



To give or not to give? Blood for pediatric trauma patients prior to pediatric trauma center arrival

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Abstract

Purpose This study evaluates the indications, safety and clinical outcomes associated with the administration of blood products prior to arrival at a pediatric trauma center (prePTC).

Methods Children (≤ 18 years) who were highest level activations at an ACS level 1 pediatric trauma center (PTC) from 2009–2019 were divided into groups:(1) patients with transport times < 4 h who received blood prePTC (*preBlood*) versus (2) age matched controls with transport times < 4 h who only received crystalloid prePTC (*preCrystalloid*).

Results Of 1269 trauma activations, 38 met *preBlood* and 38 met *preCrystalloid* inclusion criteria. A similar volume of prePTC crystalloid infusion was observed between cohorts ($p = 0.311$). *PreBlood* patients evidenced greater hemodynamic instability as demonstrated by higher prePTC pediatric age-adjusted shock index (SIPA) scores. *PreBlood* patients showed improvement in lactate ($p = 0.038$) and hemoglobin ($p = 0.041$) levels upon PTC arrival. *PreBlood* patients received less crystalloid within 12 h of PTC admission ($p = 0.017$). No significant differences were found in blood transfusion volumes within six ($p = 0.293$) and twenty-four ($p = 0.575$) hours of admission, nor in mortality between cohorts ($p = 0.091$).

Conclusions The administration of blood to pediatric trauma patients prior to arrival at a PTC is safe, transiently improves markers of shock, and was not associated with worse outcomes.

Keywords Crystalloid · Blood transfusion · Pediatric trauma · Prehospital

Introduction

Hemorrhage is associated with approximately 30% of traumatic deaths and is a leading cause of potentially preventable death [1, 2]. Current American College of Surgeons (ACS) Advanced Trauma Life Support (ATLS) guidelines for the

management of acute hemorrhage and hemorrhagic shock recommend an initial 20 mL/kg bolus of an isotonic fluid followed by an early balanced resuscitation with blood products [3]. Despite these recommendations, many pediatric patients are resuscitated with far more than 20 mL/kg of crystalloid before blood is given [4, 5]. Trauma-induced coagulopathy

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may rapidly develop after severe injury and initiating crystalloid resuscitation without the inclusion of balanced blood product transfusion has been associated with worsening acidosis and ensuing suppression of essential coagulation factors [6, 7]. As a result, crystalloid resuscitation strategies intended to treat hypovolemia may worsen acidosis, coagulopathy, and shock [7]. Prior work has also demonstrated that children may be more susceptible to trauma-induced coagulopathy [6, 7]. By halving the volume of crystalloid and using an early, balanced resuscitation with blood products, physicians caring for traumatically injured adult patients have seen a reduction in acidosis and subsequent improvement in coagulation parameters [7].

Improved outcomes have been shown in adult trauma patients when restrictive prehospital crystalloid resuscitation is combined with a balanced, hemostatic resuscitation using blood products [8–10]. In the few pediatric studies investigating restrictive crystalloid use with early administration of blood products, overall improvement in several markers of coagulopathy and shock have been seen [11–13]. These studies by Moors et al. [11], Potter et al. [12], and Fahy et al. [13] highlight the safety of transfusing pediatric patients prior to arrival at a pediatric trauma center (prePTC), with no transfusion reactions reported. Despite these positive findings, prePTC blood transfusion protocols for pediatric trauma patients have not gained widespread adoption. This is partly due to the scarcity of data surrounding the indications, safety, outcomes, and mortality associated with prehospital transfusion in the pediatric population [13]. Another hinderance may be the perceived complexity of maintaining and safely transfusing blood products in emergency, mobile environments.

The current study aims to evaluate the indications, safety, and clinical outcomes associated with prePTC blood transfusion in pediatric trauma patients. We chose to compare patients who received blood products prior to arrival at a PTC (*preBlood*), to a cohort of patients who received crystalloid alone (*preCrystalloid*)—but who ultimately received blood within 6 h of PTC arrival. By comparing the first group to the latter, we sought to create a comparison cohort with similar illness severity that might have benefited from earlier transfusion in the prePTC setting. We hypothesized that pediatric patients who received prePTC blood products would have improved shock indices and less coagulopathy on arrival at the PTC, decreased in-hospital transfusion requirements, improved clinical outcomes, and lower mortality, compared to those who received crystalloid alone prior to arrival at the PTC.

