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Pediatric trauma: Blood product transfusion characteristics in a pediatric emergency department, a single center experience

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ABSTRACT

Aim: To investigate clinical and laboratory data, management and outcomes of pediatric trauma patients who initially received blood product transfusions.
Methods: Between January 2011-January 2021, traumatic children who underwent blood product transfusions within 24 h of arrival at the emergency department were included. Demographics, clinical and laboratory data, Injury Severity Score (ISS), volume of transfused blood products and crystalloid boluses in 24 h were recorded. Massive transfusion (MT) was defined as transfusion of ≥40 mL/kg of all blood products in 24 h.
Results: Among 32 cases, 8 (25.0 %) patients met the MT threshold criterion. Length of pediatric intensive care unit (PICU) stay and mechanical ventilation (MV) were longer for patients who received MT although there was no difference for age, ISS, volume of crystalloid boluses, length of hospital stay, and 30-day mortality between those who received MT or not. Volume of crystalloid boluses was higher in patients who died than those who survived but the volume of blood products was similar for two groups. An APTT value of >37.5 s was identified as a predictor of 30-day mortality (OR = 48.000, 95 % CI: 3.704-621.998, p: 0.003).
Conclusion: Children who received MT had longer durations of MV and PICU stay than those who did not receive, but there was no significance for ISS, volume of crystalloid boluses, hospital stay, or mortality between two groups. Volume of crystalloid boluses was higher in patients who died than those who survived. An APTT value of >37.5 s can be used to predict 30-day mortality.

1. Introduction

Trauma is the leading cause of preventable death in children with the two principal etiologies being traumatic brain injury (TBI) and hemorrhagic shock [1].

While children are thought to have higher physiologic reserve than adults, severely injured patients may require transfusion of blood products and, in some of these cases, the amount of blood products may reach or exceed the threshold of massive transfusion (MT) [2]. Aggressive resuscitation strategies, the cornerstone of trauma management, were advocated to increase the circulating volume and to maintain end-organ perfusion [3]. "Massive transfusion" refers to the administration of a high volume of blood products over a period of time with various definitions [4] such as greater than 40 mL/kg in 4 h or 24 h, or 70 mL/kg in 24 h, or more than 50 % of total estimated blood volume in 3 h/12 h/24 h and the total blood volume in 24 h [5]. Recent studies defined MT as 40 mL/kg of total blood products administered during the first 24 h of admission [6–8].

Traumatic injury may lead to the release of clotting factors, which generate clinically significant coagulopathy known to be associated with increased mortality [9]. Trauma-related coagulopathy is a well-documented component of the lethal triad that also involves hypothermia and acidosis [10]. At the same time, aggressive crystalloid resuscitation, which leads to dilution of clotting factors, may also worsen early coagulopathy [9]. Pediatric trauma patients with hemorrhage are known to have a high mortality rate of 30–40 % [3,9]. Approximately 50 % of deaths occur within 6 h after trauma, most of them occurring in the first hour [11]. Thus, it is crucial to identify the optimal timing and composition of resuscitation for these cases [9].

In this study, we aimed to investigate clinical and laboratory data,

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management, and outcomes of pediatric trauma patients who initially received blood product transfusions in a pediatric emergency department (ED).

2. Materials and methods

2.1. Study design

This is a single-center retrospective chart review performed in the pediatric ED of a tertiary hospital with approximately 120,000 pediatric ED admissions per annum. The study was approved by the Institutional Review Board of the Dokuz Eylul University Faculty of Medicine (approval number: 2020/01-02).

Children aged 0–18 years who arrived at the pediatric ED by ambulance or self-transport due to trauma and underwent blood product transfusion within 24 h of arrival between January 2011 and January 2021 were included. We used International Classification of Diseases (ICD) codes to identify patients. We obtained data from a computer database, electronic medical records, blood bank records, medical charts, and nursing records. All investigations were performed and recorded by a pediatric emergency fellow and a pediatric resident. Children with burns or asphyxiation mechanisms of injury, known coagulopathies, and anticoagulant drug use were excluded from the study, as were those who underwent either blood product transfusion or crystalloid bolus in another facility and were then referred to our hospital and those with insufficient information.

