Development of prehospital assessment findings associated with massive transfusion

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BACKGROUND: Massive transfusion is frequently a component of the resuscitation of combat casualties. Because blood supplies may be limited, activation of a walking blood bank and mobilization of necessary resources must occur in a timely fashion. The development of a risk prediction model to guide clinicians for early transfusion in the prehospital setting was sought.

STUDY DESIGN AND METHODS: This is a secondary analysis of a previously described data set from the Department of Defense Trauma Registry from January 2007 to August 2016 focusing on casualties undergoing massive transfusion. Serious injury was defined based on an Abbreviated Injury Scale score of 3 or greater by body region. The authors constructed multiple imputations of the model for risk prediction development. Efforts were made to internally validate the model.

RESULTS: Within the data set, there were 15540 patients, of which 1238 (7.9%) underwent massive transfusion. In the body region injury scale model, explosive injuries (odds ratio [OR], 3.78), serious extremity injuries (OR, 6.59), and tachycardia >120/min (OR, 5.61) were most strongly associated with receiving a massive transfusion. In the simplified model, major amputations (OR, 17.02), tourniquet application (OR, 6.66), and tachycardia >120 beats/min (OR, 8.72) were associated with massive transfusion. Both models had area under the curve receiver operating characteristic values of greater than 0.9 for the model and bootstrap forest analysis.

CONCLUSION: In the body region injury scale model, explosive mechanisms, serious extremity injuries, and tachycardia were most strongly associated with massive transfusion. In the simplified model, major amputations, tourniquet application, and tachycardia were most strongly associated.

Hemorrhage is the leading cause of potentially survivable death in US military combat casualties. Blood transfusions are frequently administered during the resuscitation of severely wounded combat casualties, especially within the first 6 to 12 hours, when death from hemorrhage is most likely to occur.[1–3] One definition of massive transfusion is 10 or more units of red blood cells (RBCs) or whole blood (WB) within the first 24 hours of admission.[2,3] Current US military damage control resuscitation guidelines recommend the use of WB or component therapy that mimics WB with RBCs, plasma, and platelets in a 1:1:1 ratio,[3–5] which has been associated with improved survival from traumatic injury. Timely activation of massive transfusion protocols is imperative during resuscitation. However, in the combat setting, at times there is limited access to cold-stored WB or blood components. During those times, walking blood banks are activated to supply fresh WB. While walking blood bank activation

ABBREVIATIONS: DoDTR = Department of Defense Trauma Registry; ICD-9 = International Classification of Diseases, 9th edition; LTOWB = low-titer group O whole blood; POI = point of injury; SI = shock index.

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can occur relatively quickly, it still takes time to identify, screen, and obtain blood. Earlier activation will likely result in earlier resuscitation with fresh WB.[6]

Approximately 5% of all patients admitted to military treatment facilities in Iraq and Afghanistan require massive transfusions.[7–9] There is increased survival with early activation of massive transfusion protocol, and it is imperative to identify those casualties who are likely to receive a massive transfusion in the prehospital setting at the point of injury (POI).[7,9–11] Multiple prediction and scoring models have been developed in efforts to help identify the need for massive transfusion in trauma patients in both civilian and combat settings, including the Trauma-Associated Severe Hemorrhage Score system, the Emergency Transfusion Score, the McLaughlin Score, and the Assessment of Blood Consumption scoring system.[2,11–13] Each of these predictive systems vary in their specificity and range of preidentification factors, such as decreased blood pH and depleted hemoglobin, used to predict the need for massive transfusion.[2,12] Both the Trauma-Associated Severe Hemorrhage (TASH) Score and Assessment of Blood Consumption (ABC) scoring system also incorporate injury mechanisms, including penetrating injury and unstable/open fracture, as factors that contribute to the need for massive transfusion.[11,12] While they are useful prognostic tools, these existing scoring systems have several important limitations. First, they use laboratory data that are unavailable in the prehospital combat setting.[2,11–14] They similarly make use of imaging data to clarify injury patterns for prognostic purposes. Finally, their derivation used data from the civilian setting that do not feature the signature injury of the recent conflicts: explosives.[9] Explosive injuries may be associated with a higher incidence of coagulopathy, which can significantly increase the need for massive transfusion.[15] Furthermore, given that noncompressible torso hemorrhage accounts for 67% of potentially survivable death due to hemorrhage,[34] it brings to question whether penetrating torso wounds would be an indicator. A military unique scoring system that factors in combat-specific injury mechanisms and patterns is therefore needed to accurately and rapidly identify patients in a combat environment who would benefit from massive transfusion.