Material and methods

Setting

Children’s Hospital Colorado (CHCO) is the only American College of Surgeons verified Level 1 PTC in Colorado

and serves the neighboring states of Montana, Wyoming, North and South Dakota, Nebraska, and New Mexico. The Colorado Multiple Institutional Review Board approved this study under a waiver of informed consent.

Study design and population

A retrospective review was conducted of all highest-level trauma activations at CHCO between January 2009 to December 2019 to identify patients (≤ 18 years), who arrived at the PTC within 4 h from the time of their injury. Patients were included if brought directly from the scene or as a transfer from an outside hospital. The timeframe of 4 h from the time of injury to arrival at the PTC was chosen because this is the approximate maximum transport time when patients are transported directly from the scene to our trauma center. Patients were placed into one of two groups based on the resuscitative fluids they were given in the prePTC setting. The *preBlood* group received crystalloid and blood products prior to arrival at the PTC, whereas the *preCrystalloid* group only received crystalloid. The *preCrystalloid* patient cohort was further narrowed to those receiving a blood product transfusion within 6 h of arrival to the PTC. This additional selection criterion produced a comparison cohort that required transfusion soon after their arrival at the PTC. Patients were excluded if they had missing transport times, missing transfusion volume or crystalloid volume data, and if > 18 years old. The matched cohort was created using a nearest neighbor statistical matching algorithm with a Euclidean measure of distance to match patients by transport time (defined as the time from injury to arrival at the PTC.)

Data collection

Patient data were collected through an electronic medical record bioinformatics inquiry and an additional review of patient electronic medical records. Data included demographics, prePTC vital signs, Glasgow Coma Scale (GCS), time from injury to PTC arrival, PTC arrival vital signs, injury type, referring facility lab values, PTC admission lab values, and injury severity score (ISS). Additionally, total crystalloid volumes infused before arrival to the PTC and within the first 12 h following admission to the PTC were collected. Crystalloid administration volumes were further classified as low (0–39.9 mL/kg), mid (40–59.9 mL/kg), and high (≥ 60 mL/kg), as previously defined by the literature [4]. Blood volumes and product types [red blood cells (RBC), fresh frozen plasma (FFP), and platelets (PLT)] were also recorded. Complications and clinical outcomes were documented.

Patient heart rate (HR) and systolic blood pressure (SBP) measurements were used to calculate SIPA scores in the field

and upon PTC arrival. Shock index pediatric age-adjusted (SIPA) is a well-validated measure for identifying shock in pediatric trauma patients and has been shown to be superior to traditional, age-adjusted vital signs [14]. Elevated *pre-hospital* SIPA scores herald poor patient outcomes, as does trending *prehospital* SIPA scores over time [15]. Elevated in-hospital SIPA scores are associated with the need for transfusion, worse patient outcomes and increased mortality [16]. SIPA scores were compared to established cutoff values to categorically define the values as either elevated or not elevated [17, 18]. SIPA has only been validated in patients greater than 1 year of age. Therefore, normal age-appropriate HR and SBP values were used to calculate (HR/SBP) cutoff values for patients less than 1 year-old.

Statistical analysis

Demographics, blood product and crystalloid volumes, and clinical outcomes data are presented as medians with interquartile ranges for continuous variables. Categorical variables are described as frequencies and proportions. Percent change was calculated for SIPA scores and lab values. Kruskal–Wallis or Chi-Square testing was done to evaluate group differences depending on the variable type. Statistical significance was defined as $p \leq 0.05$, with the α error level designated at 0.05. All analyses were performed using R (R Foundation for Statistical Computing, Vienna, Austria, <http://www.R-project.org/>).