Demographics, trauma mechanism, initial body temperature, Glasgow Coma Scale (GCS) score, heart rate (HR), respiratory rate (RR), blood pressure, clinical findings, laboratory results, radiologic investigations, applied treatments, and the need for respiratory support or cardiopulmonary resuscitation (CPR) in the ED were recorded. Variables were ascertained upon arrival to the ED. Age-adjusted hypotension and tachycardia were recorded using published heart rate and blood pressure norms [12]. Hypothermia was defined as body temperature of <36 °C. Coagulopathy was defined as an international normalized ratio (INR) value of ≥ 1.5.

The Abbreviated Injury Scale (AIS) score for each body region and Injury Severity Score (ISS) [13] were calculated for each patient. The AIS quantifies injuries of various body regions from 1 (minor injury) to 6 (non-survivable) and the ISS is calculated by summing the squares of the three highest AIS scores for three different body regions, with total scores ranging from 1 to 75. Severe TBI was defined as a head AIS of ≥ 3. The BIG score was calculated as follows: base deficit + (2.5 × INR) + (15 - GCS score) [14]. The shock index (SI), which is calculated by dividing the child's heart rate into systolic blood pressure, was obtained. The pediatric age-adjusted SI (SIPA) value, derived from the SI, was considered abnormal if greater than previously reported cut-off values (Table 1) [15].

Data including timing and volumes of crystalloid boluses and the number of units of blood products, transfused as packed whole blood (WB), packed red blood cells (PRBCs), fresh frozen plasma (FFP), platelets (PLTs), and cryoprecipitate, were obtained. Units were converted to volume in milliliters using the average volume of component units administered. We estimated blood products based on the following volumes per unit: a volume of 250 mL was used for each unit recorded of PRBCs, 200 mL was used for FFP, 200 mL for PLTs, 500 mL for WB, and 50 mL for cryoprecipitate transfusions. Crystalloid boluses and the volume of blood products were converted to milliliters per kilogram of body weight for each subject. Volumes of crystalloid boluses per kilogram of body weight, volumes of each type of blood product, and volumes in total in the first 24 h were calculated. Missing weights were imputed with the 50th percentile weight of the Centers for Disease Control for age and gender [16]. Blood product ratios used for each patient were recorded and patients were divided into two groups according to the ratio of FFP:PRBC, with a low-ratio group of $<1:2$ and high-ratio group of $\geq 1:2$ [17]. Transfusion of greater than or equal to 40 mL/kg of all blood products in 24 h was defined as MT, as previously reported by Neff et al. [8]. The blood groups of the patients, utilization of type-specific or O Rh (-) typed PRBC utilization, use of recombinant factor VIIa or tranexamic acid, MT complications (hypo/hyperkalemia, leukopenia, thrombocytopenia, acidosis, hypothermia, etc.), and morbidities associated with blood product transfusion (sepsis, multiorgan failure, acute respiratory distress syndrome, transfusion-related acute lung injury, compartment syndrome, transfusion reactions, acute renal failure, thromboembolism, etc.) were recorded.

Finally, surgical interventions, admission to the ward or pediatric intensive care unit (PICU), transfer to another hospital, length of mechanical ventilation (MV) and stay in the hospital, prognosis, and mortality were recorded. Mortality was recorded within two categories as 4-h and 24-h mortality, in which deaths occurred within 4 or 24 h after arrival to the pediatric emergency department, and as 30-day mortality.

2.2. Statistical analysis

All statistical analyses were performed using SPSS 22.0 for Windows. Categorical and continuous variables were reported as frequencies and percentiles and as means with standard deviations (SDs) or medians with interquartile ranges (IQRs). A Chi-square test was used to evaluate the difference of categorical variables. The Mann-Whitney U test was used to compare non-parametric variables and Student's t test was used for parametric data. Multivariable analysis was performed using logistic regression to determine predictors of mortality. Values of $p < 0.05$ were considered statistically significant.

