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ORIGINAL RESEARCH

Limits of Transfusion Burden as a Predictor of Mortality in Severely Injured Trauma Patients

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Background: Severe hemorrhage remains a leading cause of early and preventable mortality in trauma patients. While massive transfusion protocols (MTPs) have improved resuscitation strategies, the prognostic value of transfusion burden alone remains unclear. This study evaluated the reliability of total blood product and blood cooler issuance as predictors of mortality in trauma MTP and assessed the added prognostic value of early laboratory parameters, neurological status on arrival and injury severity scores.

Methods: We conducted a retrospective cohort study of adult trauma patients requiring MTP activation upon arrival to a Level I trauma center between January 2023 and May 2025. Demographic, clinical, transfusion, and first laboratory data obtained within 15 to 30 minutes of presentation were analyzed. Blood cooler utilization was categorized as ≤5, 6–10, or >10 coolers. Outcomes were defined as survival or death at the conclusion of MTP.

Results: A total of 135 patients were included; 36 (26.7%) expired during MTP activation. Non-survivors received significantly greater numbers of red blood cells, plasma, and total blood products requiring higher numbers of blood coolers. They also demonstrated more severe coagulopathy, higher lactate levels, greater metabolic derangement, lower platelet counts, hypothermia, lower Glasgow Coma Scale scores, and higher injury severity. Kaplan Meier and Cox regression analyses showed no statistically significant association between cooler category and survival. A transfusion threshold of ≥36 total blood units yielded modest predictive performance (accuracy 69.6%) using Youden's index. Integration of laboratory markers significantly improved mortality prediction models (AUC from 0.62 to 0.78).

Conclusion: In trauma patients requiring MTP activation, mortality was driven primarily by injury severity, neurologic status, and early physiologic derangements. Blood product utilization demonstrated limited prognostic value in isolation but contributed meaningfully when combined with laboratory and clinical parameters. Blood cooler notifications may serve as useful adjuncts to prompt timely clinical reassessment.

Keywords: massive transfusion protocol, transfusion medicine, trauma, blood transfusion

Introduction

Severe hemorrhage is the leading cause of early and preventable mortality in trauma setting, and severe trauma poses a significant challenge to global public health as it is estimated to be responsible for 8% of all mortalities each year.[1] Over the last 20 years, several efforts were made to enhance the availability, timing and administration of blood products to trauma patients in both civilian and military settings and assessed the different outcomes associated.[2,3] Massive transfusion protocols (MTPs) were designed and extensively revised to address this imperative need in timely and safely manners, especially that recent studies showed uncontrolled hemorrhage contribute to approximately 50% of mortality within the initial 24 hours post trauma.[4] The definition of MTP is dynamic and includes several parameters: transfusion of more than 10 units of red blood cells (RBCs) within 24 hours or administration of blood products exceeding 50% of the patient's total blood volume over a 3 hour period or transfusion of more than 4 units of RBCs within a single hour in cases of ongoing hemorrhage.[4]

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MTPs follow a specific ratio, and the most extensively studied and established ratio is 1:1:1 and 2:1:1 (RBC: Plasma: random donor platelet), both which have been established as equivalent in terms of mortality at 24 hours and 30 days.[5] Importantly, the scope of MTP extends beyond component ratios to include timely activation and coordinated delivery of blood products. Current American College of Surgeons guidelines recommend early initiation of MTP, with blood coolers delivered within 15 minutes of protocol activation.[6] Furthermore, the implications of viscoelastic testing modalities such as thromboelastographgy (TEG) and rotational thromboelastometry (ROTEM) have tremendously helped in guiding hemostatic resuscitation in addition to the role of medications such as tranexamic acid (TXA), pro- thrombin complex (PCC) and activated factor VIIa which have additional benefits in selected clinical scenarios.[3]

The risk of mortality in trauma patients depends on several factors which include age, mechanism of injury, initial Glasgow coma scale (GCS), ISS, TRISS and number of RBC transfusions.[7,8] Blood products are critical and limited healthcare resources, and shortages continue to pose significant challenges for blood banks and transfusion medicine services.[9] For example, in July 2024, the American Red Cross reported a decline of more than 25% in the national blood supply, prompting an urgent appeal for blood donations, particularly for type O blood and platelets.[10] These shortages have prompted consideration of strategies to limit blood product utilization beyond defined thresholds, as excessive use of these limited resources may compromise availability for ongoing massive transfusion protocols (MTPs) and subsequent patients in need. This concern is particularly relevant in the setting of ultra-massive transfusion (UMT), commonly defined as the administration of more than 20 units of red blood cells within a 24 hour period.[11,12] Prior studies have demonstrated a strong association between extreme transfusion requirements and mortality. In the overall trauma population, transfusion of approximately 56 RBC or whole blood units has been associated with a 90% predicted 24 hours mortality, with this threshold increasing to approximately 71 units among patients with penetrating injuries. Furthermore, earlier work reported 100% mortality among patients who received 81–90 RBC units within the first 4 hours of admission. However, significant survival can still be achieved among patients requiring extremely large volumes of blood transfusion.[11,13] In addition to number of blood units transfused, several studies investigated laboratory values like lactate, base deficit, prothrombin time (PT), partial thromboplastin time (PTT), INR, D- dimer, hemoglobin, leukocyte count, platelet count, and the new biomarker high mobility group box 1 (HMGB-1, ie. amphoterin) and their utilization as predictors of mortality.[4,14]

In this manuscript, we sought to evaluate the reliability of the total number of transfused blood units as a predictor of mortality in severely injured trauma patients. We also aimed to assess the prognostic value of the first laboratory parameters collected on arrival to trauma bay, Glasgow Coma Scale (GCS), and injury severity scores in predicting mortality. Additionally, we examined whether early notifications based on the cumulative number of blood units transfused (assessed in terms of the number of blood coolers issued by the blood bank) impact patient survival by alerting treating physicians to escalating transfusion requirements and providing an opportunity for timely reassessment of clinical trajectory and potential futility.