Goal of this study

We developed a risk prediction model for US and coalition personnel likely to receive massive transfusion to guide the prehospital medical personnel decision making for starting blood in the field.

METHODS

Ethics

The US Army Institute of Surgical Research regulatory office reviewed protocol H-16-005 and determined it was exempt from Institutional Review Board oversight. We obtained only deidentified data.

Data acquisition

We used a series of emergency department (ED) procedural and diagnostic codes to search for subjects within the Department of Defense Trauma Registry (DoDTR) for the creation of the data set, which we have previously described.[16] This is a secondary analysis of the previously published data focusing on US forces, other nations' forces, and government military contractors that received at least 10 units or more of red blood cells (RBCs) or whole blood within the first 24 hours of hospitalization.

DoDTR description

The DoDTR, formerly known as the Joint Theater Trauma Registry, is the data repository for the Department of Defense of trauma-related injuries.[16–20] The DoDTR includes data for demographics, injury-producing incidents, diagnoses, treatments, and outcomes following injuries. The registry includes US/non-US military and US/non-US civilian personnel from the point of injury to final disposition during war and peacetime. The DoDTR includes patients admitted to a Role 3 (fixed-facility) or forward surgical team with an injury diagnosis from the International Classification of Diseases, 9th edition (ICD-9) between 800 and 959.9, near-drowning/drowning with associated injury (ICD-9 994.1) or inhalational injury (ICD-9 987.9) and trauma occurring within 72 hours from presentation to a facility with surgical capabilities. The registry defines prehospital as any location before reaching a Role 3 military treatment facility to include the Role 1 (POI, casualty collection point, battalion aid station) and Role 2 (temporary limited-capability forward-positioned hospital inside combat zone without surgical support).

Data analysis

We defined serious injuries as those resulting in an Abbreviated Injury Scale (AIS) score of 3 or greater by body region.[21,22] We compared study variables using a t test for continuous variables expressed as means with standard deviations, Wilcoxon rank-sum test for ordinal variables expressed as medians and interquartile ranges, and chi-squared test for nominal variables expressed as numbers and percentages. Odds ratios (ORs) are presented with 95% confidence intervals. For reporting of univariable ORs, we used a binary regression model. We performed all analyses with computer software (Excel version 10, Microsoft;) JMP Statistical Discovery version 13, SAS).

We used a series of variables for model development, mechanism of injury (explosive, gunshot wound, motor vehicle collision), tourniquet application, serious injury to the head/neck, face, thorax, abdomen, extremities, and skin, hypotension (<90 mm Hg systolic), tachycardia (120/min or greater), and major amputations proximal to elbow or knee (Appendix 1). We ran multiple imputations of this model for development. To validate the findings of this model, we performed a bootstrap forest analysis. We operated under the assumption that prehospital care was documented correctly.

TABLE 1. Description of casualties undergoing massive transfusion versus the remainder of the data set

		Baseline cohort (n = 14299)	Massive transfusion cohort (n = 1238)	p value
	Age	25 (22-30)	24 (21-38)	<0.001
	Male	13930 (97.4)	1221 (98.6)	0.008
Patient Category	US forces, n (%)	10734 (75.0)	931 (75.1)	<0.001
	Coalition, n (%)	2026 (14.1)	233 (18.8)	
	Contractors, n (%)	1541 (10.7)	75 (6.0)	
Mechanism of Injury	Explosion, n (%)	8446 (59.0)	1035 (83.5)	<0.001
	Gunshot wound, n (%)	2220 (15.5)	173 (13.9)	
	MVC, n (%)	1009 (7.0)	11 (1.0)	
	Other, n (%)	2626 (18.3)	20 (1.6)	
Location	Afghanistan, n (%)	10031 (70.1)	929 (74.9)	<0.001
	Iraq, n (%)	4270 (29.8)	310 (25.0)	
Injury score	Composite, n (range)	5 (2-11)	25 (18-34)	<0.001
Serious injuries by body region	Head/neck, n (%)	1296 (9.0)	219 (17.6)	<0.001
	Face, n (%)	47 (0.3)	13 (1.0)	<0.001
	Thorax, n (%)	1147 (8.0)	327 (26.3)	<0.001
	Abdomen, n (%)	603 (4.2)	341 (27.5)	<0.001
	Extremities, n (%)	2453 (17.1)	1034 (83.4)	<0.001
	Skin, n (%)	225 (1.5)	117 (9.4)	<0.001
Outcome	Survival, n (%)	14080 (98.4)	1082 (87.3)	<0.001

MVC = motor vehicle collision.