3. Results

A total of 32 patients [median age 8.8 years (IQR 2.0–15.1), 20 males (62.5 %)] were enrolled throughout the study period. Fourteen (43.8 %) of them were aged >12 years, being the most common age group. The most common trauma mechanism was out-of-vehicle traffic accident (n: 15, 46.9 %), followed by falling (n: 10, 31.3 %). Of the 32 patients, 30 (93.8 %) presented with blunt and 2 (6.3 %) with penetrating trauma, and 28 (87.5 %) patients had multiple trauma while 4 (12.5 %) had isolated trauma. Twenty-two (68.8 %) of the patients had GCS scores of ≤ 8, and the mean ISS score was 38.1 ± 12.3 (min: 6.0, max: 75.0). Five patients (15.6 %) arrived to the ED while CPR was being performed and it was continued in the hospital for 3 of them. Twenty-four (75.0 %) patients underwent MV and, of them, 20 patients were intubated before arrival and 4 were intubated after arrival to the ED. The median length of MV was 3.4 (IQR: 0.7–6.4) days. Inotropes were administered for 15 (46.9 %) patients. Twelve patients underwent operations at a median of 8.5 (IQR 2.2–66.0) h after arrival to the emergency department.

In terms of use of blood products, all patients received PRBCs with a median volume of 16.0 mL/kg (IQR: 12.5–25.0). Nineteen (59.4 %) received FFP transfusion with a median volume of 10.0 mL/kg (IQR: 8.0–15.0) and, among them, 12 patients were transfused at high and 7 at low FFP:PRBC ratios. One patient received tranexamic acid treatment. None of the patients received any WB, PLT, or cryoprecipitate transfusions or recombinant factor VIIa. Among all transfusions, 8 (25.0 %)

Table 1
Normal pediatric vital signs based on age groups with calculated SIPA threshold values.

Age in years	Heart rate (beats/min)	Systolic blood pressure (mmHg)	SIPA threshold value
1–3	70–110	90–110	1.2
4–6	65–110	90–110	1.2
7–12	60–100	100–120	1.0
>12	55–90	100–135	0.9

SIPA: Shock index, pediatric age-adjusted.

cases met the MT threshold criterion. Twenty-three (71.8 %) patients received transfusions with a non-identical but compatible blood group product. Transfusion complications were observed in 9 (28.1) cases, with thrombocytopenia being the most common complication occurring in 5 (15.6 %) cases, followed by hypocalcemia in 2 (6.3 %) cases, hypothermia in one case (3.1 %), and hyperkalemia in one (3.1 %) case. All patients received crystalloid boluses with a median volume of 40.0 mL/kg (IQR: 20.0–75.0).

Of the 32 children, 4 (12.5 %) of them were admitted to the ward and 16 (50.0 %) to the PICU. Median length of stay was 5.0 (IQR: 2.0–8.0) h in the emergency department and 4.5 (IQR: 0.8–11.7) days in the PICU; total length of stay was 2.5 (IQR: 0.1–10.5) days. Eleven (34.4 %) patients were transferred to the PICU of another facility. Of the 32 children, 6 (18.8 %) were discharged with severe complications (with neurological and respiratory complications) and 20 (62.5 %) died. Among the latter, 8 deaths occurred within the first 4 h, 4 deaths between 4 and 24 h, and 8 deaths >24 h after arrival to the pediatric emergency department. Accordingly, 4-h mortality was calculated as 25.0 %, 24-h mortality as 37.5 %, and 30-day mortality as 62.5 %.

Children who received MT had a higher rate of tachycardia, lower body temperature at arrival to the ED, and higher rate of inotrope use than those who did not receive MT (p: 0.024, p: 0.040, p: 0.014). No initial laboratory parameters differed between these two groups. Length of PICU stay, length of MV, and transfusion complication rates were also higher for patients who received MT (p: 0.006, p: 0.024, p: 0.023). No difference was found for age, ISS scores, the volume of crystalloid boluses, length of stay in the hospital, and 4-h, 24-h, or 30-day mortality between the two groups (Tables 2–4). To prevent confusion, we excluded cases of severe TBI, but mortality rates still remained similar for the two groups (p: 0.327).

