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CHARACTERIZATION OF UNEXPECTED SURVIVORS FOLLOWING A PREHOSPITAL PLASMA RANDOMIZED TRIAL

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Abstract

Background: Prehospital plasma improves survival for severely injured trauma patients transported by air ambulance. We sought to characterize the unexpected survivors, patients who survived despite having high predicted mortality following traumatic injury.

Methods: The Prehospital Air Medical Plasma (PAMPer) trial randomized severely injured patients (n=501) to receive either standard care (crystalloid) or two units of prehospital plasma followed by standard care fluid resuscitation. We built a generalized linear model to estimate patient mortality. Area under the receiver operating characteristic curve (AUC) was used to evaluate model performance. We defined unexpected survivors as patients who had a predicted mortality >50% and survived to 30 days. We characterized patient demographics, clinical features,

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Author Contributions

All authors meet authorship criteria for this manuscript as described below. All authors have seen and approved the final manuscript as submitted. The first author (DSG) had full access to all data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Conception and design: DSG, JLS, FXG, JBB; Acquisition of data: JLS, FXG, JBB, BJD, RSM, BGH, JAC, HAP; Analysis and interpretation of data: DSG, JLS, FXG, JBB; All authors participated in the manuscript preparation and editing.

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and outcomes of the unexpected survivors. Observed to expected (O/E) ratios and Z-statistics were calculated using model-estimated mortality for each cohort.

Results: Our model predicted mortality better than ISS or RTS parameters and identified 36 unexpected survivors. Compared to expected survivors, unexpected survivors were younger (33 [24, 52] vs. 47 [32, 59] years, $P=0.013$), were more severely injured (ISS 34 [22, 50] vs. 18 [10, 27], $P<0.001$), had worse organ dysfunction and hospital resource outcomes (MOF, ICU and hospital length of stay, and ventilator days), and were more likely to receive prehospital plasma (67 vs. 46%, $P=0.031$). Nonsurvivors with high predicted mortality were more likely to receive standard care resuscitation ($P<0.001$). Unexpected survivors who received prehospital plasma had a lower observed to expected mortality than those that received standard care resuscitation (O/E 0.56 [0.33–0.84] vs. 1.0 [0.73–1.32]). The number of prehospital plasma survivors (24) exceeded the number of predicted survivors ($n=10$) estimated by our model ($P<0.001$).

Conclusions: Prehospital plasma is associated with an increase in the number of unexpected survivors following severe traumatic injury. Prehospital interventions may improve the probability of survival for injured patients with high predicted mortality based on early injury characteristics, vital signs, and resuscitation measures.

Keywords

Prehospital; Plasma; Hemorrhage; Unexpected Survivors

Introduction

Traumatic injury is a leading cause of preventable death.^{1, 2} Recent advances in trauma care emphasize the importance of administering blood and blood components as soon as possible following injury.^{3, 4} The Prehospital Air Medical Plasma (PAMPer) trial, a prospective, multicenter, randomized controlled trial, demonstrated that prehospital plasma improves survival by 10% in severely injured trauma patients at risk for hemorrhagic shock and transported by air ambulance.^{4, 5} The PAMPer trial results suggest that prehospital plasma prevented mortality for a group of patients who may have died without early plasma resuscitation, but the demographic, injury, and outcome attributes of unexpected survivors have not been adequately characterized. It is not known whether prehospital interventions such as plasma prevent mortality from uncommon complications or intervene at a critical time point in patients who would not have survived their injuries.

An analysis of unexpected outcomes following traumatic injury may inform more effective management strategies or improve our understanding of how injured populations respond to interventions. Unexpected death may expose failures while unexpected survival may indicate effective practices that should be applied to all patients.⁶ Identifying the plasma unexpected survivors may also enable a more targeted allocation of resources to those who would receive the greatest benefit. However, it is challenging to identify and characterize those patients who would have died had they not received an intervention.