Results

Demographics and injury characteristics

During the study period, 1,269 patients arrived at the PTC as highest-level trauma activations. Thirty-eight patients who arrived at the PTC within 4 h from the time of their injury received a blood transfusion before arrival to the PTC; these patients comprised the *preBlood* cohort. Thirty-eight additional patients were matched to comprise the *preCrystalloid* group. All (38/38) *preBlood* patients and 79% (30/38) of the *preCrystalloid* patients arrived as transfers to the PTC from an outside hospital. The median age was 7.5 years (IQR 2.1, 11.5) for the *preBlood* cohort and 5.5 years (IQR 2.5, 10.0) for the *preCrystalloid* patients. There was no significant difference in age between groups ($p = 0.799$). No significant differences were observed in gender, ISS, GCS, or trauma type (Table 1).

Clinical characteristics

Nearly all *preBlood* patients (36/38, 95%) had elevated SIPA scores immediately following injury, compared to 76% (29/38) of *preCrystalloid* patients ($p = 0.050$). There was no significant difference in the overall number of patients with elevated SIPA scores upon PTC arrival among the *preBlood* and *preCrystalloid* patients (28/38, 74% vs. 23/38, 61%,

Table 1 Demographics, injury, and clinical characteristics^a

	PreBlood (n = 38)	PreCrystalloid (n = 38)	p value
Age	7.50 (2.10, 11.50)	5.50 (2.46, 10.00)	0.799
Male Sex	23 (60.5%)	21 (55.3%)	0.816
Weight	24.50 (14.25, 44.75)	19.00 (13.50, 35.50)	0.371
ISS	29.50 (21.00, 42.75)	28.000 (18.75, 38.00)	0.489
GCS on arrival to PTC	3.000 (3.00, 6.75)	3.000 (3.00, 6.00)	0.732
TBI	24 (64.9%)	25 (65.8%)	1.000
NAT	4 (10.5%)	8 (21.1%)	0.345
GSW	6 (15.8%)	2 (5.3%)	0.262
BLSI	7 (18.4%)	7 (18.4%)	1.000
Time from injury to arrival at PTC	2.87 (2.08, 3.58)	2.742 (2.10, 3.13)	0.352
PTA SIPA	1.91 (1.45, 2.68)	1.42 (1.29, 1.94)	0.006
PTA SIPA elevated	36 (94.7%)	29 (76.3%)	0.050
ED SIPA	1.39 (1.08, 1.92)	1.29 (0.98, 1.62)	0.226
ED SIPA elevated	28 (73.7%)	23 (60.5%)	0.329

ISS Injury Severity Score; *TBI* Traumatic Brain Injury; *NAT* non accidental trauma; *GSW* gunshot wound; *BLSI* blunt liver or spleen injury; *PTA* prior to arrival; *SIPA* shock index pediatric age adjusted; *GCS* Glasgow Coma Scale; *FAST* focused assessment with sonography for trauma; *ED* emergency department; *CPR* cardiopulmonary resuscitation; *PTC* pediatric trauma center

^aData are presented as medians with interquartile ranges Q1 & Q3 for continuous variables. Categorical variables were described as frequencies and proportions. Kruskal–Wallis or Chi-Square testing was done depending on the variable type to determine *p* values

$p=0.329$). The percent decrease in SIPA values from time of injury to arrival at the PTC was -19% (IQR -45% , 5%) for the *preBlood* patients, versus -11% (IQR -28% , 10%) for the *preCrystalloid* patients.

Blood and crystalloid volumes prior to arrival at the PTC

The volume of crystalloid that the *preBlood* and *preCrystalloid* patients received prior to arrival at the PTC did not significantly differ [36.2 mL/kg (25.0, 51.5) vs. 29.2 mL/kg (8.4, 49.2), $p=0.311$]. Similarly, prePTC crystalloid administration categories did not significantly differ between the groups, with 60% (23/38) of *preBlood* and 66% (25/38) of *preCrystalloid* patients having received low-volume crystalloid administration. Eighteen percent (7/38) of *preBlood* and 13% (5/38) of *preCrystalloid* patients received mid-volume crystalloid administration, and 21% (8/38) of *preBlood*, and 24% (9/38) of *preCrystalloid* patients received high levels of crystalloid administration as defined in the methods. The median amount of blood product transfused in the *preBlood* patients prior to PTC arrival was 16.0 mL/kg (IQR: 9.4, 25.0). The breakdown of blood products transfused in the *preBlood* patients prior to arrival at the PTC was as follows:

87% received pRBCs, 34% FFP, and 13% PLTs. Additional fluid data are shown in Table 2.