In terms of FFP:PRBC ratios, children who received transfusion with a high FFP:PRBC ratio were older in age [age in years [median (IQR)]: 15.5 (4.7–16.0) versus 6.0 (1.3–13.7), p: 0.029] and had higher ISS scores [mean ± SD (min-max): 44.2 ± 10.6 (41.0–44.5) versus 34.0 ± 12.0 (27.0–41.0), p: 0.011] than those who received a low ratio, but there was no difference for length of stay or mortality rates between the groups. Additionally, there was no difference for length of stay or mortality in terms of FFP:PRBC ratio groups for those who received MT and those who did not.

Compared to patients who survived, patients who died within 30 days of arrival had lower initial body temperatures and platelet counts; higher rate of a GCS score of ≤8; higher prothrombin time, activated partial thromboplastin time (APTT), INR, and lactate levels; lower pH and bicarbonate values; and higher ISS scores and higher AIS scores for thoracic injury ($p < 0.05$). Total volume of crystalloid boluses (mL/kg) was also higher in patients who died (p: 0.003), but the volume of blood products was similar for these two groups (Tables 2–4). We divided patients into two groups as having severe TBI or not. Among the severe TBI group, children who died also had higher ISS scores and had received higher volumes of crystalloid boluses (p: 0.014, p: 0.049). Interestingly, in the non-severe TBI group, ISS scores were similar for patients who died and those who did not, but the volumes of total crystalloid boluses were still higher among children who died (p: 0.313, p: 0.026). The SIPA was similar for those who survived and those who did not in the severe TBI group (p: 0.199), but among the patients with non-severe TBI, patients who died had higher initial SIPA values (p: 0.009) (Table 5).

To predict 30-day mortality, multivariable analysis was performed, and among the parameters of a GCS score of ≤8, an ISS score of ≥25, having received MT, and crystalloid bolus volume of ≥40 mL/kg, a GCS score of ≤8 was identified as a predictor. When we added APTT to these parameters, an APTT value of >37.5 s was identified as a predictor of 30-day mortality (Table 6).

When we evaluated 4-h mortality, similarly, we found that initial body temperatures and platelet counts were lower and lactate levels were higher ($p < 0.05$). In contrast, although ISS values were similar for the two groups (p: 0.066), head AIS scores were higher in children who died within 4 h of arrival to the ED (p: 0.009). In terms of 24-h mortality, children who died were found to have lower initial body temperatures, platelet counts, and pH values and both higher ISS and head AIS scores than those who survived the initial 24 h. The BIG score was similar for children who survived and those who did not, and also for those who received MT and those who did not.

4. Discussion

Massive transfusion has been extensively evaluated in combat populations, in which severely injured patients experience a greater risk of mortality from hemorrhage [4]. Cannon et al. evaluated pediatric trauma patients during combat operations and reported that female sex, isolated head injury, ISS score, age-adjusted tachycardia, presence of coagulopathy, and increasing base deficit were independent predictors of mortality [18]. However, implementation of MT has not demonstrated a clear survival benefit for pediatric trauma patients [4]. In addition, MT itself has several risks resulting in significant morbidity and mortality [19].

Cannon et al. reported that mortality decreased among patients who received MT despite more injuries due to explosions, more head injuries, and greater injury severity [18]. In contrast, Chidester et al. reported no difference in mortality for children who received MT and those who did not. In addition, FFP:PRBC ratios and crystalloid volumes were similar for these two groups [10]. Shroyer et al. concluded that children who underwent MT were older, had lower GCS scores, were more likely to be hypothermic, and had sustained more severe injuries and that there was no difference in length of hospital stay for patients who received any blood product transfusion and MT [20]. In our study, we found that patients who received MT had higher HR, lower body temperature, and longer PICU stay and duration of MV than those who did not receive MT, but there was no difference for age, ISS score, volume of crystalloid boluses, length of stay in the hospital, or mortality. Pieracci et al. reported that deaths in children who received early PRBC transfusions (<6 h after the injury) were commonly due to TBI leading to a state of

Table 2
Demographics and clinical findings of the patients who received massive transfusion or not and, those who resulted in mortality or not.

