final number of subjects in this investigation was only 46 over a 7-year period. Small sample size has been an issue in all MBT studies. To facilitate comparison, our study was designed to be similar in methodology to that of Vaslef and colleagues, although no attempt was made to replicate their research. To gain sufficient power, the ongoing study of survival following massive transfusion must involve larger sample sizes.

While this model was able to predict survival with 70% accuracy in the first day after injury, many factors besides the patient characteristics, transfusion volume, and laboratory data studied play an important role in determining trauma patient outcome. Future research regarding massive blood transfusion should include additional relevant variables. Two potentially important variables were not examined in this study: (1) volume of crystalloid resuscitation fluid, and (2) amount of cell-saver recovered blood or autotransfused chest blood. These variables were excluded because neither was consistently documented in the trauma registry. Other limitations of this study include the retrospective use of existing databases for primary case selection.

CLINICAL IMPLICATIONS

Intuitively, there would seem to exist an upper limit after which transfusion of further precious blood resources would no longer improve trauma patient survival. Nonetheless, the results of this study are consistent with other published data, which demonstrate that, although MBT is clearly associated with high mortality rates, no such futility point has yet been defined. Adding data derived from the patient’s second hospital day, a factor that has not been previously examined, did not contribute additional predictive information.

Reasons for a limited relationship between transfusion volume and survival remain elusive but may be found in the considerable variability of trauma patient presentation. Patients given lower volumes of blood may actually be more severely injured; they simply do not live long enough to consume massive blood resources, making transfusion volume an inadequate predictor of survival. On the basis of this and previous research, it would seem that defining the point of medical futility based solely on the volume of blood products transfused, during either the first or second day, is currently not supported by research. The search for other markers of survival, in conjunction with MBT, must continue. At present, there are no data to justify limiting massive blood transfusion based on infused volume alone, and nurses must remain advocates for their patients on this important issue.

REFERENCES