As explosives, gunshot wounds, and motor vehicle collisions accounted for most casualties in our data set, only these three mechanisms of injury were included as mutually exclusive, binary variables.[16] We excluded other mechanisms of injury to avoid variable dissociation from the model. Variables without a p value of at least 0.20 were excluded from development of the models. Vital sign values are based on the lowest documented blood pressure (<90 mm Hg vs. ≥90) and the maximum documented heart rate (<120/min vs. ≥120/min) within the ED due to limitations in prehospital documentation of vital signs.[23] We defined a major amputation as proximal to the knee or elbow.

RESULTS

Our initial search from January 2007 to August 2016 captured 28222 casualties, which we have previously described. We removed host national personnel from our data set, of which 15540 casualties remained: US forces (75.1%), other nations' forces (14.5%), and contractors (10.3%). Within that 15540, a total of 1238 (7.9%) underwent massive transfusion (Table 1).

Tourniquet application occurred more frequently (64.8% vs. 11.0%, $p < 0.001$) in massive transfusion recipients. Upper extremity amputations and lower extremity amputations proximal to the digit occurred more frequently in the massive transfusion group (9.3% vs. 0.5%, $p < 0.001$; 49.6% vs. 2.3%, $p < 0.001$, respectively). Upper extremity amputations at or above the elbow and lower extremity amputations at or above the knee were higher in the massive transfusion group (3.6% vs. 0.1%, $p < 0.001$; 29.9% vs. 0.5%, $p < 0.001$, respectively). Tachycardia over 120 per minute occurred more frequently (59.0% vs. 8.5%, $p < 0.001$), with similar findings for hypotension less than 90 mm Hg systolic (29.5% vs. 1.9%, $p < 0.001$).

In our first model development, we focused on serious injuries based on the AIS by body region. We found that explosive injuries (OR, 3.78), serious extremity injuries (OR, 6.59), and tachycardia with a rate of greater than 120/min (OR 5.61) were most strongly associated with receiving a massive transfusion (Table 2). Our area under the curve receiver operating characteristic (AUROC) for this model was 0.943 with a sensitivity of 0.89 and specificity of 0.86. Per bootstrap forest analysis, our model had strong fit for predicting both massive transfusion recipients (AUROC, 0.945) and nonrecipients (AUROC, 0.945).

We then developed a simplified model without the use of AIS measurements and limited the injury assessment to only that of major amputations (upper or lower extremity). We found that amputations (OR, 17.02), tourniquet application (OR, 6.66), and tachycardia greater than 120 beats/min (OR, 8.72) were all associated with massive transfusion (Table 3). Our AUROC for this model was 0.87, with a sensitivity of 0.84 and specificity of 0.82. On bootstrap forest analysis, our model had strong fit for predicting both

TABLE 2. Multivariable analysis for the Abbreviated Injury Scale–based model

Variable	Odds ratio (95% CI)
Mechanism of injury—explosive	3.78 (1.96-7.30)
Mechanism of injury—gunshot wound	3.09 (1.55-6.17)
Serious head/neck injury	1.72 (1.15-2.57)
Serious facial injury	6.80 (1.39-33.14)
Serious thorax injury	2.81 (2.01-3.93)
Serious abdomen injury	4.44 (3.15-6.27)
Serious extremity injury	6.59 (4.81-9.04)
Serious skin injury	3.56 (1.91-6.62)
Tourniquet application	4.61 (3.43-6.18)
Hypotension (systolic <90 mm Hg)	2.18 (1.53-3.12)
Tachycardia (heart rate > 120 beats/min)	5.61 (4.33-7.27)

TABLE 3. Multivariable analysis for the simplified model

Variable	Odds ratio (95% CI)
Major amputation (upper or lower)	17.02 (12.94-22.38)
Tourniquet application	6.66 (5.73-7.74)
Tachycardia (heart rate > 120 beats/min)	8.72 (7.51-10.14)

massive transfusion recipients (AUROC, 0.87) and nonrecipients (AUROC, 0.87).