Variable	Massive transfusion (+) (n: 8)	Massive transfusion (-) (n: 24)	p^*	Mortality (+) (n: 20)	Mortality (-) (n: 12)	$p^\dagger$
Male gender, n (%)	5 (62.5)	15 (62.5)	0.668	13 (65.0)	7 (58.3)	0.724
Age in years, median (IQR)	2.5 (1.2–11.2)	11.5 (4.3–15.7)	0.127	11.5 (2.2–15.7)	6.1 (1.3–15.0)	0.668
Tachycardia, n (%)	6 (75.0)	12 (50.0)	**0.043**	8 (40.0)	10 (83.3)	0.108
Hypotension, n (%)	3 (37.5)	9 (37.5)	0.668	9 (45.0)	3 (25.0)	0.227
Body temperature (°C), mean ± SD (min-max)	35.0 ± 0.5 (34.2–36.0)	35.8 ± 0.8 (34.0–37.0)	**0.040**	35.2 ± 0.6 (35.0–36.0)	36.1 ± 0.7 (35.5–36.6)	**0.010**
Hypothermia, n (%)	5 (62.5)	5 (20.8)	**0.031**	8 (40.0)	2 (16.0)	0.056
Glasgow Coma Scale score ≤ 8, n (%)	7 (87.5)	15 (62.5)	0.140	17 (85.0)	5 (41.5)	**0.001**

* Comparison of the patients who received massive transfusion or not.
† Comparison of the patients who resulted in mortality or not. SD: Standard deviation, IQR: interquartile range.

Table 3
Laboratory findings, Injury Severity Score and Abbreviated Injury score values of the patients who received massive transfusion or not and, those who resulted in mortality or not.

Variable	Massive transfusion (+) (n: 8)	Massive transfusion (-) (n: 24)	p^*	Mortality (+) (n: 20)	Mortality (-) (n: 12)	$p^\dagger$
Hemoglobin (g/dL), median (IQR)	8.9 (4.8–12.5)	9.1 (7.0–11.1)	0.814	9.1 (6.3–12.0)	9.3 (7.2–11.3)	0.899
Platelet count/mm^3, median (IQR)	208,500.0 (110,700.0–324,700.0)	312,000.0 (199,700.0–371,000.0)	0.325	211,600.0 (110,700.0–277,700.0)	347,000.0 (308,100.0–430,000.0)	**0.005**
Prothrombin time (seconds), median (IQR)	18.7 (17.7–20.9)	17.9 (14.0–23.0)	0.582	35.8 (17.8–28.2)	16.4 (13.8–19.6)	**0.003**
Activated partial thromboplastin time (seconds), median (IQR)	46.4 (39.4–54.7)	40.5 (28.7–107.0)	0.452	79.5 (46.2–142.7)	30.3 (27.9–43.0)	**<0.001**
International normalized ratio, median (IQR)	1.6 (1.5–2.0)	1.6 (1.2–2.1)	0.839	2.0 (1.5–2.5)	1.4 (1.2–1.8)	**0.007**
Fibrinogen (mg/dL), median (IQR)	1.8 (1.2–2.3)	1.1 (1.0–2.0)	0.351	1.7 (0.9–2.6)	1.3 (1.0–1.7)	0.304
D-dimer (μg/mL), mean ± SD (min-max)	33.0 ± 4.5 (28.0–37.0)	26.5 ± 12.5 (4.6–36.6)	0.612	30.9 ± 6.8 (20.0–36.0)	26.1 ± 13.6 (12.2–36.5)	0.942
pH, mean ± SD (min-max)	7.0 ± 0.2 (6.6–7.3)	7.1 ± 0.1 (6.6–7.3)	0.408	7.0 ± 0.2 (6.9–7.2)	7.2 ± 0.1 (7.1–7.2)	**0.030**
Lactate (mmol/L), median (IQR)	7.0 (3.4–10.8)	4.5 (2.9–7.5)	0.391	7.0 (3.4–10.8)	4.5 (2.9–7.5)	0.069
Bicarbonate (mmol/L), mean ± SD (min-max)	13.2 ± 5.3 (7.6–21.0)	14.3 ± 4.9 (3.8–21.0)	0.525	12.0 ± 5.0 (3.8–21.0)	16.8 ± 6.2 (10.0–21.0)	**0.037**
Base excess (mmol/L), median (IQR)	−16.5 (-21.8 to -6.1)	−9.5 (-15.4 to -7.1)	0.325	−15.4 (-22.0 to -7.7)	−8.5 (-11.2 to -4.5)	0.079
Abnormal SIPA, n (%)	5 (83.0)	15 (68.2)	0.432	11 (55.0)	9 (75.0)	0.528
BIG score, median (IQR)	3.1 (-3.0–6.7)	0.0 (-6.4–6.7)	0.376	0.0 (-5.6–8.6)	0.1 (-5.0–6.4)	0.843
Injury Severity Score, mean ± SD (min-max)	37.5 ± 10.3 (18.0–48.0)	38.3 ± 13.0 (6.0–75.0)	0.650	42.0 ± 11.5 (18.0–75.0)	32. ± 11.3 (6.0–43.0)	**0.021**