Lab results

PreBlood patients had significantly higher lactate levels [7.0 (IQR: 6.0, 10.0) vs. 3.5 (IQR: 3.3, 4.8) $p=0.011$] at the referring facilities, when compared to *preCrystalloid* patients. Upon arrival at the PTC there was no significant difference in initial lactate values between the two cohorts [2.9 (IQR: 1.8, 4.3) vs. 3.0 (IQR: 2.0, 4.9), $p=0.738$]. However, *preBlood* patients demonstrated a significant improvement in lactate following transport and arrival at the PTC [-62% (IQR: -75% , -48%) when compared to the *preCrystalloid* cohort [-8% (IQR: -27% , 10%); $p=0.038$]. Although there was no significant difference between the groups' base deficit (BD) values prior to PTC arrival, upon arrival at the PTC the *preBlood* patients had significantly lower BD values [-9.5 (IQR: -14.0 , -6.9) vs. -6.0 (IQR: -10.2 , -4.7), $p=0.004$]. Despite these findings, there was no significant difference in percent change for either group's BD values from prePTC to arrival at the PTC (*preBlood*: median 0% (IQR: -63% , 25%); *preCrystalloid*: median -22% (IQR: -29% , -7%); $p=0.892$).

Table 2 Blood product and transfusion data^a

	PreBlood (n=38)	PreCrystalloid (n=38)	p value
PTA crystalloid (mL/kg)	36.165 (25.00, 51.50)	29.17 (8.41, 49.17)	0.311
PTA Blood (mL/kg)	16.01 (9.41, 25.00)	NA	NA
Received pRBC PTA	33 (86.8%)	NA	NA
PTA pRBC (mL/kg)	10.00 (6.25, 22.64)	NA	NA
Received FFP PTA	13 (34.2%)	NA	NA
PTA FFP (mL/kg)	0.00 (0.00, 6.40)	NA	NA
Received PLT PTA	5 (13.2%)	NA	NA
PTA PLT (mL/kg)	0.00 (0.00, 0.00)	NA	NA
Total transfusion within 4 h of arrival at PTC (mL/kg)	14.58 (0.00, 45.16)	22.50 (9.69, 41.67)	0.446
pRBC transfused within 4 h of arrival at PTC (mL/kg)	11.19 (0.00, 30.33)	15.81 (7.43, 33.65)	0.336
FFP transfused within 4 h of arrival at PTC (mL/kg)	0.00 (0.00, 17.04)	0.00 (0.00, 17.56)	0.777
PLT transfused within 4 h of arrival at PTC (mL/kg)	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)	0.646
Total transfusion within 6 h of arrival at PTC (mL/kg)	17.71 (1.99, 55.52)	26.97 (13.49, 41.67)	0.293
pRBC transfused within 6 h of arrival at PTC (mL/kg)	12.50 (0.00, 32.38)	18.26 (10.18, 33.65)	0.239
FFP transfused within 6 h of arrival at PTC (mL/kg)	0.00 (0.00, 17.04)	0.00 (0.00, 17.56)	0.969
PLT transfused within 6 h of arrival at PTC (mL/kg)	0.00 (0.00, 3.30)	0.00 (0.00, 0.00)	0.696
Total Transfusion within 24 h of arrival at PTC (mL/kg)	28.21 (8.69, 55.52)	27.92 (15.16, 41.67)	0.575
pRBC transfused within 24 h of arrival at PTC (mL/kg)	16.15 (8.46, 32.38)	18.90 (12.10, 33.65)	0.509
FFP transfused within 24 h of arrival at PTC (mL/kg)	4.34 (0.00, 19.41)	4.67 (0.00, 17.56)	0.692
PLT transfused within 24 h of arrival at PTC (mL/kg)	0.00 (0.00, 6.09)	0.00 (0.00, 0.00)	0.578
Crystalloid infused within 12 h of arrival at PTC	52.25 (30.86, 96.71)	86.82 (52.15, 123.04)	0.017