DISCUSSION

We report indicators that may allow for early prehospital prediction for massive transfusion requirement in the deployed combat setting. In our study of US casualties presenting to EDs in Iraq and Afghanistan, massively transfused patients comprised 7.9% of the population.[8,9] This is a comparatively larger proportion relative to previous studies that report a massive transfusion rate of 4.8% in casualties reporting to combat support hospitals and is likely a factor of our registry search methods isolating only casualties with an intervention performed.[1] Tourniquet and hemostatic applications were higher in the massive transfusion group, as well as airway intervention, prehospital tranexamic acid and prehospital blood product administration. Both upper and lower extremity amputations were also more prevalent in the massive transfusion group. Using ED vitals as a surrogate for the prehospital setting due to limitations in prehospital data availability, we saw a significant contribution of tachycardia and hypotension as predictors of receipt of massive transfusion.

Several studies have identified hypotension and tachycardia as physiological indicators in patients receiving massive transfusion.[11,14] However, hypotension and tachycardia are defined differently. Because of the variability in the definition of hypotension and tachycardia, some have used the shock index (SI) as a method to predict massive transfusion. Zhu et al.[24] recently performed a retrospective analysis using SI and pulse pressure on 102 massive transfusion patients. They found a 0.78 positive predictive value of mortality with pulse pressure less than 45 and an SI greater than 1 was 0.78 for all patients. These data are not directly applicable to the military setting, as their patient population was older (42 years) and had 66% blunt mechanism. A recent study in India of 254 patients used prehospital physiologic measurements to assess accuracy of massive transfusions; the most relevant is the SI.[25] They also used an additional definition of massive transfusion: four or more RBC units within the first 4 hours of hospital admission. The area under the curve was 0.798 (95% confidence interval, 0.739-0.848), which, as a single data point, is lower than our findings.

Other variables that we identified have also been associated with massive transfusion in previous studies. Expectedly, massive transfusion patients in our study were more likely to be injured through explosive mechanisms and had a lower survival rate than the nonmassive transfusion cohort. Massively transfused patients sustained more serious injuries to all body regions. Interestingly, most massively transfused patients (83.4%) sustained serious extremity injuries, compared with only 17.1% of the baseline cohort reporting extremity injuries. These findings are consistent with several other hospital studies and provide more robust information regarding prehospital indicators that may predict the need for massive transfusion in combat casualties. The OR of massive transfusion for torso wounds fell between 2.70 (2.19-3.34) and 4.24 (3.38-5.34). This is much lower than the extremity wounding but is still a valuable tool the combat medic or corpsman at the POI if evaluating for the possibility of massive transfusion.

As the recognition of early blood transfusion on mortality in the critically wounded becomes clear, efforts began to move blood and blood components into the prehospital setting. Medical evacuation was the first to use it on a regular basis. However, the Committee on Tactical Combat Casualty Care changed its guidelines in 2014 to recommend WB as the fluid resuscitation of choice.[26] This led to the 75th Ranger Regiment developing a fresh WB program using low-titer group O whole blood (LTOWB).[27] As this program grew and matured, with the assistance of the Armed Services Blood Program, the US Army Institute of Surgical Research, and US Central Command, cold-stored LTOWB began to be shipped into Afghanistan, with the first unit being used within 1 week.[28] The prehospital use of LTOWB is currently being evaluated. However, within the past 3 years, efforts have identified that medical evacuation use of blood products can have an impact on mortality. Shackelford et al.[29] demonstrated a sixfold early survival benefit when any blood product is given within 34 minutes of wounding. Kotwal[30,31] has published studies that have recognized the benefit of early prehospital blood transfusions. Finally, Howard et al.[32] did a second look at Kotwal's Golden Hour Policy paper, which identified 83% lower odds of mortality for casualties with injury severity score of 25 or greater.

Our objective is to identify prehospital predictors of massive transfusion that are concrete and rapidly and easily assessable. As we aim to develop a prediction model using only data that are available in the prehospital setting, variables that require testing at a hospital were not analyzed for this study. Our results build upon previously identified variables in developing a potentially reliable prediction model that will help frontline trauma providers in identifying patients that likely require massive transfusion using information readily available to them in the prehospital combat setting.

