Published in final edited form as:

Surgery. 2017 February ; 161(2): 538–545. doi:10.1016/j.surg.2016.08.023.

Early plasma transfusion is associated with improved survival after isolated traumatic brain injury in patients with multifocal intracranial hemorrhage

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Abstract

Background—Plasma-based resuscitation improves outcomes in trauma patients with hemorrhagic shock, while large animal and limited clinical data suggest that it also improves outcomes and is neuroprotective in the setting of combined hemorrhage and traumatic brain injury (TBI). However, the choice of initial resuscitation fluid including the role of plasma is unclear for patients after isolated TBI.

Methods—We reviewed adult trauma patients admitted from January 2011 to July 2015 with isolated TBI. “Early plasma” was defined as transfusion of plasma within 4 hours. Purposeful multiple logistic regression modeling was performed to analyze the relationship of early plasma and in-hospital survival. After testing for interaction, sub-group analysis was performed based on pattern of brain injury on initial head CT: epidural hematoma, intraparenchymal contusion, subarachnoid hemorrhage, subdural hematoma, or multifocal intracranial hemorrhage (MIH).

Results—Of the 633 isolated TBI patients included, 178 (28%) who received early plasma were more severely injured, coagulopathic, hypoperfused, and hypotensive on admission. Survival was similar in the early plasma versus no early plasma groups (78% versus 84%, $p=0.08$). After adjustment for covariates, early plasma was not associated with improved survival (odds ratio [OR] 1.18, 95% confidence interval [CI] 0.71 – 1.96).

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Abstract has been accepted for presentation at the Scientific Forum of the American College of Surgeons Clinical Congress 2016, Washington D.C.

Disclosures: All other authors report no conflicts of interest.

On subgroup analysis, multifocal intracranial hemorrhage (MIH) was the largest subgroup with 242 patients. Of these, 61 (25%) received plasma within 4 hours. Within-group logistic regression analysis with adjustment for covariates found that early plasma was associated with improved survival (OR 3.34, 95% CI 1.20 – 9.35).

Conclusion—Although early plasma transfusion was not associated with improved in-hospital survival for all isolated TBI patients, early plasma was associated with increased in-hospital survival in those with MIH.

Keywords

traumatic brain injury; plasma; resuscitation

INTRODUCTION

Traumatic brain injury (TBI) is estimated to cause up to half of trauma deaths¹ and is a significant cause of morbidity and long-term disability. Presently, there is no effective therapy for primary brain injury caused by the traumatic insult. Current treatments are therefore aimed at reducing the risk factors of secondary brain injury: hypoxia, hypoperfusion, hypoglycemia, and excitotoxicity.² Hypotension, in particular, is extremely harmful; a study by Chesnut et al found that a single episode of hypotension (systolic blood pressure [SBP] <90 mmHg) was associated with a 150% increase in mortality after severe TBI.³ Fluid resuscitation is instrumental in mitigating these risk factors after TBI, but the optimal regimen including type, timing, and volume of fluids is unknown.⁴ Isotonic crystalloid such as normal saline has traditionally been the fluid of choice, but its use is not supported by good evidence.

The advent of “damage control resuscitation” with the use of plasma as the primary volume expander is associated with improved outcomes in trauma patients presenting with hemorrhagic shock.^{5,6,7} This effect may be due to plasma’s ability to repair endothelial injury and reduce vascular permeability, which has been demonstrated in vitro and in animal models of hemorrhagic shock.^{8,9,10} In a large animal model of combined TBI and hemorrhagic shock, plasma-based resuscitation reduced secondary brain injury¹¹ and improved neurologic recovery.¹² This benefit was attributed to improved cerebral perfusion, mitigation of glutamine-mediated excitotoxicity, and reduced mitochondrial dysfunction with plasma resuscitation.¹³ However, there is little data on the role of plasma in the treatment of isolated TBI. We hypothesized that early plasma transfusion would be associated with improved in-hospital survival in patients who presented with isolated TBI.