Massive Transfusion Protocol Process and Notification System

At our institution, trauma bay initially provides 3 units of O negative RBCs and 3 units of liquid A plasma, those units are readily available refrigerated in the trauma bay. Subsequent units are issued from the blood bank and follow a 3:3:1 ratio. Each round includes 3 units of RBCs and 3 units of plasma; odd-numbered rounds include 1 unit of platelets, while even numbered rounds include cryoprecipitate. The blood bank labels the fifth cooler with a sign indicating that it is the fifth cooler being issued and the tenth cooler with a sign indicating that it is the tenth cooler. This process serves to alert the trauma team of the cumulative number of blood product units administered, prompting reassessment of the patient's clinical status and allowing the team to reevaluate the ongoing appropriateness, futility, or continuation of the resuscitation.

Materials and Methods

This study is a retrospective cohort study of adult trauma patient who required activation of the massive transfusion protocol upon arrival to our level I trauma center at the University of South Alabama Medical Center in Mobile, Alabama between January 2023 and May 2025. The study included adult patients (age 18 ≥ years) who were transported either via ground or air within 60 minutes of trauma. They were identified through the institutional trauma registry and cross

referenced with the blood bank database using records of MTP activation to ensure comprehensive inclusion of all patients meeting study criteria during the study period. Patients who were deceased on arrival, who did not require massive transfusion due to minor trauma and did not require comprehensive laboratory testing were excluded.

Electronic medical records and the laboratory information system were reviewed to collect epidemiologic, demographic, clinical, and laboratory data, including the number and type of blood components transfused during MTP activation. All cases had a documented final disposition (survived or deceased) at the conclusion of the MTP code activation.

Demographic and clinical variables included age, initial vital signs upon presentation, Glasgow Coma Scale (GCS) score on admission, Trauma and Injury Severity Score (TRISS), and injury site, type and mechanism. On admission, level of consciousness was assessed using the Glasgow Coma Scale (GCS) and categorized into three groups for analysis. A GCS score of 13–15 was classified as mild, a score of 9–12 as moderate, and a score of 3–8 as severe. Patients were assigned to these categories based on their initial GCS value at presentation, and all subsequent comparisons between groups were made according to this classification.[15] TRISS values were grouped into three risk strata: scores from 0.00 to 0.50 were classified as "low survival", scores from 0.51 to 0.75 as "moderate risk", and scores greater than 0.75 as "high risk." This categorization is in tandem with prior uses of TRISS around the 50% survival threshold to distinguish poor from favorable prognoses and to identify potentially preventable deaths.[16,17]

Transfusion related variables included duration of MTP activation, number and type of blood components transfused (red blood cells, plasma (fresh frozen plasma and liquid plasma group A), platelets and cryoprecipitate) and number of blood bank coolers issued. Accordingly, for analytical purposes, the number of blood coolers issued was categorized as less than or equal to 5 coolers, six to ten coolers, or more than 10 coolers in this manuscript.

Laboratory data were obtained from the first samples collected within 15 to 30 minutes of arrival to the trauma bay and included complete blood count (CBC), ABO/Rh blood group, comprehensive metabolic panel (CMP), coagulation studies (PT, PTT, and INR), liver function tests (ALT and AST), serum lactate, and arterial blood gas (ABG) analysis.

Statistical analyses were performed using RStudio (version 2024.9.0). Comparisons between patients who expired and those who survived at the conclusion of the MTP activation were conducted using Fisher's Exact test and Wilcoxon tests, as appropriate. Survival analysis was performed using Kaplan–Meier methods, with hazard ratios estimated through Cox proportional hazards regression models. Optimal cut-off points were determined using the Youden index for the total number of blood products used during the MTP code. A p value ≤ 0.05 was considered statistically significant.

Results

Our cohort study included a total of 135 adult patients who presented to trauma bay requiring MTP code activation. Ninety-nine patients were alive at the end of the MTP code and 36 expired. Comparative analysis between the two groups revealed statistically significant differences.