Several methods have been established to predict and assess outcomes following trauma. The Injury Severity Score (ISS) and the Revised Trauma Score (RTS) were both developed

to characterize injury severity.^{7, 8} Similar approaches have been applied to identify trauma unexpected survivors, patients who survive despite high predicted mortality (>50%) following injury.⁹ It is difficult to predict an individual patient's likelihood of survival without evaluating robust pre- and in-hospital characteristics, outcomes, and a range of trauma systems, injury patterns, and patient demographics. Mortality metrics carry limitations and may fail to predict long-term outcomes, to generalize across heterogeneous patient populations, or to account for changing management practices.¹⁰ Outcome assessments are further complicated by survivor bias, as patients who are more seriously injured and live are also more likely to have worse organ dysfunction and greater medical resource utilization. To overcome challenges associated with estimating patient mortality, we sought to leverage data from the PAMPer trial, a recently completed, randomized trial which included severely injured patients, robust prehospital data, long-term outcomes, and a positive survival benefit.

Previous studies in military settings attribute unexpected survival to advanced resuscitation strategies that mitigate the consequences of hemorrhage.⁶ An analysis of civilian trauma patients also revealed that clinically unexpected survivors received more blood products.¹¹ Our objective was to characterize the PAMPer trial unexpected survivors in order to understand the patients who lived despite a high probability of death. We hypothesized that the unexpected survivors would have higher incidence of MOF, greater hospital resource requirements, and would be more likely to receive prehospital plasma.

Methods

The PAMPer trial was a pragmatic, multicenter, cluster-randomized, phase 3 superiority trial designed to test the effect of administering plasma to severely injured trauma patients on air ambulances prior to arrival to definitive trauma care. Patients were randomized by air ambulance base to receive either standard care fluid resuscitation or two units of freshly thawed plasma followed by the standard care fluid resuscitation. The primary outcome was 30-day mortality. This study was approved by appropriate institutional review boards as described in Sperry et al., 2018⁴ and the full study protocol is publicly available ([ClinicalTrials.gov](https://clinicaltrials.gov/ct2/show/NCT01818427) ID NCT01818427)^a. The study was approved under an Emergency Exception From Informed Consent (EFIC) protocol from the Human Research Protection Office of the US Army Medical Research and Materiel Command.

We built a logistic regression model (generalized linear model with a binomial link function without accounting for clustering by site) to predict patient 30-day mortality in the PAMPer cohort. We used data from the control group (n=271) to train our model. We evaluated ISS, RTS variables, and key prehospital variables associated with survival or relevant to trauma resuscitation. We included ISS, Glasgow Coma Score (GSC) (<8), prehospital resuscitation (CPR, intubation, and fluids excluding plasma), presence of prehospital shock, emergency department (ED) systolic blood pressure (SBP), respiratory rate (RR), and International Normalized Ratio (INR), and head abbreviated injury score (AIS). ISS was treated as a continuous variable, and head AIS was treated as categorical variable.

^a<https://clinicaltrials.gov/ct2/show/NCT01818427>

To assess the performance of our model, we calculated the area under the receiver operating characteristics (ROC) curve and 95% confidence intervals with 2000 bootstrap replicates using the pROC v1.16.2¹² package. We also evaluated ISS, RTS parameters (ED SBP, RR, and GCS), and trauma injury severity score (TRISS) parameters (ISS, RTS, ED SBP, RR, and GCS, and age less than or equal to or greater than 55 years) for comparison.

We applied our model to calculate the probability of death for PAMPer trial patients. As previously described, we defined unexpected survivors as patients who had a model-estimated probability of death >50% and survived to 30 days.⁹ We characterized the unexpected survivors using summary statistics. We used the Pearson's chi-square test to compare plasma vs. standard care arms for survivors and nonsurvivors with predicted mortality >50%. We also calculated observed to expected mortality ratios with 95% confidence intervals (CIs) across the arms of the PAMPer trial. Finally, we used our model results to calculate the Z-Statistic (Z) associated with survival in the prehospital plasma arm, using the control arm to derive baseline cohort survival characteristics.^{13, 7}

We analyzed clinical data, performed summary statistics, and built and tested our models using R Version 3.6.3.¹⁴ We used descriptive statistics to characterize patient demographics, injury characteristics and outcomes. Categorical variables are presented as frequencies and percentages and tested using the Pearson's Chi-square test. Continuous variables are expressed as medians and interquartile ranges (IQRs) and tested using Mann-Whitney U or Kruskal-Wallis test, as appropriate. The Fisher's exact test was used for categorical variables with small sample sizes ($n \leq 5$). Statistical significance was determined at the probability (P) <0.05 level.