* Comparison of the patients who received massive transfusion or not.
† Comparison of the patients who resulted in mortality or not. SD: Standard deviation, IQR: interquartile range.

Table 4
Transfusion characteristics and prognosis of the patients who received massive transfusion or not and, those who resulted in mortality or not.

Variable	Massive transfusion (+) (n: 8)	Massive transfusion (-) (n: 24)	p^*	Mortality (+) (n: 20)	Mortality (-) (n: 12)	$p^\dagger$
Volume of blood products (mL/kg), median (IQR)	47.5 (40.2–53.7)	15.0 (10.5–22.5)	**<0.001**	19.0 (11.2–40.0)	18.0 (13.5–32.0)	0.769
Transfusion with a high FFP:PRBC ratio, n (%)	5 (62.5)	14 (58.4)	0.104	8 (40.0)	4 (33.3)	0.503
Transfusion complications, n (%)	5 (62.5)	7 (29.2)	**0.023**	6 (30.0)	3 (25.0)	0.369
Volume of crystalloid boluses (mL/kg), median (IQR)	67.5 (45.0–96.2)	35.0 (20.0–67.5)	0.058	60.0 (40.0–85.0)	20.0 (20.0–39.7)	**0.003**
Inotrope use, n (%)	7 (87.5)	8 (33.3)	**0.013**	13 (65.0)	2 (16.7)	**0.010**
Length of mechanical ventilation (days), median (IQR)	8.1 (0.2–11.5)	0.1 (0.1–1.0)	**0.024**	0.2 (0.1–2.39)	6.0 (2.5–9.0)	0.066
Length of stay in PICU (days), median (IQR)	12.0 (8.8–17.5)	2.0 (0.4–5.0)	**0.006**	8.0 (0.3–12.0)	6.0 (2.0–7.0)	0.949
Length of stay in hospital (days), median (IQR)	12.0 (0.3–22.2)	0.7 (0.1–8.7)	0.059	12.0 (0.3–22.2)	0.7 (0.1–8.7)	**0.003**
Mortality, n (%)						
4-h	1 (12.5)	7 (29.2)	0.333			
24-h	3 (37.5)	9 (37.5)	0.668			
30-day	7 (75.0)	14 (58.3)	0.344			

* Comparison of the patients who received massive transfusion or not.
† Comparison of the patients who resulted in mortality or not. SD: Standard deviation, IQR: interquartile range, PICU: pediatric intensive care unit, FFP: fresh frozen plasma, PRBC: packed red blood cell.

shock, while only 30 % of them died due to uncontrolled hemorrhage [21]. Likewise, in our study, although ISS values were similar for children who survived and those who died within 4 h after arrival, head AIS scores were higher in the cases that ended in death.

Debate also exists regarding the proper ratio of blood products that should be used to improve survival and minimize morbidity in exsanguinating subjects [10]. There is little evidence supporting the use of component-based transfusion utilizing rigid strategies and blood product ratios for the pediatric population [22]. Cannon et al. concluded that a high FFP:PRBC ratio did not improve survival [23]. In contrast, Cunningham et al. reported that survival was improved for children who were transfused with a high FFP:PRBC ratio at 4 h and at 24 h [7]. Butler et al. showed that in massively transfused children, higher FFP:PRBC ratios were associated with lower 24-h mortality [17]. Noland et al. found a survival benefit with a 1:1 FFP:PRBC ratio for children who received MT [11]. There are also a few single-center civilian studies that did not find an association between mortality and FFP:PRBC transfusion ratio [24,25]. In our study, mortality rates were similar for patients who received and did not receive transfusions with high FFP:PRBC ratios in the MT group and among all cases. In contrast to the studies by Cannon et al. [23] and Cunningham et al. [7], children who received transfusions with high FFP:PRBC ratios were older in age.