Patients who expired during MTP received substantially greater volumes of blood or number of blood products compared with survivors. The median number of red blood cell (RBC) units transfused was significantly higher in the expired group (11.00 [7.00–21.25]) than in the surviving group (7.00 [4.00–13.00]; p = 0.01). Similarly, patients who expired received more plasma (fresh frozen plasma and liquid A plasma) units (10.00 [4.75–19.00] vs. 6.00 [3.00–13.50]; p = 0.04). The total number of all blood units required during MTP was also greater among those who expired, with median of 23.50 [12.75–47.25] compared with 14.00 [7.00–32.50] in survivors (p = 0.04). In addition, the duration of MTP activation was significantly prolonged in the surviving group, with a median duration of 24 hours versus 14 hours among expired patients (p = 0.03). Cooler number utilization during MTP was significantly associated with patient outcome (p = 0.01). Among patients who survived to the end of the MTP, most required five or fewer coolers (78.8%), whereas smaller proportions required six to ten (16.2%) or more than ten coolers (5.1%). In contrast, patients who expired more frequently required higher numbers of coolers, with only 58.3% receiving five or fewer coolers, while 22.2% required six to ten and 19.4% required more than ten coolers. Patients who expired at end of MTP code had significantly lower body temperature compared with non-expired patients (median [IQR]: 35.5°C [34.6–36.0] vs. 36.3°C [35.9–36.7]; $p < 0.01$). Systolic and diastolic blood pressures, heart rate, respiratory rate, and oxygen saturation were comparable between expired and non-expired patients (Table 1).

Table 1 Baseline Demographic and Clinical Characteristics of Trauma Patients Undergoing Massive Transfusion Protocol Activation, Stratified by Survival at the End of the Code Activation

	Alive (n = 99)	**Expired (n = 36)**	***p*-value**
Demographics			
Age, years, median (IQR)	42 (30.00–57.00)	41 (25.75–58.00)	0.45
Male gender, n (%)	79 (79.8)	31 (86.1)	0.56
Race, n (%)			0.19
Asian	0 (0.0)	1 (2.8)	
Black or African American	54 (54.5)	19 (52.8)	
Native American	1 (1.0)	0 (0.0)	
White	40 (40.4)	14 (38.9)	
Other	4 (4.0)	2 (5.6)	
Ethnicity (Not Hispanic/Latino), n (%)	94 (94.9)	34 (94.4)	1.00
Initial Vital Signs			
Temperature, °C, median (IQR)	36.30 (35.88–36.70)	35.50 (34.60–36.00)	<0.01
Systolic blood pressure, mmHg, median (IQR)	92.00 (78.00–110.00)	86.00 (70.00–120.00)	0.42
Diastolic blood pressure, mmHg, median (IQR)	56.50 (44.75, 64.25)	54.50 (36.75, 62.50)	0.28
HR, beats/min, median (IQR)	110.00 (94.00–133.00)	109.00 (77.00–133.00)	0.33
RR, beaths/min, median (IQR)	21.00 (18.00–24.00)	22.00 (18.00–28.00)	0.74
Oxygen saturation, %, median (IQR)	97.00 (92.00–100.00)	94.00 (88.00–98.00)	0.06
Transfusion Characteristics			
RBC units, median (IQR)	7.00 (4.00–13.00)	11.00 (7.00–21.25)	0.01
Plasma units, median (IQR) (Fresh Frozen Plasma and Liquid A Plasma)	6.00 (3.00–13.50)	10.00 (4.75–19.00)	0.04
Platelet units, median (IQR)	1.00 (1.00–2.50)	2.00 (1.00–4.00)	0.02
Cryoprecipitate pools units, median (IQR)	0.00 (0.00–2.00)	2.00 (0.00–2.00)	0.19
Total blood units, median (IQR)	14.00 (7.00–32.50)	23.50 (12.75–47.25)	0.04
Less than 6 coolers issued, n (%)	75 (75.8)	19 (52.8)	0.02
6-10 coolers issued, n (%)	19 (19.2)	10 (27.8)	0.40
More than 10 coolers issued, n (%)	5 (5.1)	7 (19.4)	0.02
Duration of MTP, median (IQR))	1.00 (0.23–1.64)	0.58 (0.10–1.05)	0.03
ABO Blood Group, n (%)			0.89
A	40 (40.4)	13 (36.1)	
B	49 (49.5)	19 (52.8)	
AB	1 (1.0)	0 (0.0)	
O	49 (49.5)	19 (52.8)	
Rh positive, n (%)	50 (50.5)	20 (55.6)	0.75

Patients who expired exhibited significantly more severe coagulopathy, reflected by higher median (IQR) INR values (1.89 [1.38–2.21] vs. 1.33 [1.17–1.53]; p < 0.01), prolonged prothrombin time (18.55 seconds [18.30–22.40] vs. 16.50 seconds [15.30–18.40]; p < 0.01), and extended activated partial thromboplastin time (52.00 seconds [36.75–79.00] vs. 32.00 seconds [29.00–39.00]; p < 0.01). Platelet counts were also significantly lower among expired patients (107.50 × 10^3/μL [67.25–193.25] vs. 272.00 × 10^3/μL [112.00–474.00]; p < 0.01). Metabolic abnormalities were more pronounced in the expired cohort, with significantly higher median (IQR) glucose levels (148.50 mg/dL [101.75–256.75] vs. 108.00 mg/dL [95.00–132.00]; $p < 0.01$), creatinine levels (1.71 mg/dL [1.20–2.24] vs. 0.94 mg/dL [0.64–1.43]; $p < 0.01$), and phosphorus concentrations (6.85 mg/dL [4.48–9.20] vs. 3.70 mg/dL [2.90–4.70]; $p < 0.01$). Lactate levels were markedly elevated in patients who expired (9.30 mmol/L [5.85–17.30] vs. 2.00 mmol/L [1.40–4.55]; $p < 0.01$). The distribution of electrolytes including sodium, potassium, chloride, magnesium and CO2 was statistically significant but within the reference range defined by the laboratory or slightly above the upper limit posing no clinical significance (Table 2). Indicators of injury severity and neurological status further distinguished the two groups. Glasgow Coma Scale

