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Application of the Berlin definition in PROMMTT patients: the impact of resuscitation on the incidence of hypoxemia

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IRB approval – The original PROMMTT study as well as this secondary analysis was approved at each study site and the Data Coordinating Center by the local institutional review boards. The US Army Human Research Protections Office also provided second level review and approval for PROMMTT.

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Abstract

Introduction—Acute lung injury following trauma resuscitation remains a concern despite recent advances. Utilizing PROMMTT study population, the risk of hypoxemia and potential modifiable risk factors are studied.

Methods—Patients with survival > 24 hours with at least 1 ICU day were included in the analysis. Hypoxemia was categorized utilizing the Berlin definition for ARDS: none (PaO_2 to FiO_2 ratio (P/F) > 300 mmHg), mild (P/F = 201–300), moderate (P/F = 101–200) or severe (P/F < 100). The cohort was dichotomized into those with none or mild hypoxemia and those with moderate or severe injury. Early resuscitation was defined as that occurring 0–6 hours from arrival, late resuscitation was defined as that occurring 7–24 hours. Multivariate logistic regression models were developed controlling for age, gender, mechanisms of injury, arrival physiology, individual AIS scores, blood transfusions and crystalloid administration.

Results—58.7% (731/1245) met inclusion criteria. Hypoxemia occurred in 69% (mild 24%, moderate 28%, severe 17%). Mortality was highest (24%) in the severe group. During early resuscitation (0–6 h), logistic regression revealed age (OR 1.02, CI 1.00–1.04), chest AIS (OR 1.31, CI 1.10–1.57) and intravenous crystalloid fluids given in 500 mL increments (OR 1.12 CI 1.01–1.25) as predictive of moderate or severe hypoxemia. During late resuscitation, age (OR 1.02, CI 1.00–1.04), chest AIS (OR 1.33, CI 1.11–1.59) and crystalloids given during this period (OR 1.05 CI 1.01–1.10) were also predictive of moderate to severe hypoxemia. RBC, plasma and platelet transfusions (whether received during early or late resuscitation) failed to demonstrate an increased risk of developing moderate/severe hypoxemia.

Conclusion—Severe chest injury, increasing age and crystalloid-based resuscitation, but not blood transfusions, were associated with increased risk of developing moderate to severe hypoxemia following injury.

Level of Evidence—I

Keywords

PROMMTT; resuscitation; hypoxemia; lung injury; trauma

BACKGROUND

Acute lung injury (ALI) in severely injured trauma patients has been historically associated with exposure to crystalloid and blood product transfusions utilized during the initial resuscitation.^{1,2} Specifically, the development of hypoxemia within a traumatically injured population has been closely associated with significant transfusion requirements with rates of acute respiratory distress syndrome (ARDS) approaching 60% in those receiving greater than 10 units of red blood cells (pRBC) over 24 hours.³ Several authors have shown increased risk for each additional unit of pRBC received, and plasma (FFP) remains most closely associated with development of transfusion related acute lung injury (TRALI).^{3–5} With the integration of damage control resuscitation techniques in many major civilian trauma centers, massive transfusion protocols now favor a resuscitation strategy with more balanced ratios of plasma to pRBCs and with limitation of crystalloid. Although mortality benefit has been shown for those patients receiving more balanced resuscitations, concern remains regarding the impact of this strategy on significant hypoxemia.^{5–7} To date, this remains largely uninvestigated in the era of damage control resuscitation.

In 2011, a consensus conference was convened in Berlin to refine the definition of ARDS. The resulting criteria, known as the Berlin Definition of Acute Respiratory Distress Syndrome, were published in May 2012 with the support of the major critical care organizations worldwide.⁸ The traditional terminology of ALI was dropped in favor of an alternative and more discriminatory stratification of ARDS into degrees of hypoxemia. Utilizing the Prospective Observational Multicenter Major Trauma Transfusion study (PROMMTT), the prevalence and risk factors for the development of hypoxemia as defined by the Berlin criteria was investigated.⁹

METHODS

Study Population

PROMMTT was a prospective, multicenter observational study conducted at ten Level 1 trauma centers from July 2009 to October 2010. Criteria for inclusion were major trauma activations arriving from the scene and surviving for at least 30 minutes after emergency department (ED) admission, age > 15 years old, and the transfusion of at least 1 unit of pRBC within 6 hours.⁹ The PROMMTT study was approved by the institutional review boards of each study site and the Data Coordinating Center (DCC). The US Army Human Research Protections Office also provided second level review and approval of the PROMMTT study.