Results

The PAMPer trial assessed 30-day mortality for 501 severely injured patients, of which 230 received prehospital plasma. The PAMPer cohort included mostly men (72.7%) with blunt trauma injuries (82.4%) and a median ISS of 22. Approximately half of these patients received prehospital intubation (51.1%). The overall 30-day mortality rate was 29.6%. Mortality at 30 days was lower in the plasma group (23.2% vs. 33.0%; difference, -9.8%; 95% CI, -18.6 to -1.0%; $P=0.03$). Due to the design of the trial and the need for fluid resuscitation among hypotensive patients, patients who received prehospital plasma also received less prehospital crystalloid and packed red blood cells (PRBC).

Our model predicted 30-day mortality for PAMPer patients better than ISS and RTS or TRISS variables (AUC [95%CI] ISS = 0.701 [0.644–0.759]; RTS = 0.781 [0.732–0.832]; TRISS = 0.798 [0.750–0.846]; our model = 0.840 [0.794–0.887], Figure 1). We identified 36 unexpected survivors from the PAMPer cohort. Overall, patients with greater injury severity had a greater model-predicted mortality (Figure 2). Compared to expected survivors ($n=276$), unexpected survivors were younger (33 [24, 52] vs. 47 [32, 59] years, $P=0.013$), more severely injured (ISS 34 [22, 50] vs. 18 [10, 27], $P<0.001$), and had greater organ dysfunction and hospital resource requirements (MOF, ICU and hospital length of stay, and ventilator days). Unexpected survivors had greater incidence of TBI (56% vs. 23%, $P<0.001$) and worse head injuries as measured by GCS (3 [3, 4] vs. 14 [7, 15], $P<0.001$) and

head AIS (3 [2, 4] vs. 0 [0, 2], $P<0.001$). Unexpected survivors were also more likely to receive prehospital CPR (11% vs. 0%, $P<0.001$), intubation (89% vs. 32%, $P<0.001$), and plasma (67% vs. 46%, $P=0.031$). There were no differences between unexpected and expected survivors in terms of mechanism of injury (blunt vs. penetrating), transport time, or origin of transport (scene vs. outside facility) (Table 1).

We further compared unexpected nonsurvivors, expected survivors, expected nonsurvivors, and unexpected survivors. Unexpected nonsurvivors were older than expected survivors, while unexpected survivors were younger than expected nonsurvivors. Unexpected survivors were also characterized by high rates of prehospital cardiopulmonary resuscitation (CPR), and most unexpected survivors were intubated in the prehospital setting. Survivors had higher incidence of MOF and length of stay compared to nonsurvivors, and all unexpected survivors developed MOF. There was no difference in sex, prehospital shock, or transport time among the four cohorts (Table 1).

Nonsurvivors with predicted mortality ($>50\%$) were more likely to receive standard care prehospital resuscitation (43 vs. 18) while survivors were more likely to receive prehospital plasma (24 vs. 12) ($P<0.001$, Figure 3). Unexpected survivors who received prehospital plasma had a lower observed to expected mortality (O/E 0.56 [0.33–0.84] vs. 1.0 [0.73–1.32]). The number of deaths predicted by our model ($n=44$) was nearly equal to the observed number of deaths ($n=43$) for standard care patients. However, the number of prehospital plasma survivors ($n=24$) exceeded the number of predicted survivors ($n=10$) estimated from our model ($Z=5.7$, $P<0.001$).