METHODS

Study design

Approval was obtained from the University of Texas Health Science Center at Houston Institutional Review Board. We queried our trauma registry to perform a single-institution, retrospective study of consecutive highest-level adult trauma patients (≥ 16 years of age) admitted between January 2011 and July 2015. To identify patients with isolated TBI, we first screened for patients with head/neck Abbreviated Injury Scale (AIS) ≥ 3 and AIS of all

other body regions <3. Patients were then excluded if they had a negative initial head CT scan, fewer than 2 head CT scans, known prehospital warfarin use, or uncontrolled hemorrhage, which was defined as activation of a massive transfusion protocol or continued hemorrhage despite basic hemostatic maneuvers such as external compression or wound packing. Patient demographics including age, sex, Glasgow Coma Score (GCS), admission vital signs, admission base excess, admission activated clotting time on thromboelastography, Injury Severity Score, Abbreviated Injury Scale score, ICU-free days, in-hospital survival, discharge location, and mechanism of injury (blunt versus penetrating) were obtained from patient records. Patients were dichotomized into “early plasma” and “no early plasma” groups based on transfusion of any plasma within 4 hours of hospital presentation. In-hospital survival was defined as being alive at time of discharge and discharge to anywhere other than hospice.

Head CT analysis

Initial head CTs are obtained based on admission GCS, mechanism of injury, and the discretion of the attending trauma surgeon. After the head CTs are interpreted by the trauma team and a radiologist, appropriate consultations are requested from neurosurgery. If the initial head CT is abnormal, a second head CT is obtained within 6 hours to evaluate for stability versus progression of the presenting brain injury. However, a second head CT is not obtained if the injury is deemed “nonsurvivable” by the attending neurosurgeon. Therefore, the criterion of 2 head CT scans identifies patients with severe, but potentially survivable, injury who may benefit from early plasma transfusion. Patients were categorized into mutually-exclusive subgroups based on the dominant brain lesion on the initial head CT: epidural hematoma, subdural hematoma, intraparenchymal contusion, subarachnoid hemorrhage, or multifocal intracranial hemorrhage (MIH). MIH was defined as at least two different types of brain lesion without a dominant lesion (Figure 1). Progression of head injury was defined as an increase in the size of intracranial hemorrhage compared to findings on the initial head CT as determined by the attending radiologist.

Laboratory analysis

Blood samples are obtained from highest-level trauma patients immediately upon arrival to the emergency department and are sent for blood gas analysis, basic metabolic panel, complete blood count, and rapid thromboelastography (r-TEG). R-TEGs are run on a Thromboelastograph 5000 (Hemoscope Corp., Niles, IL) with clinically relevant data available within 5 minutes. The activated clotting time (ACT) is a measure of the amount of time needed to initiate clot formation and is dependent on plasma clotting factor activity. At our institution, we use ACT 128 seconds as a plasma transfusion trigger when bleeding is suspected or confirmed; a previous study performed at our institution found that this cutoff predicted need for massive transfusion within 6 hours of presentation in multiply-injured trauma patients.¹⁴

Statistical Analysis

Statistical analysis was performed using Stata 14.1 (StataCorp LP, College Station, TX). Data are reported as median values with interquartile range (IQR) or proportions as appropriate. Nonparametric comparisons of continuous variables were performed using the

Wilcoxon rank-sum test for two groups or the Kruskal-Wallis test for more than two groups. Categorical data was analyzed by Chi-square test. A purposeful multiple logistic regression model was performed to assess the effect of early plasma transfusion on in-hospital survival. Covariates were chosen if they were significant at the $p < 0.20$ level on univariate analysis and are easily available within 30 minutes of patient arrival to the ED.¹⁵ A test for interaction was performed to detect a possible subgroup effect based on the pattern of brain injury on initial head CT, followed by subgroup analysis. Beside initial covariate selection for the purposeful multiple logistic regression model, a two-tailed significance level of $\alpha < 0.05$ was used for all statistical tests.