Hypoxemia Categorizations

The categorization of hypoxemia was based on the Berlin definitions of ARDS created by the European Society of Intensive Care Medicine and endorsed by the American Thoracic Society and the Society of Critical Care Medicine.⁸ Hypoxemia was categorized as severe (PaO_2 to FiO_2 ratio (P/F) < 100 mmHg), moderate (P/F 101–200 mmHg), mild (P/F 201–300 mmHg) or none (P/F > 300 mmHg). PaO_2 to FiO_2 ratios used for analysis included values collected during the first 7 days of hospitalization. If multiple values existed, the single most severe value was utilized. Patients with survival > 24 hours, a known P/F ratio, and an intensive care unit (ICU) admission were included for analysis.

Data Collection

Prospective data collection occurred under the supervision of site coordinators utilizing the standard operation procedure manual of the PROMMTT study. Real-time records of product transfusions, fluid infusions, interventions and outcomes were obtained. Following

conclusion of the active resuscitation phase as defined by PROMMTT, patients were followed daily until discharge or death.⁹ Initial ED, operative, and intensive care unit values were verified within the medical records prior to DCC submission.

Data Analysis

The database was provided to study sites in a de-identified fashion by the DCC. Demographic, injury characteristics, emergency department initial vital signs, blood product transfusion times and amounts, crystalloid (normal saline and Ringer's lactate) infusion times and amounts, P/F ratio records, mechanical ventilator usage, and outcome data were available. Demographic, resuscitation and outcome data were analyzed by hypoxemia category. The effects of early (0–6 hours after admission) and late (7–24 hours after admission) resuscitation on the development of hypoxemia were specifically examined. To determine the odds of severe to moderate hypoxemia ($P/F < 200$ mmHg) as compared to mild or no hypoxemia ($P/F \geq 200$ mmHg), odds ratios (OR) and 95% confidence intervals (CI) were calculated using logistic regression. To account for confounding variables, logistic regression was reported with both early and late resuscitation variables included in determining risk factors for the development of hypoxemia. Chi-square and Wilcoxon rank-sum tests were used to compare relevant groups as applicable. All data analysis was performed using SAS Version 9.3 (Cary NC).

RESULTS

Overall

The PROMMTT study group included 1245 patients. The cohort yielded 731 patients (59% of the cohort) with survival > 24 hours, an ICU admission and a P/F ratio recorded during the first 7 days of hospitalization (Figure 1). A single hypoxemic event was present in 505 patients (69%) with moderate (P/F 101–200 mmHg, $n = 207$ [28%]) being more frequent than mild (P/F 201–300 mmHg, $n = 174$ [24%]) or severe ($P/F < 100$ mmHg, $n = 124$ [17%]).

Demographic and Resuscitation Characteristics by Hypoxemia Severity

Table 1 outlines cohort demographics by hypoxemia category including those without hypoxemia ($P/F > 300$). The severe hypoxemia group had the highest proportion of blunt injury (84%), proportion of patients with an initial ED heart rate > 110 beats per minute (BPM) (56%), median head abbreviated injury score (AIS) (2.5), and mortality (24%). The moderate group had the highest median age (45), proportion male (80%), proportion with an initial ED systolic blood pressure < 90 mmHg (36%), median ISS (33), median ICU length of stay (15 days), and median hospital length of stay (23.1 days). Both the severe and moderate groups had the same median chest (3) and abdomen (2) abbreviated injury scale (AIS) value.