Table 2 Baseline Laboratory Values of Trauma Patients, by Survival Status at the End of the MTP Code

	Alive (n = 99)	**Expired (n = 36)**	***p*-value**
Initial Laboratory Values			
Prothrombin time (PT) (median (IQR))	16.50 (15.30, 18.40)	18.55 (18.30, 22.40)	<0.01
INR (median (IQR))	1.33 (1.17, 1.53)	1.89 (1.38, 2.21)	<0.01
Activated partial thromboplastin time (aPTT (median (IQR))	32.00 (29.00, 39.00)	52.00 (36.75, 79.00)	<0.01
White blood cell count (median (IQR))	9.99 (7.22, 12.91)	9.67 (4.27, 12.86)	0.38
Red blood cell count (median (IQR))	3.23 (2.74, 3.76)	3.26 (2.53, 4.05)	0.57
Hemoglobin (median (IQR))	9.30 (7.75, 10.60)	9.40 (8.00, 11.57)	0.44
Hematocrit (median (IQR))	29.10 (24.05, 32.45)	29.15 (24.28, 35.00)	0.45
Mean cell volume (median (IQR))	89.00 (85.05, 93.20)	90.35 (87.38, 93.97)	0.2
Mean cell hemoglobin (median (IQR))	29.20 (28.45, 29.95)	29.50 (28.90, 30.30)	0.07
Mean cell hemoglobin concentration (median (IQR))	32.20 (31.35, 33.30)	32.35 (31.67, 33.10)	0.88
Red cell diameter (median (IQR))	15.70 (14.40, 16.55)	15.20 (14.05, 15.93)	0.25
Red cell distribution width (median (IQR))	50.50 (45.00, 55.50)	49.55 (46.90, 51.80)	0.66
Platelet count (median (IQR))	272.00 (112.00, 474.00)	107.50 (67.25, 193.25)	<0.01
Mean platelet volume (median (IQR))	9.90 (9.40, 10.60)	10.10 (9.70, 10.80)	0.30
Glucose (median (IQR))	108.00 (95.00, 132.00)	148.50 (101.75, 256.75)	<0.01
Blood urea nitrogen (median (IQR))	15.50 (11.00, 24.75)	15.00 (12.00, 24.50)	0.89
Creatinine (median (IQR))	0.94 (0.64, 1.43)	1.71 (1.20, 2.24)	<0.01
Sodium (median (IQR))	140.50 (137.00, 144.75)	146.50 (142.00, 153.75)	<0.01
Potassium (median (IQR))	3.90 (3.62, 4.40)	4.40 (3.82, 5.35)	<0.01
Chloride (median (IQR))	107.00 (103.25, 111.00)	113.50 (104.50, 119.75)	0.02
CO2 (median (IQR))	26.00 (22.00, 28.00)	17.50 (13.25, 22.00)	<0.01
Calcium (median (IQR))	8.80 (8.20, 9.30)	8.75 (7.75, 9.65)	0.77

(*Continued*)

Table 2 (Continued).

	Alive (n = 99)	Expired (n = 36)	*p*-value
Magnesium (median (IQR))	2.00 (1.80, 2.20)	2.20 (1.90, 2.58)	<0.01
Phosphorous (median (IQR))	3.70 (2.90, 4.70)	6.85 (4.48, 9.20)	<0.01
Albumin (median (IQR))	2.70 (1.80, 3.00)	2.30 (1.72, 3.03)	0.55
Total bilirubin (median (IQR))	0.70 (0.30, 1.10)	0.45 (0.30, 0.60)	0.08
Alkaline phosphatase (median (IQR))	70.00 (52.00, 96.00)	65.00 (47.25, 80.50)	0.12
Alanine Aminotransferase (ALT) (median (IQR))	86.00 (39.00, 221.00)	217.00 (54.50, 737.50)	0.07
Aspartate Aminotransferase (AST) (median (IQR))	130.00 (49.00, 378.00)	257.00 (70.25, 945.75)	0.06
Lactate (median (IQR))	2.00 (1.40, 4.55)	9.30 (5.85, 17.30)	<0.01

(GCS) category at MTP activation was significantly associated with patient outcome ($p < 0.01$). Among patients who survived to the end of the MTP, the majority presented with mild GCS scores (53.5%), followed by severe (39.4%) and moderate (7.1%) categories. In contrast, patients who expired were predominantly classified as having severe GCS scores (83.3%), with substantially fewer patients in the mild (13.9%) and moderate (2.8%) categories. In contrast, TRISS risk stratification showed a significant association with mortality, with expired patients more commonly classified as high risk (52.5% vs. 19.4%) and less frequently classified as low risk (37.4% vs. 75.0%; $p = 0.001$) (Table 3).