PTA prior to arrival; PTC pediatric trauma center; pRBC packed red blood cells; FFP fresh frozen plasma; PLT platelet

^aData are presented as medians with interquartile ranges Q1 & Q3 for continuous variables. Categorical variables were described as frequencies and proportions. Kruskal–Wallis or Chi-Square testing was done depending on the variable type to determine p values

preBlood patients had significantly higher INR values at the referring facility, compared to *preCrystalloid* patients [1.5 (IQR: 1.5, 1.8 vs. 1.3 (IQR: 1.2, 1.4), $p=0.020$]; however, there was no significant difference at the PTC, where *preBlood* patient INR values had increased by 7% (IQR: – 1%, 16%) and *preCrystalloid* INR values had increased by 10% (IQR: 9%, 19%).

There was no significant difference in platelet counts or percent change in platelet counts between the two groups prior to arrival to the PTC. Upon arrival at the PTC, *preBlood* patients had significantly lower platelet counts compared to *preCrystalloid* patients [163.0 (IQR: 114.3, 200.8) vs. 269.0 (IQR: 169.0, 342.0), $p<0.001$], as shown in Table 3.

Crystalloid volumes infused after arrival at the PTC

Once at the PTC, *preBlood* patients received significantly less crystalloid (52.3 mL/kg; IQR: 30.9, 96.7) within 12 h of arrival compared to the *preCrystalloid* group (86.8 mL/kg; IQR: 52.2, 123.0; $p=0.017$). Similarly, within 12 h of arrival at the PTC, significantly more *preBlood* patients received low-level volumes (0–39.9 mL/kg) of crystalloid compared to *preCrystalloid* patients [14/38 (40%) vs. 4/38 (11%), $p=0.014$]. No significant difference existed in rates of mid-level crystalloid administration volumes (40–59.9 mL/kg) between *preBlood* and *preCrystalloid* patients [6/38 (16%) vs. 7/38 (18%), $p=1.00$]. Notably, almost half of the *preBlood* patients (17/38, 45%) received high-volume crystalloid administration (≥ 60 mL/kg), which was significantly less than the *preCrystalloid* patients (27/38, 71%) ($p=0.036$).

Blood product transfusion after arrival at the PTC

There were no significant differences between the two groups in the volumes of blood products transfused within the first six and 24 h of arrival at the PTC. Within the first 6 h of arrival, *preBlood* and *preCrystalloid* patients were transfused 17.7 mL/kg and 27.0 mL/kg of blood products, of which pRBC accounted for 12.5 mL/kg and 18.3 mL/kg, respectively. Within the first 24 h of arrival at the PTC the *preBlood* and *preCrystalloid* patients were transfused 28.2 mL/kg and 27.9 mL/kg of blood products, respectively, of which 16.2 mL/kg and 18.9 mL/kg were pRBC, and 4.3 mL/kg and 4.2 mL/kg were FFP. Further breakdown of blood product and crystalloid infusion volumes is shown in Table 2.

Operation after arrival at the PTC

Thirteen percent (5/38) of *preBlood* patients had an operation within 6 h of arrival at the PTC compared to 29%

(11/38) of *preCrystalloid* patients ($p=0.16$). Sixteen percent (6/38) of *preBlood* patients and 32% (12/38) of *preCrystalloid* patients went to the operating room within 12 h of arrival at the PTC ($p=0.18$). Sixteen percent (6/38) of *preBlood* and 37% (14/38) of *preCrystalloid* patients had an operation within 24 h of arrival at the PTC ($p=0.07$). Laparotomies were performed in three (8%) *preBlood* and one (3%) *preCrystalloid* patients. Three (8%) *preBlood* and nine (24%) *preCrystalloid* patients had a craniectomy or craniotomy. Three *preCrystalloid* patients received the remaining procedures with one patient (3%) undergoing an escharotomy, one patient (3%) underwent femoral stabilization, and one patient (3%) was taken to the operating room for incision and drainage.