There is also a paucity of data on the ideal volume of blood products or crystalloid that should be administered as part of the initial resuscitation for the pediatric trauma population [9]. It remains unclear whether commonly used resuscitative fluids, including crystalloid or blood products, are linked with adverse outcomes constituting a mere surrogate for injury severity or representing a truly causative effect [3].

Table 5
Comparison of patients who did and did not die within 30 days after arrival according to TBI severity groups.

		Mortality (+) (n: 14)	Mortality (-) (n: 6)	*p* value
Severe TBI (+) (n: 20)	Abnormal SIPA, n (%)	6 (42.8)	4 (66.6)	0.182
	Injury Severity Score, mean ± SD (min-max)	41.0 ± 7.1 (27.0–57.0)	30.8 ± 8.3 (18.0–41.0)	**0.014**
	Volume of crystalloid boluses (mL/kg), median (IQR)	62.5 (36.2–80.0)	20.0 (18.0–40.0)	**0.049**
	Volume of blood products (mL/kg), median (IQR)	15.0 (10.0–33.0)	15.0 (13.0–45.0)	0.965
		Mortality (+) (n: 6)	Mortality (-) (n: 6)	*p* value
Severe TBI (-) (n: 12)	Abnormal SIPA, n (%)	6 (100.0)	3 (50.0)	**0.009**
	Injury Severity Score, mean ± SD (min-max)	44.1 ± 18.7 (31.5–57.0)	33.8 ± 15.6 (6.0–43.0)	0.313
	Volume of crystalloid boluses (mL/kg), median (IQR)	67.5 (39.7–88.7)	20.0 (20.0–46.5)	**0.026**
	Volume of blood products (mL/kg), median (IQR	26.0 (14.8–40.0)	21.0 (13.5–30.0)	0.584

SD: Standard deviation, IQR: interquartile range, SIPA: Shock index, pediatric age-adjusted, TBI: traumatic brain injury.

Table 6
Multivariable analysis to predict 30-day mortality.

	Variable	Odds Ratio	95 % Confidence Interval	*p*
1	**GCS score of ≤8**	21.700	1.951–243.498	**0.012**
	ISS score of ≥25	1.738	0.021–144.107	0.806
	Having received MT	0.335	0.026–4.265	0.399
	Crystalloid bolus volume of ≥40 mL/kg	9619	0.842–109.941	0.069
2	**GCS score of ≤8**	0.000	0.000- –	0.999
	ISS score of ≥25	1.304	0.013–128.149	0.910
	Having received MT	0.473	0.027–8.255	0.608
	Crystalloid bolus volume of ≥40 mL/kg	7.918	0.563–111.434	0.125
	APTT >37.5 s	48.000	3.704–621.998	**0.003**

GCS: Glasgow Coma Scale, ISS: Injury Severity Score, MT: massive transfusion, APTT: activated partial thromboplastin time. 1: Multivariable analysis was performed, and among the parameters of a GCS score of ≤8, an ISS score of ≥25, having received MT, and crystalloid bolus volume of ≥40 mL/kg, a GCS score of ≤8 was identified as a predictor. 2: When we added APTT to these parameters, an APTT value of >37.5 s was identified as a predictor of 30-day mortality.