Table 3 Injury Severity and Characteristics Stratified by Survival Status at the End of MTP Code Activation

	Alive (n = 99)	Expired (n = 36)	*p*-value
Injury Severity and Characteristics			
GCS, median (IQR)	13.00 (3.00–15.00)	3.00 (3.00–5.00)	<0.01
GCS category, n (%)			<0.01
Mild	53 (53.5)	5 (13.9)	
Moderate	7 (7.1)	1 (2.8)	
Severe	39 (39.4)	30 (83.3)	
TRISS, median (IQR)	0.79 (0.14–0.95)	0.11 (0.00–0.46)	<0.01
TRISS Category More than 50%, n (%)	62 (62.6)	9 (25.0)	<0.001
TRISS category, n (%)			<0.01
	Low risk	37 (37.4)	27 (75.0)
	Moderate risk	10 (10.1)	2 (5.6)
	High risk	52 (52.5)	7 (19.4)
Injury Location, n (%)			
Abdomen	37 (37.4)	10 (27.8)	0.40
Chest	50 (50.5)	24 (66.7)	0.14
Upper extremities	18 (18.2)	6 (16.7)	1.0

(*Continued*)

Table 3 (Continued).

	Alive (n = 99)	Expired (n = 36)	*p*-value
Lower extremities	26 (26.3)	3 (8.3)	0.46
Pelvis/groin	30 (30.3)	8 (22.2)	0.48
Head/neck	20 (20.2)	11 (30.6)	0.05
Neck only	2 (2.0)	2 (5.6)	0.62
Injury type, Penetrating, n (%)	47 (47.5)	16 (44.4)	0.907
Injury Mechanism, n (%)			0.54
Fall	4 (4.0)	3 (8.3)	
Gunshot	40 (40.4)	15 (41.7)	
Motor Vehicle Accident	37 (37.4)	15 (41.7)	
Other Blunt Mechanism	6 (6.1)	0 (0.0)	
Other Penetrating Mechanism	7 (7.1)	1 (2.8)	
Pedestrian	5 (5.1)	2 (5.6)	

To evaluate whether cooler utilization, as a surrogate for the number of blood units transfused, was associated with survival at the end of MTP code, we performed Kaplan- Meier survival analysis and Cox proportional hazards regression using cooler category as the sole predictor. No additional covariates were included, as the objective of this analysis was to assess the predictive value of cooler usage (number of blood units transfused) alone. Survival differences between groups were assessed using the Log rank test. Cox regression results are presented as hazard ratios (HR) with 95% confidence intervals (CI). The Kaplan Meier survival analysis included the 135 patients distributed across three cooler categories: Less than six coolers (n = 99), Six to ten coolers (n = 24), and more than ten (n = 12). The number of observed events (expired) was 21 for the first group, 8 for the second group, and 7 for the third group. Median survival could not be estimated for less than six coolers group due to insufficient events, whereas the median survival for six to ten group was 2.45 units (95% CI: 1.67- NA) and for more than 10 group was 1.80 units (95% CI: 1.50- NA). Overall, no statistically significant differences in survival were observed between cooler types (Figure 1). Cox proportional hazards regression analysis was performed to evaluate the association between blood cooler utilization and time to mortality at end of MTP (Table 4). Compared with patients who received fewer than 6 coolers (reference group), receipt of 6–10 coolers was not significantly associated with mortality (HR 1.18; 95% CI, 0.52–2.67; p = 0.69). Similarly, receipt of more than 10 coolers was associated with a higher, but non-significant, hazard of death (HR 1.77; 95% CI, 0.75–4.19; p = 0.19). Overall, the model demonstrated limited discriminatory ability (concordance = 0.48), and global tests of model fit were not statistically significant (likelihood ratio p = 0.50; Wald p = 0.40; score test p = 0.40).

A Youden index was applied to identify an optimal cutoff for the total number of units transfused during a massive transfusion protocol (MTP) to predict mortality (expired at the end of MTP code). The optimal cutoff identified was ≥36 units. At this threshold, the sensitivity was 44.4%, specificity 78.8%, and overall accuracy 69.6% (Figure 2).

Receiver operating characteristic (ROC) curve analysis was performed to evaluate the predictive ability of the total number of blood products for in-hospital mortality. When considered alone, the number of blood units transfused demonstrated modest discriminatory performance, with an area under the curve (AUC) of 0.62. Incorporation of additional clinical and laboratory parameters, including prothrombin time (PT), activated partial thromboplastin time (APTT), creatinine, and lactate, substantially improved model discrimination, increasing the AUC to 0.78. These findings indicate that while number of blood products alone provides limited prognostic information, integration of physiological and laboratory data markedly enhances the ability to predict mortality in trauma patients (Figure 3).