The volume of crystalloid and units of blood products given in the first 24 hours after admission was examined by hypoxemia categories (Table 2). Crystalloids in half-liter increments differed among groups ($p = 0.003$) with the moderate and mild groups receiving the most crystalloid. The number of pRBC units transfused by hypoxemia category also differed significantly ($p = 0.0001$). Those with moderate hypoxemia received the most blood during the first day (6 [4–12] units). The greatest quantity of plasma transfused was to the severe group (6 [2–11] units) and the amounts transfused did differ significantly among groups ($p < 0.0001$). Platelet use differed significantly among groups ($p = 0.001$) with the moderate group being transfused the most (0 [0–12] units). The ratio of plasma to pRBC and platelets to pRBC during the first 24 hours of resuscitation was delineated by hypoxemia category. No significant differences in the ratio of plasma to pRBC were detected among the

groups; however, the ratio of platelets to pRBC did differ ($p = 0.02$) with the moderate group receiving the highest ratio (0 [0–0.71]).

Determination of Risk Factors for Severe to Moderate Hypoxemia

The association of early (0–6 hours after admission) and late resuscitation (7–24 hours) variables to the development of severe to moderate hypoxemia ($P/F < 200$ mmHg) were determined. On univariate analysis, significant risk factors from early resuscitation included male gender, blunt injury, head and chest AIS, the units of blood, plasma and platelets, and crystalloids received during the first 6 hours of care (Table 3). Multivariate analysis found only increasing age (OR 1.02 [CI 1.00–1.04], $p = 0.047$), chest AIS (OR 1.31 [CI 1.10–1.57], $p = 0.003$), and crystalloid by 500 mL increments (OR 1.06 [CI 1.00–1.12], $p = 0.04$) to be significant independent risk factors for severe to moderate hypoxemia. For each 500 mL of crystalloid received early, there was a 6% increased incidence of severe to moderate hypoxemia.

For multivariate analysis of late resuscitation, increasing age (OR 1.02 [CI 1.00–1.04], $p = 0.04$), chest AIS (OR 1.33 [CI 1.11–1.59], $p = 0.002$), and crystalloid were significant risk factors for severe to moderate hypoxemia (Table 4). Crystalloid received between 7–24 hours was associated with a 5% additional odds for development of severe to moderate hypoxemia (OR 1.05 [CI 1.01–1.10], $p = 0.03$) for each 500 mL of crystalloid given. The amounts of pRBC, plasma and platelets transfused, whether given early or late, failed to demonstrate an increased risk of developing severe to moderate hypoxemia. Higher volumes of early platelet transfusion were associated with a decreased risk of severe to moderate hypoxemia (OR 0.94 [CI 0.89–1.00] $p = 0.04$).

DISCUSSION

Uncontrolled hemorrhage in traumatically injured patients continues to be a major etiology for early death despite continued work to correct coagulopathy through the early institution of plasma and platelet-rich transfusion practices.^{10,11} Even with widespread implementation of blood product rich resuscitations, little is known regarding the direct association of such strategies in terms of pulmonary dysfunction. At the bedside, lung injury after trauma can range from mild hypoxemia to severe ARDS.^{12,13}

In an effort to create uniformity for a diverse population of patients with lung injury and to standardize research criteria, the American-European Consensus Conference definition of ARDS was created in 1994.¹⁴ Patients with acute hypoxemic respiratory failure, bilateral infiltrates on chest radiographs and a lack of evidence for left atrial hypertension were divided into those with acute lung injury (ALI) if the P/F ratio was < 300 mmHg and ARDS if the P/F was < 200 mmHg. As applied to trauma patients, this definition was viewed as controversial. It is possibly too broad for such a diverse patient population and may have poor specificity for identifying patients at risk.^{15,16} In hopes of addressing issues of reliability, validity for mortality, and complexity with current criteria, the European Society of Intensive Care Medicine convened a conference in Berlin 2011 to improve upon the 1994 AECC definitions.⁸ The new definition included the development of ARDS within 7 days of a known insult, bilateral opacities on chest radiograph or computed tomography, respiratory failure not fully explained by cardiac failure and positive end-expiratory pressure of at least 5 cm H₂O. Patients with mild ARDS have mild hypoxemia with P/F 201–300 mmHg, moderate ARDS patients have moderate hypoxemia of 101–200 mmHg and those with severe ARDS have severe hypoxemia of $P/F < 100$ mmHg. The definition of acute lung injury was removed.