We compared arms of the trial to assess whether these results are due to differences in patient or injury characteristics. Among the unexpected survivors, 12 received standard care resuscitation and 24 received prehospital plasma (Table 2). Demographics and injury characteristics were similar across arms of the trial. All unexpected survivors, irrespective of trial arm, developed MOF. Plasma patients received less prehospital PRBC. Blood transfusion requirements in the first 24 hours of hospitalization were lower in the plasma arm but this did not reach statistical significance. Plasma patients also had lower admission INR values. These findings were similar to the primary study results.⁴

Injury characteristics and severity were similar for unexpected survivors ($>50\%$ mortality) who received plasma and expected nonsurvivors ($>50\%$ mortality) who received standard care resuscitation (Table 3), suggesting the plasma intervention may have played a role in determining survival outcome differences. Injured patients with a predicted mortality of $<50\%$ across the arms were not statistically different (plasma=11% vs standard care=11%, $p=0.86$), as would be expected due to the overall lower rate of mortality.

Discussion

Despite major improvements in trauma resuscitation over the last few decades, mortality from hemorrhage continues to occur within the first few hours of arrival to definitive trauma care. These analyses highlight the importance of the prehospital arena and proximity to the time of injury for improving outcomes.^{15, 3, 16, 4} In an interventional, randomized, clinical

trial with a demonstrated mortality benefit as the primary outcome, there exists a cohort of patients who may not have survived without the intervention. It is possible that interventions may minimize complications and benefit those patients who would be expected to survive. Alternatively, early, targeted interventions may be associated with survival among a cohort unlikely to survive their injuries. Characterizing the factors associated with unexpected survival may enable more efficient management practices that improve the probability of survival for injured patients in the prehospital environment.

The current results demonstrate that plasma is associated with an increase in the number of unexpected survivors following traumatic injury, with no differences found in those with low predicted mortality. Compared to patients expected to survive their injuries, unexpected survivors had an inherently higher predicted mortality, were younger, were more severely injured with greater incidence of TBI, were more likely to receive prehospital CPR, and had worse outcomes (MOF, ICU and hospital length of stay, and ventilator days). Unexpected survivors were also more likely receive prehospital plasma, while nonsurvivors and expected survivors were more likely to receive standard care resuscitation. The current unexpected survivor characterization highlights the magnitude of this intervention effect and solidifies the understanding that early interventions as close to the time of injury as feasible are important.

Predicted mortality calculations have been applied to assess outcomes and trauma center performance.^{7, 17} These methods typically rely on large populations of patients and may not accurately predict survival across all injury and patient characteristics.¹⁸ We were able to overcome these obstacles by using data from the PAMPer trial. Our model results predicted mortality within the PAMPer cohort better than ISS or RTS variables alone. Unexpected survivor analysis may be ineffective if the characteristics used to derive the model and those of the study cohort are different. As management practices evolve, we would expect to see an increase in survivors of injuries previously thought to be incompatible with life.¹¹ We circumvented these issues by building and testing our model with a randomized cohort of similarly-injured patients over the same time period.

Based on the results of the PAMPer trial, we hypothesized that the 10% reduction in mortality for the prehospital plasma patients (n=230) would result in approximately 23 patients who survived due to the plasma intervention. Our model identified 36 unexpected survivors, of which 24 received prehospital plasma. While it is impossible to ascertain causality in this study, our model estimates are reasonable based on the findings of the original analysis.

Prehospital plasma was associated with an increase in the number of survivors predicted by our model. Recent studies have suggested that prehospital plasma may have a greater benefit for patients based on injury type and hemorrhage severity.^{19, 20} In this study, prehospital plasma was associated with an increase in the number of unexpected survivors, patients who had significantly worse injury severity, and presumably hemorrhage, and who were more likely to have TBI. Our results are also consistent with previous studies that demonstrated an association between unexpected survival and blood administration.^{11, 6} An analysis of patients in military settings found that the majority of cases associated with unexpected

survival were attributed to advanced resuscitation strategies to treat trauma-associated hemorrhage.⁶ Previous analyses were unable to assess prehospital fluid administration. Our analysis suggests that the prehospital phase of care is important for increasing the probability of survival to 30 days for injured patients. It is hypothesized that early, prehospital administration of plasma, rather than crystalloid fluid, may have downstream effects on the immune response to or endotheliopathy of trauma.²¹ Our work suggests that future efforts to understand survival following injury should also consider prehospital variables and interventions.