RESULTS

There were 5,831 highest level adult trauma activations between January 2011 and July 2015. Of these, 1,192 had head/neck AIS ≥ 3 and AIS of all other body regions < 3 . Excluded were 559 patients (301 had a negative initial head CT, 54 had no initial head CT, 167 had no follow-up head CT, 23 had known prehospital warfarin use, and 14 had uncontrolled hemorrhage). Less than 1% of patients who had a negative initial head CT had delayed appearance of intracranial injury on a subsequent head CT, and only one patient in this group had cause of death listed as TBI. Of the patients who had no initial head CT or no follow-up head CT, 95% of these patients had non-survivable TBI with a median time to death of 12 hours. There were 633 patients included for analysis. These patients were predominantly male and victims of blunt trauma (Table 1).

Blood product utilization

The patients who received early plasma ($n=178$, 28%) were more severely injured, had higher incidence of severe TBI, were more likely to be hypotensive and/or coagulopathic, and had fewer ICU-free days (all $p < 0.05$). There was no significant difference in age, gender, mechanism of injury, progression of head injury, or survival between the early plasma and no early plasma groups. There was no difference in the prehospital use of aspirin, clopidogrel, or dabigatran between the two groups (Table 2). Of the patients who received early plasma, the majority received 1 or 2 units only (Figure 2). Most patients in the early plasma group (Table 3) did not receive RBCs. Patients received concomitant RBC and plasma for strong suspicion or evidence of bleeding. Patients who received solely FFP were transfused for a variety of indications, most commonly due to coagulopathy (ACT > 128 seconds on admission rapid TEG) or hypoperfusion/shock (Table 4).

Multiple logistic regression model

We constructed a purposeful multiple logistic regression model using an initial set of covariates which are available soon after patient arrival to the ED and were significant on univariate analysis at the $p < 0.20$ level. Four covariates were included in the final model as dichotomous variables: age > 55 , GCS ≤ 8 , ACT > 128 , and SBP < 90 . Using this model, we found that early plasma transfusion was not associated with improved in-hospital survival in all 633 patients (odds ratio [OR] 1.18; 95% confidence interval [CI] 0.71 – 1.96).

Sub-group analysis

Patients were divided into subgroups based on brain injury pattern on initial head CT scan (Table 5). There were significant differences in age, mechanism of injury, hypoperfusion, injury severity, early plasma transfusion, progression of head injury, and survival among the different subgroups on univariate analysis (all $p < 0.05$). For example, patients presenting with SDH were older and had the worst survival, while patients presenting with EDH were younger and had the best survival. Patients with EDH, SAH, and SDH were more often victims of blunt trauma, while patients with MIH and IPC had higher incidence of penetrating trauma.

There were 242 patients with MIH, which interestingly was the largest subgroup (37%). We found significant interaction between presence of MIH and utilization of early plasma in the logistic regression model ($p < 0.04$), indicating a subgroup effect. In the MIH group, 61 (25%) received early plasma; these patients were more likely to present with severe TBI, hypotension, hypoperfusion, more severe injuries, and coagulopathy (all $p < 0.05$). However, there were no significant differences in age, mechanism, ICU-free days, or survival (Table 6). Using a multivariate logistic regression model with the previously mentioned dichotomous variables (age > 55 , GCS ≤ 8 , ACT ≥ 128 , and SBP < 90), we found that early plasma transfusion was significantly associated with improved in-hospital survival in the MIH subgroup (OR 3.34, 95% CI 1.20 – 9.35, $p = 0.03$). Early plasma was not significantly associated with improved survival in non-MIH patients (OR 0.75, 95% CI 0.40 – 1.38).