The Berlin Definition of hypoxemia has not been previously examined in the trauma patient population. Additionally, hypoxemia in the era of damage control resuscitation has not been well described for the severely injured trauma population. Furthermore, those studies that do exist suffer from retrospective data collection and a lack of clarity regarding the temporal nature of fluid and blood product transfusions. In a prospective observational cohort of severely injured patients, the PROMMTT study group, hypoxemia was common (69%) and associated with fatal outcomes (13–24%). Severe to moderate hypoxemia was related to chest injury severity, increasing age, and increasing crystalloid infusion in early and late resuscitation.

Hypoxemia originating from direct chest injury may be responsible for localized capillary leak from the direct transmission of force but also may be implicated in inciting an inflammatory cascade responsible for widespread and bilateral injury. In our study cohort, chest AIS as a surrogate for direct thoracic injury was associated with an increased risk of developing severe to moderate hypoxemia in both phases of resuscitation. This finding further validates the work of groups that have previously described predictive models for ARDS in an injured population. In these models developed specifically for trauma patients, chest injury was a significant predictor.^{17–19}

The finding that age is a risk factor for hypoxemia was also consistent with previously published work demonstrating a higher incidence of ARDS in older trauma patients.^{17,19} Though age is widely accepted as a correlate of the development of acute hypoxemia in trauma patients, the complex interplay of age and ARDS has not been fully elucidated.²⁰ Given that age is non-modifiable, the role of other modifiable risk factors, like resuscitation, may be even more important for elderly trauma patients and warrants further study.

Common to both the early and late phase of resuscitation was the negative consequences of crystalloid administration upon the development of severe to moderate hypoxemia. Even at relatively small clinical volumes, each half-liter increment was associated with a 5–6% increased risk of hypoxemia. Prior clinical studies implicating increasing crystalloid volumes as problematic for ARDS development have been plagued with bias as the data were extrapolated retrospectively from chart review.^{12,21} In contrast, the present study collected the crystalloid volumes real-time and the demonstration of fairly profound negative effects of very modest volumes of crystalloid on development of hypoxemia is troubling. This further supports the position that every effort should be made to minimize crystalloid in patients suspected of or known to be experiencing hemorrhage.

Though crystalloids are historically (over the last 45 years) ubiquitous in the initial approach to fluid resuscitation in hemorrhagic shock, the negative effects of crystalloid infusions are becoming better understood. Crystalloid infusions in the hemorrhagic patient have been associated with cardiac and pulmonary complications as well as alterations in the coagulation cascade due to cellular and inflammatory disturbances that occur after exposure, leading to morbidity.^{22–24} Possible explanations for these findings may be related to the fact that crystalloid infusions fail to correct early coagulopathy present in hemorrhaging patients. With ongoing coagulopathy, blood loss worsens, necessitating volume expansion with crystalloid, which may ultimately potentiate a continuing morbid cycle.²⁵ As such, an accentuated inflammatory response occurs at multiple end organ sites, resulting in capillary leak within lung parenchymal tissue, poor gas exchange and hypoxemia. In those patients requiring active blood product resuscitation, especially those requiring a massive transfusion, the ratio of crystalloid to pRBC should be monitored to avoid these known complications.²⁶

In view of the early coagulopathy of hemorrhagic shock, great concern has been raised as to the possible ill effects of blood product rich resuscitations.²⁷ Arguments against such strategies focus on the possibly higher rates of hypoxemia directly related to increased inflammatory pulmonary states primed by blood product transfusion and the possible higher incidence of TRALI that may occur.²⁸ The risk of TRALI varies by the blood products transfused and ranges from 1 case per 5000 units of pRBC to 1 per 2000 units of plasma to 1 per 400 units of platelets and is the leading cause of transfusion related deaths in the United States.^{28–30} However, lower rates of TRALI have been associated with the restriction of transfusions from female donors (1:12000).³¹