The PAMPer trial enrolled patients between 18 and 90 years of age based on physiological responses to injury.⁴ It is expected that patients may respond differently to injury based on age.^{6, 22} Our analysis suggests that older patients are less likely to survive their injuries, while younger patients are more likely to survive despite more severe injuries, consistent with previous analyses.¹¹ Our study does not account for the effects of age or pre-injury health which may be important factors to consider in subsequent studies of the response to injury. Although the PAMPer trial excluded patients if they had a traumatic cardiac arrest that lasted longer than 5 minutes, 4 of the 36 unexpected survivors and 11 of the 61 expected nonsurvivors received prehospital CPR. This analysis may add further weight to the argument that more aggressive prehospital interventions can increase the probability of long-term survival.

In the original analysis, there were no measured adverse outcomes associated with prehospital plasma.⁴ In this analysis, we show that unexpected survivors had greater incidence of MOF and more days in the ICU, on mechanical ventilation, and in the hospital. This result is likely due to survival bias. Unexpected survivors are likely to require more intensive treatment, suffer greater organ dysfunction, and require longer hospital stays. Among the four cohorts studied in this analysis, survivors were more likely than nonsurvivors to develop MOF and have greater hospital resource utilization. The association between unexpected survival and incidence of MOF is also consistent with previous analysis of trauma unexpected survivors.¹¹

There are several limitations of our analysis which should be considered in the interpretation of our work. First, this was a secondary analysis of a prospective randomized trial which was not prespecified. Variability in pre- and in- hospital factors (prehospital times and provider-level differences) introduce bias. We are limited by the possibility of non-random missing data and survival bias, and the number of patients with unexpected outcomes was small relative to the overall cohort. This model did not account for site clustering and assumes that patient populations are similar. However, when we fit our model to account for site randomization, this did not affect our conclusions. While our model predicts survival with reasonable accuracy, it may not be generalizable to other patient populations. However, the purpose of our analysis is to examine expected and unexpected outcomes within the PAMPer cohort. It is impossible to prove causality or ascertain which patients survived due to the plasma intervention. There were differences in randomization across study arms (prehospital PRBC and crystalloid and admission INR values). The unexpected survivors were more likely to result from the plasma arm, and thus the demonstrated differences in INR and transfusion may be due to prehospital plasma, similar to the primary analysis. It is also

possible that model results are due to variable clinical factors other than the plasma intervention. We optimized our model for mortality prediction within this cohort. When we tested a version of our model without prehospital resuscitation fluids or INR, we found similar results with reduced accuracy. The methods used in our analysis may be useful for other trauma trials with a demonstrated survival benefit, but our findings may be specific to injury patterns, patient characteristics, and prehospital interventions studied.

In conclusion, prehospital plasma is associated with an increase in the number of unexpected survivors following severe traumatic injury and hemorrhage. This finding is novel and the current methodology utilized may be useful for benefit assessment in future injury related clinical trials. Prehospital plasma may increase the probability of survival for injured patients with high predicted mortality based on their injury characteristics and early pre- and in-hospital factors.

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Figure 1:

Receiver operating characteristics (ROC) curve for the model used in this analysis. Area under the curve (AUC) = 0.840 [0.794–0.887]. Grey shading represents the 95% confidence interval.

Figure 2:

Probability of death versus injury severity score (ISS) among survivors. The open circles represent patients who received standard care resuscitation and the filled squares represent patients who received prehospital plasma. Unexpected survivors are defined as patients above probability of death=50% (dashed line).

Figure 3: Probability of death (>50%) versus injury severity score (ISS) among survivors (grey symbols) and nonsurvivors (black symbols) across trial arms. Data from survivors (Figure 2) included for comparison.