DISCUSSION

Plasma-based resuscitation is associated with improved outcomes in hemorrhaging trauma patients,^{5,6,7} while earlier access to plasma by making ready-to-transfuse thawed or liquid universal donor plasma available on aeromedical transport in the pre-hospital setting¹⁶ and in the emergency department¹⁷ have led to improved outcomes at our institution. One quarter of trauma patients present with an acute trauma-induced coagulopathy,¹⁸ and plasma-based resuscitation addresses this directly.¹⁹ The Pragmatic, Randomized Optimal Platelet and Plasma Ratios (PROPPR) trial randomized severely injured trauma patients to a high and low plasma and platelet ratio transfusion groups (1:1:1 versus 1:1:2 plasma:platelet:RBC) and demonstrated reduced risk of exsanguination in the high ratio group.²⁰

In the setting of concomitant hemorrhage and TBI, observational data and well-performed large animal studies suggest a benefit with plasma-based resuscitation. In porcine models, resuscitation with plasma reduced secondary brain injury compared to resuscitation with crystalloid or artificial colloid,¹¹ suggesting that plasma induced repair of endothelial injury and reestablished the blood-brain barrier. This is consistent with other studies in animal hemorrhage models where plasma repaired the pulmonary endothelial injury induced by hemorrhagic shock.^{8,9,10} A retrospective study by Peiniger et al analyzed 1,250 massively transfused trauma patients with and without TBI and found that a high plasma:RBC transfusion ratio of $> 1:2$ was an independent predictor of decreased mortality (OR 0.48, 95% CI 0.29 – 0.81) in patients with TBI.²¹ However, another retrospective study by Spinella et al examined 850 massively transfused patients and found that a high plasma:RBC

transfusion ratio was associated with increased survival in non-TBI patients, while a high platelet:RBC ratio was associated with survival in TBI patients.²²

The optimal regimen in the initial resuscitation after isolated TBI is less clear, however. Guidelines published by the Brain Injury Foundation recommend isotonic crystalloid for any hypotensive TBI patient in the prehospital setting.²³ However, the quality of evidence for this recommendation is low (class III studies or class II studies with conflicting findings), and the authors state further investigation is needed to identify an ideal fluid for the initial resuscitation of TBI. Hypertonic saline has been proposed due to its ability to decrease intracranial pressure and improve cerebral perfusion pressure in animal models and patients with severe TBI.²⁴ However, a randomized control trial which randomized isolated blunt TBI patients to prehospital resuscitation with normal saline, hypertonic saline, or hypertonic saline/dextran showed no difference in 6-month neurologic outcome or 28-day survival.²⁵ The use of colloids is controversial due to a post-hoc subgroup analysis in the Saline versus Albumin Fluid Evaluation (SAFE) trial which demonstrated increased mortality in TBI patients resuscitated with 4% albumin versus normal saline.²⁶ Breakdown of the blood brain barrier is known to persist for several days after TBI,²⁷ and albumin molecules could theoretically leak across the disrupted blood brain barrier, increasing cerebral edema and secondary brain injury. In contrast, plasma-mediated repair of the blood-brain barrier may have prevented this from occurring in the large animal studies cited above.^{11,12,13}

In this study, we retrospectively analyzed the association between early plasma transfusion and in-hospital survival in trauma patients presenting with isolated TBI. To our knowledge, this is the first such study in the literature. We found that early plasma transfusion was associated with a survival benefit in those presenting with MIH on the initial head CT, but there was no association in patients presenting with other injury types. While there are clear differences in the resuscitation needs between hemorrhaging and isolated TBI patients – relating to intravascular volume deficit, for example – some benefits of plasma resuscitation are likely applicable to both groups. The incidence of coagulopathy after isolated TBI has been reported as 23%²⁸ (similar to that of the general trauma population) and is certainly a risk factor for increased morbidity and mortality in TBI^{28,29} and in general trauma¹⁸ patients. However, it has not been proven if correction of coagulopathy per se results in improved outcomes in trauma patients, and the coagulopathy after TBI may be mechanistically different from that of non-TBI trauma.³⁰ Additionally, although much of the focus of plasma resuscitation is on coagulopathy and replacement of clotting factors, repair of endothelial injury with reestablishment of the blood-brain barrier and subsequent limitation of edema and secondary brain injury may play vital roles.^{11,12} Other plasma-mediated neuroprotective effects observed in a porcine model of concomitant hemorrhage and TBI include mitigation of excitotoxicity and reducing mitochondrial dysfunction,¹³ but it is unknown if these benefits also occur in the setting of isolated TBI.