In retrospective older studies preceding the damage resuscitation era, red blood cell transfusions have been described as a risk factor for the development of lung injury in trauma patients with the negative consequences being cumulative as more units are transfused.^{2,3,12} In a more recent prospective study with patients receiving a massive transfusion, pRBC volumes transfused within the first 12 hours of resuscitation are associated with multi-organ failure whereas plasma and crystalloid are not.³² However, the transfusion of plasma and platelets has also been described as a risk factor in the development of acute lung injury.^{5,33,34} Based upon historical data, as damage control resuscitation has gained popularity, concern over the increased patient exposure to plasma and the association with ARDS or hypoxemia has understandably remained.

Importantly, our prospective study failed to demonstrate a negative association of pRBC and plasma exposure to the development of hypoxemia in a cohort in which survival was increased with a more balanced blood product resuscitation.³⁵ Previous work has demonstrated that an early balanced blood product infusion with limited crystalloid leads to improved survival, lower amounts of products transfused, and fewer inflammatory consequences.³⁶ Our work demonstrated that, higher volumes of early platelet transfusion were associated with a protective effect for avoiding severe to moderate hypoxemia. This likely reflects the positive effect of a more balanced ratio of pRBCs to FFP to platelets in patients receiving higher platelet amounts compared to those who did not.^{37,38} Utilizing a prospective, observational study specifically designed to document the timing, type, and quantity of resuscitation products and transfusions during active resuscitation provides a major advancement in understanding the role of crystalloid and blood products on development of pulmonary complications.

The focus of this work was to elucidate modifiable interventions of care during the first 24 hours of admission. By dividing the first 24 hours into early (0–6 hours) and late (7–24 hours) periods, interventions during the active resuscitative phase of care could be distinguished from a later phase characterized by patients approaching physiologic equilibrium. The major modifiable risk factor identified in this study was the quantity of crystalloid infused. Prior research has focused on the quantity and type of blood product exposure as risk factors for pulmonary morbidity and has ignored the deleterious inflammatory and dilutional effects of crystalloids.^{3–5} The present study appears to dispel this myth. Blood products themselves, and specifically, plasma were not statistically significant predictors of pulmonary complications defined as significant hypoxemia utilizing the Berlin definition. In contrast, crystalloid volumes appear to be more relevant during the first day of care than the total blood exposure as a contributory cause of severe to moderate hypoxemia.

We recognize several limitations of the current study. Documentation of pulmonary outcomes is limited to hypoxemia as defined by P/F ratios and ventilator usage rather than more specific data relating to chest radiographic findings and ventilator settings. The observational nature of this work limited documentation of adverse effects, specifically

TRALI, and the specific etiologies for lung injury. Thus, the possibility exists that unknown or undocumented variables may be responsible for associations to acute hypoxemia rather than those investigated. Finally, survival bias is inherent in works that require the evolution of clinical entities to occur such as hypoxemia. The inclusion of patients that died before 7 days of care with a known P/F ratio may effect statistical analysis of hypoxemic events that often take several days to develop.

CONCLUSION

Hypoxemia as delineated by the Berlin definition is common in trauma patients experiencing resuscitation from active hemorrhage. Known non-modifiable risk factors of advanced age and chest injury continue to be associated with hypoxemia in this population. The incremental amount of crystalloid provided rather than the amount of blood products transfused to these patients during the first day of care appears to be the modifiable risk factor for lung injury. Care should be taken to limit the amount of crystalloid exposure in this high pulmonary risk population.

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Figure 1.

Algorithm of inclusion criteria for hypoxemia analysis. Those included for final analysis had an intensive care unit admission, lived > 24 hours and had a recorded PaO₂ to FiO₂ ratio.