Complications and outcomes

There were no transfusion reactions documented for *preBlood* patients in the prePTC setting. There was, however, one transfusion reaction in one *preBlood* patient and one in a *preCrystalloid* patient after arrival at the PTC. There were no significant differences in outcomes between the two groups, including pneumonia, acute renal failure, deep vein thrombosis, sepsis, ventilator days, intensive care unit (ICU) length of stay (LOS), hospital LOS, or mortality (Table 4).

Discussion

The administration of prePTC blood to pediatric trauma patients is safe. Patients who received prePTC blood did not experience a greater risk of complications (transfusion reaction, pneumonia, acute renal failure, deep vein thrombosis, sepsis), nor did they experience worse clinical outcomes (ventilator days, ICU LOS, hospital LOS, or mortality). These findings endorse prePTC transfusion safety and support a growing body of literature suggesting that harm can result from crystalloid-only resuscitation and delays to transfusion [4, 5, 10, 17]. Interestingly, in comparison with the *preBlood* group, the *preCrystalloid* cohort received more blood and crystalloid within 6 and 12 h of arrival at the PTC, suggesting they might have benefited from earlier transfusion. This finding is bolstered by the observation that *preBlood* patients exhibited greater improvements in markers of shock and coagulopathy on arrival at the PTC. This is an important finding, considering hemorrhagic shock is a leading cause of preventable death in severely injured pediatric patients, who are at risk of trauma-induced coagulopathy [1, 6, 7].

A study in the Netherlands evaluating the effectiveness of pRBC transfusion in the prehospital setting found that in a cohort of ten critically ill children, two of whom were

Table 3 Lab results^a

	PreBlood (n = 38)	PreCrystalloid (n = 38)	p value
PrePTC lactate			0.011
N-missing	27	29	
Median(Q1,Q3)	7.00 (6.00, 9.95)	3.50 (3.30, 4.74)	
ED lactate			0.738
N-missing	20	19	
Median(Q1,Q3)	2.91 (1.83, 4.32)	3.00 (1.99, 4.87)	
PrePTC base deficit			0.360
N-missing	31	27	
Median(Q1,Q3)	- 8.00 (- 17.20, - 7.00)	- 7.00 (- 8.70, - 6.50)	
ED base deficit			0.004
N-missing	0	1	
Median(Q1,Q3)	- 9.50 (- 14.00, - 6.85)	- 6.00 (- 10.20, - 4.70)	
PrePTC INR			0.020
N-missing	25	33	
Median(Q1,Q3)	1.50 (1.47, 1.79)	1.34 (1.23, 1.40)	
ED INR			0.280
N-missing	7	3	
Median(Q1,Q3)	1.57 (1.36, 1.83)	1.49 (1.34, 1.69)	
PrePTC platelet count			0.263
N-missing	14	22	
Median(Q1,Q3)	299.50 (235.50, 325.00)	307.00 (268.00, 418.25)	
ED platelet count			<0.001
N-missing	4	2	
Median(Q1,Q3)	163.00 (114.25, 200.75)	269.00 (169.00, 342.00)	
PrePTC hemoglobin			0.472
N-missing	11	20	
Median(Q1,Q3)	11.10 (8.55, 12.90)	11.55 (10.20, 13.00)	
ED hemoglobin			0.147
N-missing	1	1	
Median(Q1,Q3)	11.20 (8.80, 14.00)	9.60 (8.20, 11.60)	
PrePTC PTT			0.103
N-missing	28	34	
Median(Q1,Q3)	45.80 (33.38, 56.73)	29.00 (28.18, 30.58)	
ED PTT			0.088
N-missing	5	3	
Median(Q1,Q3)	40.00 (31.00, 60.50)	34.00 (29.00, 41.75)	
ED fibrinogen			0.259
N-missing	21	27	
Median(Q1,Q3)	125.00 (80.00, 196.00)	166.00 (120.00, 231.00)	
ED D-DIMER			0.970
N-missing	23	31	
Median(Q1,Q3)	20.00 (11.83, 20.00)	20.00 (9.70, 20.00)	
ED white blood cell count			0.058
N-missing	4	2	
Median(Q1,Q3)	13.00 (9.60, 20.14)	17.83 (11.92, 23.72)	