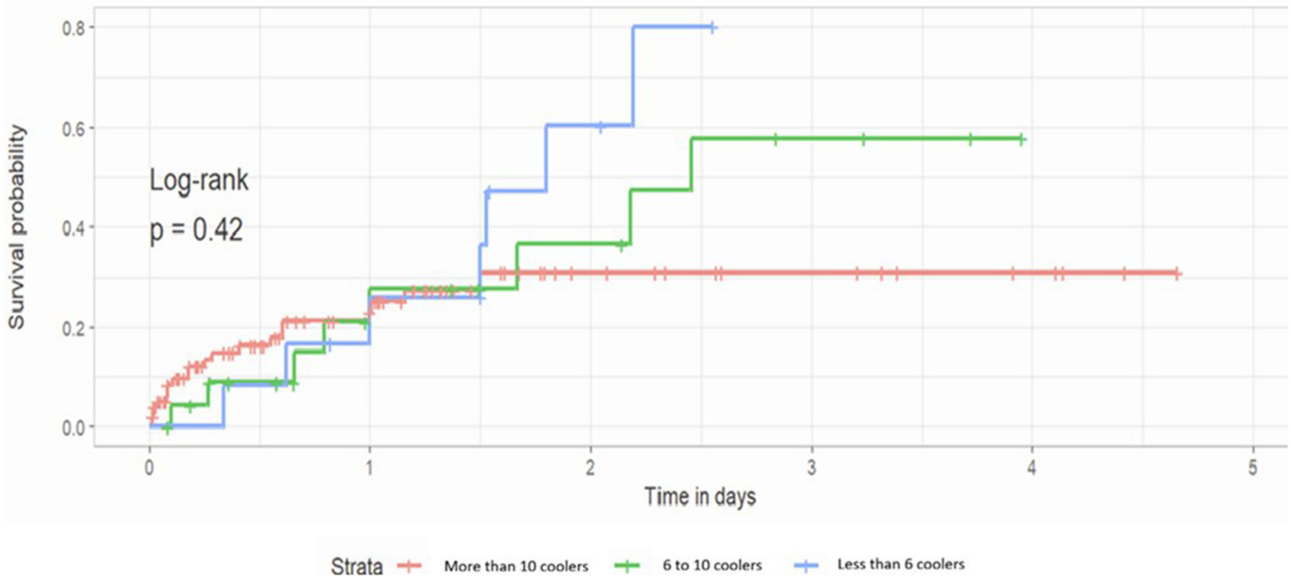

Figure 1 Kaplan–Meier survival curves by cooler category. No significant differences in survival were observed between groups indicating that cooler utilization (number of blood units transfused) alone is not a reliable predictor.

Discussion

In this study, several clinical, laboratory, and resuscitation related factors distinguished patients who survived at the end of the massive transfusion protocol (MTP) activation from those who expired. Overall, the findings highlight that mortality in the setting of massive hemorrhage is closely linked to both the severity of injury and the physiologic derangements present at admission, as well as the intensity of resuscitative efforts required.

Patients who expired required substantially greater blood units compared with survivors ultimately leading to more blood coolers issued. This pattern is consistent with the well-recognized association between high transfusion requirements and increased mortality in trauma related hemorrhages.[11,18] The higher total blood product utilization in the expired group likely reflects both greater hemorrhage severity and more profound hemodynamic instability. Interestingly, despite receiving fewer blood products, survivors had a significantly longer duration of MTP activation. This may suggest that prolonged but controlled resuscitation is more feasible in patients with less catastrophic injury, whereas those who expired may have deteriorated rapidly despite aggressive early transfusion.

Marked differences in initial laboratory parameters further underscore the severity among patients who expired. These individuals presented with significantly more pronounced coagulopathy, as evidenced by elevated INR, prolonged APTT and lower platelet count. Coagulopathy is a central component of the "lethal triad" in trauma and is strongly associated with mortality.[19,20] Similarly, metabolic derangements including elevated glucose, creatinine, phosphorus and particularly lactate were more severe in the expired cohort. Lactate levels in the expired group were more than fourfold higher than in survivors, reflecting severe tissue hypoperfusion and shock. Although differences reached statistical significance between the two groups for sodium, potassium, chloride, CO2 and magnesium, all values remained within reference ranges or slightly higher than the upper limit posing no clinical significance, suggesting limited clinical relevance in predicting the outcome of MTP.

Table 4 Cox Proportional Hazard Regression Analysis Based on Cooler Utilization (Number of Blood Units Transfused)

Variable	Hazard Ratio (HR)	95% Confidence Interval	p-value
<6 coolers	Reference	-	-
6–10 coolers	1.18	0.52–2.67	0.69
>10 coolers	1.77	0.75–4.19	0.19