Table 1

Demographics of study cohort by hypoxemia severity (n=731)

	Severe Hypoxemia P/F < 100 (n=124)	Moderate Hypoxemia P/F 101–200 (n=207)	Mild Hypoxemia P/F 201–300 (n=174)	No Hypoxemia P/F >300 (n=226)	p-value
Age (years)	37 (23–52)	45 (28–57)	44.5 (28–59)	31 (23–49)	<0.0001*
Male gender	74.2%	80.2%	73.0%	70.4%	0.12
Blunt Injury Rate	83.9%	74.9%	73.6%	62.0%	<0.0001*
ED SBP < 90 mmHg	28.5%	36.1%	30.1%	25.1%	0.10
ED HR > 110 BPM	56.1%	44.1%	47.7%	39.4%	0.02*
ISS	29 (22–41)	33 (22–38)	27 (17–38)	22(14–33)	<0.0001*
Head AIS	2.5 (0–4)	2 (0–4)	2 (0–4)	0 (0–4)	0.03*
Chest AIS	3 (2–4)	3 (2–4)	3 (0–4)	2 (0–3)	<0.0001*
Abdomen AIS	2 (0–3)	2 (0–3)	2 (0–3)	1.5 (0–3)	0.001*
Ventilator – free days in 30	16 (0–25)	19 (6.5–25)	15 (24.5–29)	28 (24–29.5)	<0.0001*
ICU LOS	13.8 (6–22)	15 (8–25)	9 (4.2–17)	5 (3–12)	<0.0001*
Hospital LOS	20.6 (12–32)	23.1 (12–35.6)	17 (9–26.7)	16 (8–24)	<0.0001*
Mortality	24.2%	13.0%	17.2%	9.3%	0.002*

Values provided in medians (inter-quartile ranges)

P/F: PaO₂ to FiO₂ ratio in mmHg, ED: emergency department, SBP: systolic blood pressure, HR: heart rate, BPM: beats per minute ISS: injury severity score, AIS: abbreviated injury scale, ICU: intensive care unit, LOS: length of stay

* $p < 0.05$

Table 2

Resuscitation characteristics of first 24 hours by hypoxemia severity (n=731)

	Severe Hypoxemia P/F < 100 (n=124)	Moderate Hypoxemia P/F 101–200 (n=207)	Mild Hypoxemia P/F 201–300 (n=174)	No Hypoxemia P/F >300 (n=226)	p-value
Crystalloid (half liters)	14.0 (10.0–21.9)	15.4 (10.4–23.8)	14.2 (8.3–19.6)	13.6 (9.2–19.0)	0.003 *
pRBC	6 (4–10)	6 (4–12)	5 (3–18)	4 (2–8)	0.0001 *
Plasma	6 (2–11)	5 (2–11)	4 (1–8)	4 (0–7)	<0.0001 *
Platelets	0 (0–6)	0 (0–12)	0 (0–6)	0 (0–6)	0.001 *
Plasma to pRBC ratio	0.82 (0.43–1.21)	0.76 (0.33–1.02)	0.75 (0.29–1.0)	0.67 (0–1.0)	0.12
Platelets to pRBC ratio	0 (0–0.67)	0 (0–0.71)	0 (0–0.6)	0 (0–0.55)	0.02 *
Massive Transfusion	28.2%	31.9%	23.6%	20.8%	0.051

Values provided in medians (inter-quartile ranges), all values are 24 hour totals, comparisons of blood products are per unit and crystalloid (normal saline and Ringer's lactate) are per half liter increments, massive transfusion defined as 10 units of pRBCs in 24 hours.

P/F: PaO₂ to FiO₂ ratio in mmHg, pRBC: packed red blood cells.

* $p < 0.05$

Table 3

Early resuscitation predictors of severe to moderate hypoxemia (0–6 hours).