TBI is a heterogeneous disease with different injury patterns resulting in potentially divergent clinical courses. Traditionally, EDH has been associated with 90% survival,³¹ whereas SDH and IPC are associated with much lower survival in the 40–60% range.^{32,33} However, these estimates are based on studies performed in the 1980s and 1990s, and some more recent studies have reported much higher survival rates after SDH.³⁴ Our group

reported 90% survival after SDH and IPC, 100% survival after SAH and EDH, as well as IPCs being the most likely injury type to undergo progression on subsequent head CTs in a previous study.³⁵ In this study, we observed no difference in progression of head injury between early plasma and no early plasma groups (50% versus 57%, $p=0.12$) on univariate analysis, and were unable to demonstrate a difference on multivariate logistic regression analysis (data not shown). Additionally, the survival benefit was only observed in patients with an MIH pattern of brain injury on initial head CT, which by definition is a mixture of injury types. It is unclear why increased survival was observed in this particular subgroup – further investigation is needed to answer this question.

This study has several limitations. As a single-center retrospective study, it is subject to the selection bias, potential bias from unmeasured variables, and other limitations inherent in such a design. One of the most common indications for plasma transfusion in this study was ACT 128 seconds on admission rapid TEG (Table 4). This practice is based on a previous study at our institution where this cutoff was significantly predictive of early (< 2 hours) and massive transfusion of blood products in consecutive trauma patients (14), although it has not been specifically studied in the setting of isolated TBI. Selection bias may have also been introduced by analyzing only patients with 2 head CT scans. The intent of this criterion was to exclude patients who would not be expected to benefit from plasma transfusion, i.e. those with minimal TBI and those with non-survivable TBI. The pattern of TBI-related mortality for the patients excluded based on head CT criteria, which was extremely low (<1%) for patients with negative initial head CT but extremely high (95%) for patients with no initial or no follow-up head CT, suggests that these exclusion criteria served their intended purpose. Survivability after TBI (and the decision to pursue aggressive therapy including plasma) at our institution is adjudicated by the neurosurgery attending based on clinical parameters and the result of the first head CT scan. Different philosophies regarding the pursuit of aggressive neurosurgical therapy in the setting of severe TBI may be a factor affecting outcome if this study were to be replicated at another institution. Since reversal of coagulopathy in TBI patients known to be on prehospital warfarin with plasma or prothrombin complex concentrate is clearly indicated, these patients were excluded from the analysis. A sensitivity analysis with the warfarin patients included was performed: warfarin patients overwhelmingly presented with SDH, and the results of the overall analysis and subgroup analysis were unchanged. Another potentially significant source of bias is the classification of head CTs into the 5 subgroups. These subgroups are similar to a classification scheme employed previously by Folkerson et al.³⁵ Although head CTs were interpreted by attending radiologists, the categorization of initial injury pattern was accomplished by our interpretation of the reports and therefore subject to bias.

Conclusion

Although early plasma transfusion was not associated with improved in-hospital survival for all isolated TBI patients, early plasma was associated with increased in-hospital survival in those with MIH on initial head CT scan. This retrospective review identifies a potential target population for prospective studies.

Acknowledgments

RC is supported by a T32 fellowship (grant no. 5T32GM008792) from NIGMS. Additionally, the authors thank the nurses, pharmacists, staff, residents, and fellows of the Texas Trauma Institute at Memorial Hermann Hospital – Texas Medical Center for their vigilance in patient care.