PrePTC Prior to arrival to the pediatric trauma center; *ED* emergency department; *INR* international normalized ratio; *PTT* partial thromboplastin time

^aData are presented as medians with interquartile ranges Q1 & Q3 for continuous variables. Categorical variables were described as frequencies and proportions. Kruskal–Wallis or Chi-Square testing was done depending on the variable type to determine *p* values

Table 4 Outcomes^a

	PreBlood (n = 38)	PreCrystalloid (n = 38)	p value
Pneumonia	5 (13.2%)	4 (10.5%)	1.000
Extremity Compartment Syndrome	0 (0.0%)	0 (0.0%)	1.000
Urinary tract infection	3 (7.9%)	2 (5.3%)	1.000
Acute renal failure	1 (2.6%)	0 (0.0%)	1.000
Deep vein thrombosis	0 (0.0%)	1 (2.6%)	1.000
Sepsis	0 (0.0%)	1 (2.6%)	1.000
Ventilator days	5.00 (1.00, 8.00)	4.00 (1.00, 8.00)	0.798
ICU LOS	6.00 (2.00, 13.00)	5.50 (3.00, 10.75)	0.694
Hospital LOS	6.50 (2.00, 15.75)	10.00 (5.00, 17.75)	0.137
Mortality	17 (44.7%)	9 (23.7%)	0.091

ICU intensive care unit; LOS length of stay

^aData are presented as medians with interquartile ranges Q1 & Q3 for continuous variables. Categorical variables were described as frequencies and proportions. Kruskal–Wallis or Chi-Square testing was done depending on the variable type to determine *p* values

unexpected survivors, all had improved acid–base balance, hemoglobin levels, and coagulopathy [11]. In the current study, similar improved trends were found in markers of shock, including lactate and SIPA, as well as in hemoglobin levels and INR values. These results support prePTC blood safety and are consistent with extant studies that describe the potential for hemodilution and negation of blood product benefits that accompany high volume crystalloid administration [18].

Studies by Acker et al. [4] and Coons et al. [5] showed that an infused crystalloid volume of > 60 mL/kg in the first 24 h was associated with worse outcomes, including increased hospital LOS, need for mechanical ventilation, severe anemia, and thrombocytopenia. Similarly, in a multicenter prospective observational study by Polites et al. [19] pediatric patients with hemorrhagic shock had increased odds of prolonged ventilator days, intensive care unit length of stay (LOS), and hospital LOS for each crystalloid bolus they were given before being transfused. Nearly a quarter of *preBlood* patients in the present study received a prePTC crystalloid resuscitation considered high-volume administration (≥ 60 mL/kg), and nearly half received a high-volume crystalloid resuscitation within 12 h of PTC arrival. Conversely, *preBlood* patients received significantly less crystalloid than the *preCrystalloid* patients, which further emphasizes the potential benefits of prePTC blood transfusion. While no significant differences were found in patients who went to the operating room within 6, 12, and 24 h of arrival, descriptively more *preCrystalloid* patients had operations after arrival at the PTC. This may account for some of the increased crystalloid volumes received by *preCrystalloid* patients following their arrival at the PTC.

Aggressive crystalloid resuscitation without blood product transfusion can dilute coagulation factors and worsen trauma-induced coagulopathy in adult and pediatric trauma

populations [5, 18, 19]. Bickell et al. [17] imputed aggressive prehospital fluid resuscitation in perpetuating hemorrhage due to blood pressure elevation with the concomitant dilution of hemoglobin and clotting factors. *PreBlood* patients, despite receiving similar prePTC crystalloid volumes, had lower lactate values than the *preCrystalloid* cohort. Additionally, while *preBlood* patients demonstrated no change in their base deficits, *preCrystalloid* patients had widening derangements in BD values. *PreBlood* patients also showed improvement in their hemoglobin levels upon arrival at the PTC, whereas *preCrystalloid* patients' hemoglobin levels dropped. The improvement seen in *preBlood* patients' SIPA scores on arrival at the PTC are indicative of an improvement in their shock status, most likely due to early blood product transfusion.