Hemorrhage is the leading cause of potentially survivable deaths on the battlefield, demonstrating the need for rapid control of hemorrhage in the deployed combat environment.[33] Though Kotwal and Howard demonstrated that the Golden Hour Policy was effective in decreasing mortality, in the future, we may not have that ability. Peer-to-peer conflicts have historically resulted in longer evacuation times. Therefore, establishing a reliable prediction model for massive transfusion in casualties will provide better guidance for the different echelons of care and may significantly reduce mortality in casualties. In addition to benefiting those patients that necessitate massive transfusion, this model would help avoid unnecessarily exposing patients to the potential harms of blood transfusion when it is not needed. This model will assist in appropriately allocating limited resources, an essential objective in the deployed combat setting. A predictive model will be especially applicable for the anticipated setting of future warfare in which the availability of fewer deployable hospital structures will likely lead to prolonged field care time. This highlights a need for high-level treatment guidelines for medical providers on the frontline. This study adds to the literature valuable information regarding potential predictors of the need for massive transfusion in severely injured patients. Further study is needed to effectively establish reliable prehospital predictors for massive transfusion in severely injured patients and combat casualties.

There are several limitations of this study. It is a retrospective analysis limited by data available in a combat setting. The prehospital setting in combat is rather austere and the majority of medics rely on rudimentary methods to determine if a casualty requires resuscitation. The Tactical Combat Casualty Care (TCCC) guidelines use altered mental status and/or lack of a radial pulse as indicators of hemorrhagic shock. Furthermore, the majority of medics do not carry a blood pressure cuff at the POI. This is why other, previously published predictive models have limitations in the combat prehospital setting, although it has also limited the development of this model. Robust physiologic data were not available on all patients in the prehospital setting so we had to rely on the ED vital signs as a surrogate. While we believe this is a reasonable surrogate given the limitations in prehospital data, we do not have combat-based data to support this supposition. However, due to the lack of blood and other evidence-based resuscitation tools, it is unlikely that the vital signs changed drastically before arrival, but there is a potential that they became worse. In a 2018 study, of 705 patients who had prehospital data, 134 had documented hypotension; of those, 42 patients had fluids administered, none of whom had a blood transfusion documented.[34] Additionally, factors that have been included in previous model development studies of massive transfusion patients including penetrating mechanism and presence of multiple injuries were not analyzed in this study. However, we did include explosives, which are frequently a mix of penetrating and blunt injuries. We used AIS by body region for estimating injury severity. AIS values are calculated after the care has occurred and the trained personnel score the injury based on all available information—for example, radiology data, operative reports, outcome, and so on. These values may not directly translate over into an assessment by medical personnel in the prehospital setting in real time. The data that were retrieved point to a potential starting place for a functional prediction model with information that is easily obtained in the prehospital combat setting. Furthermore, we are limited by documentation gaps within the registry, which were previously described.[35] Strengths of this study include the size of the study population as well as the general relevance of our results to the target combat casualty population. While there are newer definitions for massive transfusion, the Department of Defense currently uses 10 units within 24 hours. Also, because the number of POI blood transfusions are so few, it would have been difficult to determine how many casualties received a massive transfusion after receiving a blood product at the POI.

CONCLUSIONS

In our body region injury scale model, we found that explosive mechanisms, serious injuries to the extremities, and tachycardia were most strongly associated. In our simplified model, we found that major amputations, tourniquet application, and tachycardia were most strongly associated. Both of these models require external validation.

A. APPENDIX – INPUT VALUES FOR MODEL DEVELOPMENT

Mechanism of injury*
- Explosive
- Gunshot wound
- Motor vehicle collision

Tourniquet application
Serious injury to the head/neck
Serious injury to the face
Serious injury to the thorax
Serious injury to the abdomen
Serious injury to the extremities
Serious injury to the skin
Hypotension (<90 mm Hg systolic)†
Tachycardia (≥120 beats/min)†
Major amputations proximal to elbow or knee

*Mechanisms of injury were mutually exclusive.
†Binary variables.

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CONFLICT OF INTEREST

The authors have disclosed no conflicts of interest.

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