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Figure 1.
Example of multifocal intracranial hemorrhage (MIH). A subdural hematoma (SDH) and intraparenchymal contusion (IPC) both contribute significantly to the injury without one predominating over the other.

Figure 2.
Distribution of plasma utilization. The majority of patients who received early plasma received 1 to 2 units.

Table 1

Baseline demographics (n=633).

Variable	No plasma (n=455, 72%)	Plasma (n=178, 28%)	P value
Age	42 (27, 58)	45 (30, 62)	0.12
Male, n (%)	339 (75%)	131 (74%)	0.81
Blunt, n (%)	403 (89%)	160 (90%)	0.64
TBI severity Mild (GCS 13) Moderate (GCS 9–12) Severe (GCS 8)	90 (20%) 43 (9%) 322 (71%)	16 (9%) 8 (4%) 154 (87%)	<0.001
SBP <90 mmHg, n (%)	7 (2%)	16 (9%)	<0.001
Heart rate (bpm)	90 (75, 105)	91 (75, 110)	0.47
Base excess <−4 mEq/L, n (%)	107 (24%)	58 (33%)	0.02
Hemoglobin (g/dL)	13.8 (12.4, 14.9)	13.2 (11.9, 14.4)	<0.001
ISS	17 (14, 25)	24 (17, 27)	<0.001
r-TEG ACT 128 seconds	47 (10%)	53 (30%)	<0.001
Units of plasma given	-	2 (2, 3)	-
PHI, n (%)	225 (49%)	100 (56%)	0.13
ICU-free days	24 (9, 28)	18 (0, 27)	<0.001
Survival, n (%)	382 (84%)	139 (78%)	0.08

Data reported with median (interquartile range).

r-TEG ACT, rapid thromboelastography activated clotting time; GCS, Glasgow Coma Score; ISS, Injury Severity Score; PHI, progression of head injury; SBP, systolic blood pressure; TBI, traumatic brain injury.

Table 2

Pre-hospital use of anticoagulation and anti-platelet medication.

Variable	No plasma (n=455, 72%)	Plasma (n=178, 28%)	P value
Aspirin	21 (5%)	11 (6%)	0.42
Clopidogrel	26 (6%)	8 (4%)	0.54
Dabigatran	2 (<1%)	1 (<1%)	0.84

Data reported as n, (%).

Table 3

Pattern of PRBC and FFP utilization.

No plasma or PRBC	PRBC only	Plasma and PRBC		Plasma only
		1:1 (FFP:PRBC)	>1:1 (FFP:PRBC)	
433 (68%)	22 (3%)	58 (9%)	24 (4%)	96 (15%)

PRBC, packed red blood cells.

Data reported as n, (%).

Table 4

Indications for sole transfusion of FFP without PRBC in 96 patients.

Indication	Number of patients
Coagulopathy (r-TEG CT ≥ 128 seconds)	51 (53%)
Shock (base excess < -4 mEq/L)	22 (23%)
Operating room	8 (8%)
Bleeding	1 (1%)
Hypotension (SBP < 90 mmHg)	4 (4%)
Unclear	10 (10%)

r-TEG ACT, rapid thromboelastography activated clotting time; SBP, systolic blood pressure.

Data reported as n, (%).