Downward trends in SIPA scores are associated with improved outcomes in pediatric patients suffering from blunt traumatic injuries [20]. In a study by Phillips et al. [21] traumatically injured pediatric patients with an elevated prehospital SIPA that remained elevated on arrival to the E.D. were more likely to receive a transfusion and more likely to have worse outcomes. The downward progression in SIPA values identified in the *preBlood* cohort suggests a benefit to giving blood early; however, we were unable to demonstrate improved outcomes in this group.

This study should inform future research in restrictive crystalloid resuscitation and increased use of prePTC blood for the pediatric population. These patients can be challenging to manage, especially in the prePTC setting. It is hard to determine which children will most benefit from early transfusion and hemostatic resuscitation, and even harder to predict when and which children will decompensate. This study therefore highlights the need for point-of-care testing and/or a noninvasive, real-time method for monitoring individual-specific hemodynamic status, to aid in the

identification of children who will most benefit from early blood product administration.

Limitations

This study has several limitations. It is a retrospective study at a single center. The implementation of prePTC blood transfusion protocols is not widespread. Therefore, most patients were transferred from outside facilities. To best replicate transfer times from the injury scene, we limited our patient population to those with transport times under four hours. This significantly reduced the study sample size, as many of the patients transported to CHCO are referrals from neighboring states, with long scene, outside hospital and transport times. Additionally, some patients may have had their transfusion started at the referring hospital, whereas others during active transport. Oftentimes we were unable to establish the exact location and timing of transfusion initiation in external reports, further limiting our study population. Furthermore, nonsignificant differences ($p=0.05$) were seen in the number of patients in each cohort with elevated SIPA scores, suggesting that patients in the *preBlood* group were sicker than patients in the *preCrystalloid* group, despite our best efforts to match the cohorts. Because of the small patient selection pool, patients were unable to be matched on multiple factors.

We were unable to determine in all cases which patients received coagulation factors and/or tranexamic acid prior to arrival at our facility. Neither were we able to evaluate the impact of different blood component ratios and their associations with clinical outcomes. Lab values measuring lactate, base deficit, coagulation factors, and platelet counts were unavailable for some patients. This is a significant limitation to our analysis of lab values and the changes that may have resulted following the administration of blood and/or crystalloid products in the prePTC setting. Despite this major limitation, the study still demonstrated the safety of earlier transfusion, which should promote future prospective investigation of this important topic.

Future studies should aim to include multiple centers and prospectively enroll patients from the scene of injury instead of including transfers from outside referral emergency departments, to better emulate conditions experienced by patients transported directly from the scene. Future studies should also aim to compare groups with transport times under one hour, which would be more representative of most pediatric trauma transports. Additionally, future research efforts should be directed towards randomized controlled trials to best evaluate the outcomes associated with prehospital blood administration and blood component products, with the implementation of standardized lab collection protocols with specific time intervals.

Conclusion

This study is the first to compare matched pediatric cohorts based on transport time, stratified by prePTC blood transfusion status. Importantly, it has provided evidence for the safety and efficacy of early blood transfusion. Specifically, traumatically injured pediatric patients who received prePTC blood transfusions were more likely to have improved shock markers and reduced crystalloid needs upon arrival at the PTC. Additionally, patients who received prePTC blood did not have an increased risk of worse clinical outcomes. Thus, this study adds to a growing body of evidence that restrictive crystalloid and early blood transfusion are mutually beneficial when managing and transporting severely injured children.

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Declarations

Conflict of interest The authors have no conflicts of interest to disclose.

Ethical approval All human studies have been approved by the appropriate ethics committee of the Colorado Multiple Institutional Review Board with a waiver of informed consent and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments.

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