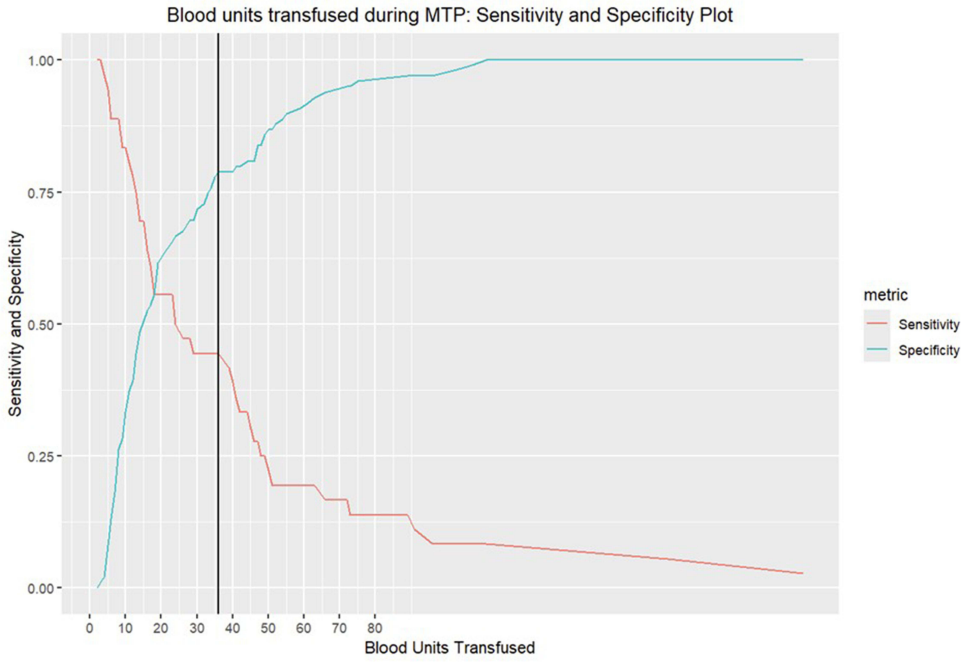

Figure 2 Youden index–derived cutoff for total units transfused during MTP predicting mortality. A threshold of ≥36 units yielded 44.4% sensitivity, 78.8% specificity, and 69.6% accuracy.

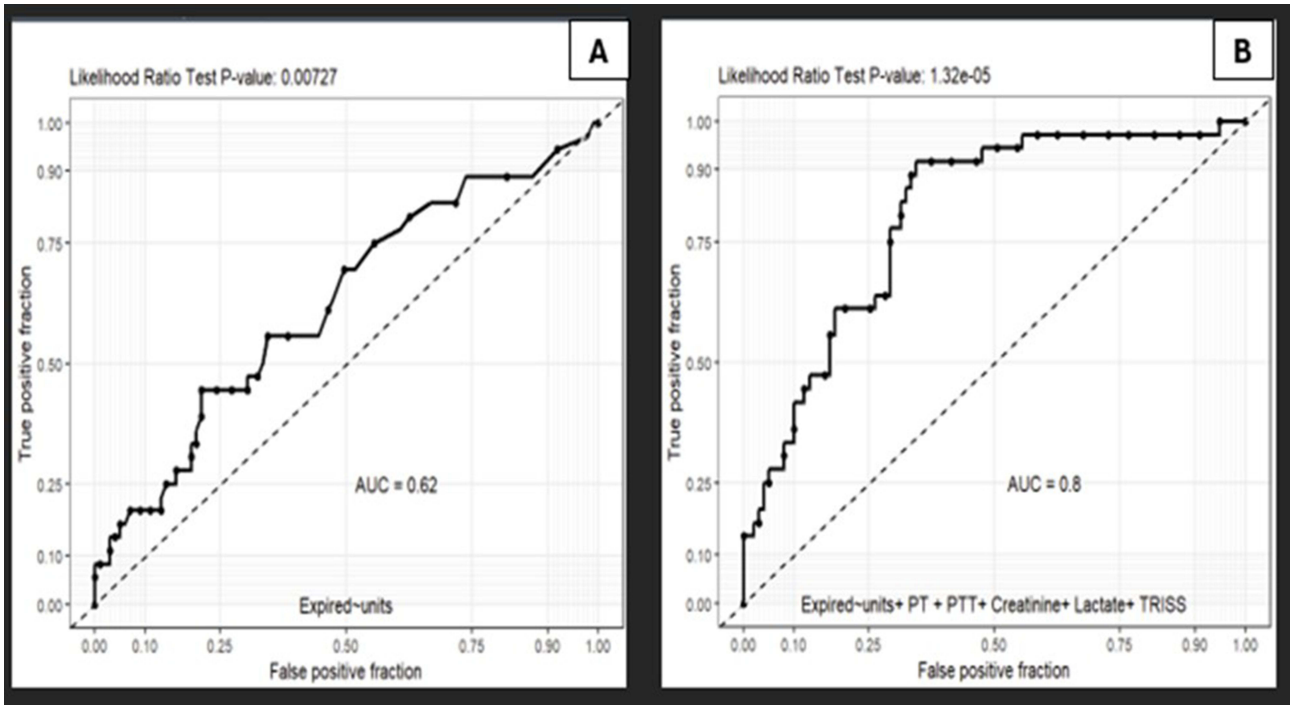

Figure 3 (**A**) ROC curve for prediction of mortality (expired) based on total number of blood units (AUC = 0.62). (**B**) ROC curve based on total number of blood units, laboratory values and TRISS scoring (AUC = 0.80).

Indicators of injury severity and neurologic status also differed substantially between groups. Patients who expired had significantly lower GCS scores and higher ISS values, confirming that they sustained more severe injuries. The markedly lower TRISS scores in the expired group further reinforce the reduced probability of survival based on

established trauma prognostic models. Together, these findings indicate that mortality was strongly associated with both the magnitude of injury and the degree of physiologic compromise at presentation.

Importantly, no significant differences were observed in other demographic or clinical variables, suggesting that the disparities in outcomes were driven primarily by injury severity and physiological derangement rather than baseline characteristics.

These results align with existing literature demonstrating that early coagulopathy, elevated lactate, and high transfusion requirements are key predictors of mortality in trauma patients undergoing massive transfusion and consistent with the current literature.[12,20,21] The findings emphasize the importance of rapid identification of high-risk patients, early correction of coagulopathy, and aggressive management of shock to improve outcomes.