	Univariate	p-value	Multivariate	p-value
Age (years)	1.01 (1.00–1.01)	0.15	1.02 (1.00–1.04)	0.047 *
Male gender	1.41 (1.00–1.98)	0.047	1.33 (0.68–2.59)	0.40
Blunt Injury	1.77 (1.27–2.48)	0.0008	1.42 (0.68–2.95)	0.35
ED SBP < 90 mmHg	1.33 (0.96–1.83)	0.08	0.90 (0.47–1.70)	0.74
ED HR > 110 BPM	1.25 (0.93–1.69)	0.13	1.16 (0.61–2.22)	0.65
Head AIS	1.10 (1.02–1.18)	0.013	1.15 (0.98–1.35)	0.10
Chest AIS	1.34 (1.23–1.47)	<0.0001	1.31 (1.10–1.57)	0.003 *
Abdomen AIS	1.08 (0.99–1.18)	0.09	1.12 (0.93–1.35)	0.25
pRBC 0–6h	1.06 (1.03–1.08)	<0.0001	1.03 (0.96–1.11)	0.42
Plasma 0–6h	1.07 (1.03–1.10)	<0.0001	1.08 (0.99–1.18)	0.08
Platelets 0–6h	1.04 (1.01–1.08)	0.02	0.96 (0.90–1.01)	0.10
Crystalloid 0–6h	1.11 (1.05–1.17)	0.0001	1.12 (1.01–1.25)	0.04 *

Values provided as odds ratios (95% confidence interval), logistic regression analysis performed of severe to moderate hypoxemia (PaO2/FiO2 ratio < 200 mmHg) vs. mild to no hypoxemia (PaO2/FiO2 > 200 mmHg). univariate variables with p < 0.15 were included in multivariate modeling, blood products comparison are per unit and crystalloid (normal saline and Ringer's lactate) are per half liter increments.

ED: emergency department, SBP: systolic blood pressure, HR: heart rate, BPM: beats per minute, AIS: abbreviated injury scale, pRBC: packed red blood cells, h: hours, IVF: intravenous fluids.

* p < 0.05

Table 4

Predictors of severe to moderate hypoxemia (0–24 hours).

	Univariate	p-value	Multivariate	p-value
Age (years)	1.01 (1.00–1.01)	0.15	1.02 (1.00–1.04)	0.04 *
Male gender	1.41 (1.00–1.98)	0.047	1.28 (0.65–2.52)	0.48
Blunt Injury	1.77 (1.27–2.48)	0.0008	1.45 (0.67–3.10)	0.34
ED SBP < 90 mmHg	1.33 (0.96–1.83)	0.08	0.92 (0.48–1.80)	0.81
ED HR > 110 BPM	1.25 (0.93–1.69)	0.13	1.07 (0.55–2.07)	0.85
Head AIS	1.10 (1.02–1.18)	0.013	1.17 (0.99–1.39)	0.07
Chest AIS	1.34 (1.23–1.47)	<0.0001	1.33 (1.11–1.59)	0.002 *
Abdomen AIS	1.08 (0.99–1.18)	0.09	1.09 (0.90–1.33)	0.38
pRBC 0–6h	1.06 (1.03–1.08)	<0.0001	1.04 (0.97–1.12)	0.30
pRBC 7–24h	1.07 (1.02–1.11)	0.003	0.94 (0.85–1.03)	0.18
Plasma 0–6h	1.07 (1.03–1.10)	<0.0001	1.09 (0.99–1.19)	0.07
Plasma 7–24h	1.06 (1.02–1.11)	0.002	1.07 (0.98–1.18)	0.14
Platelets 0–6h	1.04 (1.01–1.08)	0.02	0.94 (0.89–1.00)	0.04 *
Platelets 7–24h	1.03 (0.99–1.08)	0.20	NA	NA
Crystallloid 0–6h	1.05 (1.03–1.08)	0.0001	1.06 (1.01–1.12)	0.04 *
Crystallloid 7–24h	1.03 (1.00–1.05)	0.02	1.05 (1.01–1.10)	0.03 *

Values provided as odds ratios (95% confidence interval), logistic regression analysis performed of severe to moderate hypoxemia (PaO₂/FiO₂ ratio 200 mmHg) vs. mild to no hypoxemia (PaO₂/FiO₂ >200 mmHg). univariate variables with p 0.15 were included in multivariate modeling, blood products comparison are per unit and crystallloid (normal saline and Ringer's lactate) are per 500 mL increments.

ED: emergency department, SBP: systolic blood pressure, HR: heart rate, BPM: beats per minute, AIS: abbreviated injury scale, pRBC: packed red blood cells, h: hours, IVF: intravenous fluids.

* p < 0.05