Table 5

Demographics by TBI subgroup

Variable	MIH (n=242, 37%)	EDH (n=49, 7%)	IPC (n=106, 16%)	SAH (n=56, 9%)	SDH (n=180, 30%)	P value
Age	41 (26, 57)	31 (23, 41)	35 (23, 54)	45 (31, 61)	52 (36, 68)	<0.001
Male, n (%)	180 (74%)	40 (82%)	86 (81%)	39 (70%)	125 (69%)	0.15
Blunt, n (%)	202 (83%)	47 (96%)	91 (86%)	52 (93%)	171 (95%)	<0.001
TBI severity Mild (GCS 13) Moderate (GCS 9–12) Severe (GCS 8)	45 (19%) 19 (8%) 178 (73%)	7 (14%) 2 (4%) 40 (82%)	16 (15%) 10 (9%) 80 (76%)	13 (23%) 5 (9%) 38 (68%)	25 (14%) 15 (8%) 140 (78%)	0.72
SBP <90 mmHg, n (%)	10 (4%)	4 (8%)	2 (2%)	2 (4%)	5 (3%)	0.36
Heart rate (bpm)	91 (76, 104)	88 (69, 103)	90 (77, 106)	91 (78, 116)	90 (73, 110)	0.66
Base excess <-4 mEq/L, n (%)	58 (24%)	10 (20%)	23 (22%)	23 (41%)	51 (28%)	0.05
Hemoglobin (mg/dL)	13.7 (12.1, 14.8)	14 (12.9, 15)	13.8 (12.5, 15.1)	14.1 (12.6, 15.0)	13.3 (12.2, 14.6)	0.17
ISS	17 (14, 24)	26 (24, 30)	17 (13, 21)	15 (14, 17)	25 (17, 26)	<0.001
ACT 128 seconds	38 (16%)	7 (14%)	16 (15%)	7 (13%)	32 (18%)	0.89
Received plasma within 4h, n (%)	61 (25%)	18 (37%)	27 (25%)	12 (21%)	60 (33%)	0.14
PHI, n (%)	143 (59%)	20 (41%)	62 (58%)	20 (36%)	80 (44%)	0.001
ICU free days	23 (8, 27)	26 (13, 28)	23 (13, 27)	26 (15, 28)	20 (0, 27)	0.02
Survival, n (%)	204 (84%)	47 (96%)	95 (90%)	49 (88%)	126 (70%)	<0.001

Data reported with median (interquartile range).

MIH, multifocal intracranial hemorrhage; EDH, epidural hematoma; IPC, intraparenchymal contusion; SAH, subarachnoid hemorrhage; SDH, subdural hematoma; r-TEG ACT, rapid thromboelastography activated clotting time; GCS, Glasgow Coma Score; ISS, Injury Severity Score; PHI, progression of head injury; SBP, systolic blood pressure; TBI, traumatic brain injury.

Table 6

Demographics of the MIH subgroup

Variable	No plasma (n=181, 75%)	Plasma (n=61, 25%)	P value
Age	39 (26, 56)	42 (29, 59)	0.53
Male, n (%)	135 (75%)	45 (74%)	0.90
Blunt, n (%)	151 (83%)	51 (84%)	0.97
TBI severity Mild (GCS 13) Moderate (GCS 9–12) Severe (GCS 8)	39 (22%) 17 (9%) 125 (69%)	6 (10%) 2 (3%) 53 (87%)	0.02
SBP <90 mmHg	2 (1%)	8 (13%)	<0.001
Heart rate (bpm)	91 (76, 102)	93 (75, 113)	0.29
Base excess (mEq/L)	33 (18%)	24 (39%)	0.001
Hemoglobin (g/dL)	13.8 (12.4, 14.9)	13.1 (11.5, 14.2)	0.03
ISS	17 (14, 24)	21 (16, 26)	<0.01
ACT 128 seconds	20 (11%)	18 (30%)	0.001
Units of plasma given	-	1 (1, 2)	-
PHI, n (%)	105 (58%)	38 (62%)	0.56
ICU-free days	24 (8, 27)	20 (5, 27)	0.34
Survival, n (%)	151 (83%)	53 (87%)	0.67

Data reported with median (interquartile range).

MIH, multifocal intracranial hemorrhage; r-TEG ACT, rapid thromboelastography activated clotting time; GCS, Glasgow Coma Score; ISS, Injury Severity Score; PHI, progression of head injury; SBP, systolic blood pressure; TBI, traumatic brain injury.