Although the Kaplan Meier analysis did not yield a statistically significant p-value, this confirms that the number of coolers cannot be used to predict patient survival. Our decision to notify the clinical service about cooler usage is therefore not intended to directly affect outcomes, but rather to provide timely information that allows clinicians to re-evaluate each case using their clinical judgment. This approach ensures that decisions are guided by patient specific considerations rather than the quantity of blood units used, supporting optimal care and informed clinical decision-making. The Cox regression analysis supports the conclusion that cooler type is not a significant predictor of patient survival, as evidenced by hazard ratios close to unity and nonsignificant p-values. This reinforces the Kaplan Meier findings, indicating that the number or type of coolers used should not guide prognostic expectations. Importantly, this validates the clinical approach of providing the care team with updates on cooler usage not as a direct survival determinant but as supplementary information to prompt patient reassessment. By relying on clinical judgment rather than cooler counts alone, clinicians can better tailor management strategies, ensuring that patient care decisions are individualized and responsive to real time clinical context. This approach promotes dynamic evaluation and optimal outcomes beyond reliance on operational metrics.

In this analysis, the Youden index was applied to identify an optimal cutoff for the total number of units transfused during a massive transfusion protocol (MTP) to predict mortality (expired at the end of MTP code). The optimal cutoff identified was ≥36 blood units. At this threshold, the sensitivity was 44.4%, specificity 78.8%, and overall accuracy 69.6%. The relatively low sensitivity indicates that more than half of patients who ultimately expired would not have been correctly identified using this threshold. Conversely, although specificity is higher, relying solely on transfusion number risks overestimating risk in patients who survive despite receiving large volumes.

Receiver operating characteristic (ROC) analysis demonstrated that the total number of blood units issued has an initial ability to discriminate between survivors and non-survivors. However, when used as a sole predictor, number of blood units showed only modest discriminatory performance, indicating limited prognostic utility. These findings suggest that while transfusion burden contributes some predictive information, it does not adequately reflect the complex physiological derangements underlying mortality in critically injured or severely ill patients. The addition of laboratory markers and a validated trauma severity score resulted in a substantial improvement in model performance as shown with the increase in AUC from 0.62 to 0.80. This finding underscores the importance of incorporating objective measures of coagulation status, metabolic derangement, renal function, and overall injury severity when assessing mortality risk.

This study has several limitations that should be considered when interpreting the findings. It is a single center, retrospective study and selection bias are a recognized possibility. The relatively small sample size, particularly within higher cooler utilization categories, limited statistical power and may have contributed to the lack of significance in survival and Cox regression analyses. The study relied on initial laboratory values obtained within the first 15 to 30 minutes of arrival and did not account for dynamic changes in physiology, laboratory parameters, or transfusion ratios during the course of resuscitation. Important variables such as timing of hemorrhage control, surgical or interventional radiology interventions, use and timing of adjunctive therapies (eg., TXA, PCC, factor VIIa), viscoelastic testing results, and prehospital transfusion were not incorporated. Finally, long-term outcomes beyond survival at the end of MTP activation were not evaluated, precluding assessment of downstream morbidity and mortality. Multivariate analysis was not performed, as the analysis was designed to evaluate the prognostic value of number of blood units transfused alone. While this approach supports the study objective, it does not evaluate the significance of other established predictors.

Conclusions

In this retrospective cohort of trauma patients requiring MTP code activation, mortality (defined at the end of the MTP code) was strongly associated with injury severity, neurologic status, and early physiologic derangements rather than with blood product utilization alone. Patients who expired exhibited more profound coagulopathy, metabolic acidosis, hypoperfusion, and higher injury severity scores at presentation, in addition to requiring larger number of blood products. Although higher transfusion requirements and increased cooler utilization were more common among non-survivors, these measures demonstrated limited prognostic value when evaluated in isolation. Neither number of coolers issued or number of blood units issued alone reliably differentiated survivors and non-survivors.

Importantly, predictive performance improved substantially when number of blood units was integrated with laboratory parameters and validated trauma severity scores, underscoring the multifactorial nature of mortality in massively transfused trauma patients. These findings support the use of cumulative blood product utilization and cooler notifications as adjunctive tools to prompt timely clinical reassessment, rather than as determinants of prognosis or futility. Policies that impose limits on blood product transfusion based solely on the number of units issued are not supported by our findings and risk oversimplifying complex clinical decision-making. A comprehensive, patient-centered approach that incorporates vital signs, laboratory markers, and injury severity remains essential for informed decision-making during massive transfusion, particularly in the context of limited blood resources and escalating resuscitative demands.

Data Sharing Statement

The de-identified datasets analyzed during this study are available from the corresponding author upon reasonable request.

Institutional Review Board Statement

The study was conducted in accordance with the Declaration of Helsinki and approved by the Institutional Review Board (or Ethics Committee) of the University of South Alabama Institutional Review Board (IRB protocol: 25-191) in Mobile, Alabama on 13 May 2025.

Informed Consent Statement

Patient consent was waived due to the nature of the study, which is a retrospective study. Hence, the waiver of subject authorization was properly granted prior to data collection. The data were collected anonymously and serially coded to ensure confidentiality.

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Disclosure

The authors declare no conflicts of interest in this work.

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