Cannon et al. concluded that increased crystalloid volumes were associated with decreased mortality while greater blood product volumes were associated with increased mortality [23]. In contrast, Edwards et al. reported that increased crystalloid administration had an association with length of intensive care unit and hospital stay for both MT and high-volume transfusions as well as with increased length of MV in cases of high-volume transfusions. They also showed that crystalloid administration of >150 mL/kg in the first 24 h increased mortality [5]. Elkbuli et al. reported that crystalloid resuscitation of >60 mL/kg was associated with increased length of PICU stay without survival benefit [26]. Edwards et al. showed that trauma resuscitation with more than one crystalloid bolus was associated with increased need for blood product transfusion and worse outcomes, which included extended duration of MV and hospital stay; although the volume of blood products was similar for patients who did and did not survive, the volume of crystalloid boluses was higher among patients who did not survive [5]. In our study, the total volume of crystalloid boluses was higher among patients who died than those who survived, although the volume of blood products was similar for the two groups. However, crystalloid boluses were not found as a predictor of mortality in our multivariable analysis, which included the parameters of GCS score of ≤8, ISS score of ≥25, having received MT and crystalloid bolus volume of ≥40 mL/kg, and APTT value of >37.5 s. But it should be kept in mind that the number of cases in our study was limited. Early use of blood products instead of crystalloid boluses for ongoing volume resuscitation was also recommended for trauma-related hemorrhagic shock in the 2020 Pediatric Advanced Life Support guidelines [27]. While aggressive fluid resuscitation may rapidly improve vital signs, the overall effect on outcomes may be worse than expected [3]. Low-volume resuscitation or hypotensive resuscitation may balance the risks of trauma resuscitation with the aim of organ perfusion.

The SIPA was reported to have a correlation with ISS, ventilator use, length of hospital stay, early need for blood product transfusion, and mortality in pediatric trauma patients [15,28,29]. In our study population, the SIPA was not correlated with the ISS, need for MT, or outcomes, but among the patients with non-severe TBI, those who did not survive had higher initial SIPA values. This may be related to the fact that most of our patients had severe TBI, so the reason may be that the associated hypertension and/or bradycardia commonly present in patients with severe TBI could alter SIPA values. It was reported that in cases of head trauma, SIPA elevation upon arrival was correlated with a longer stay in the hospital [28]. However, we could not perform serial measurements of SIPA due to the retrospective nature of our study. The BIG score was shown to predict poor outcomes and was also reported as an independent predictor of mortality for pediatric trauma patients [2]. However, there was no difference in this regard between our patients who survived and those who did not, nor between those who received MT and those who did not. This could be related to the fact that our patients had very high ISS values, so the BIG score could not successfully predict outcomes among our severely injured population.

The main limitation of our study lies in its retrospective nature. We used ICD codes to identify patients, but missing data may have led to the underestimating of the real number of cases. Furthermore, the data were obtained from a single medical center, so the sample size was relatively small. In addition, trauma resuscitation practices were clinician-dependent.

In conclusion, children who received MT had longer duration of MV and PICU stay together with higher transfusion complication rates compared to those who did not receive MT, but there was no significant difference in ISS scores, the volume of crystalloid boluses, length of hospital stay, or mortality between those two groups. The total volume of crystalloid boluses was higher in patients who died than those who survived, although the volume of blood products was similar for those two groups. A GCS score of ≤8 and an APTT value of >37.5 s can be used to predict 30-day mortality in pediatric trauma patients. For the precise identification of optimal timing and treatment protocols, it is needed to have a larger number of pediatric trauma patients who received MT and conformation in further studies in this field.

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Author contributions

HÖ, MD and DY initiated and designed the study. Data collection and analysis was performed by NŞ, AU, AÖ and ŞY. The manuscript was written by NŞ, ÖT and MD. Final evaluation of the manuscript and checking of analysis was performed by MD, ÖT, HÖ and NŞ.

Availability of data and material

The data that support the findings of this study are available from the corresponding author, upon request.

Transparency document

The Transparency document associated with this article can be found in the online version.

CRediT authorship contribution statement

Nihan Şık: Conceptualization, Methodology, Writing – original draft. **Aslıhan Uzun:** Data curation. **Ali Öztürk:** Data curation. **Özlem Tüfekçi:** Visualization, Investigation. **Şebnem Yılmaz:** Supervision. **Durgül Yılmaz:** Software, Validation. **Hale Ören:** Writing – review & editing. **Murat Duman:** Writing – review & editing.

Declaration of Competing Interest

The authors declare no conflict of interest.

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