Table 1:

A comparison of expected and unexpected survival following injury. Unexpected nonsurvivors and expected survivors correspond to predicted mortality 50%. Expected nonsurvivors and unexpected survivors correspond to predicted mortality >50%. Probability (P) values for between-group comparisons determined by the Pearson's chi-square test for categorical variables and the Kruskal-Wallis test for nonparametric, continuous variables. GCS=Glasgow coma scale; ISS=Injury severity score; AIS=Abbreviated injury scale; TBI=Traumatic brain injury; SBP=Systolic blood pressure; PRBC=Packed red blood cells; CPR=Cardiopulmonary resuscitation; INR=International normalized ratio; MOF=Multiple organ failure; ICU=Intensive care unit; LOS=Length of stay.

Variable	Unexpected Nonsurvivor (n=36)	Expected Survivor (n=276)	Expected Nonsurvivor (n=61)	Unexpected Survivor (36)	P Value
Patient and Injury Characteristics					
Predicted Mortality (median [IQR])	0.16 [0.08, 0.34]	0.05 [0.02, 0.15]	0.80 [0.67, 0.94]	0.67 [0.58, 0.82]	<0.001
Age (median [IQR])	56.50 [35.00, 67.00]	46.50 [32.00, 59.00]	46.00 [25.00, 65.00]	33.00 [23.75, 52.00]	0.022
Sex (% Male)	25 (69.4)	194 (70.3)	47 (77.0)	30 (83.3)	0.31
GCS (median [IQR])	5.00 [3.00, 14.00]	14.00 [7.00, 15.00]	3.00 [3.00, 3.00]	3.00 [3.00, 4.00]	<0.001
ISS [median [IQR]	26.50 [17.00, 35.75]	18.00 [10.00, 27.00]	33.00 [20.00, 43.00]	34.00 [22.00, 50.00]	<0.001
AIS Head [median [IQR]]	3.00 [0.00, 4.00]	0.00 [0.00, 2.25]	3.00 [2.00, 5.00]	3.00 [2.00, 4.25]	<0.001
TBI (%)	20 (55.6)	63 (22.8)	43 (70.5)	20 (55.6)	<0.001
PH SBP <70 (%)	15 (41.7)	125 (45.3)	33 (54.1)	16 (44.4)	0.58
Blunt Injury (%)	35 (97.2)	223 (80.8)	58 (95.1)	30 (83.3)	0.005
Transport Time [median [IQR]]	44.00 [32.00, 63.00]	41.00 [33.00, 52.00]	44.00 [34.00, 50.00]	41.00 [35.75, 50.75]	0.87
Transferred from Hospital (%)	9 (25.0)	68 (24.6)	6 (10.2)	6 (16.7)	0.081
Prehospital					
Crystalloid [median [IQR]]	650.00 [0.00, 1262.50]	800.00 [0.00, 1500.00]	500.00 [0.00, 1300.00]	0.00 [0.00, 925.00]	0.061
Plasma Intervention (%)	16 (44.4)	127 (46.0)	18 (29.5)	24 (66.7)	0.005
PRBC [median [IQR]]	0.00 [0.00, 1.00]	0.00 [0.00, 1.00]	0.00 [0.00, 1.00]	0.00 [0.00, 0.00]	0.221
Intubation (%)	22 (61.1)	88 (31.9)	57 (93.4)	32 (88.9)	<0.001
CPR (%)	0 (0.0)	0 (0.0)	11 (18.0)	4 (11.1)	<0.001
Hospital					
INR (%)	1.27 [1.11, 1.60]	1.20 [1.10, 1.32]	1.60 [1.30, 1.90]	1.25 [1.18, 1.42]	<0.001
Massive Transfusion (%)	10 (27.8)	45 (16.3)	20 (32.8)	14 (38.9)	0.001
PRBC in 24h (median [IQR])	4.00 [2.00, 10.50]	3.00 [0.00, 6.00]	6.00 [3.00, 11.00]	5.00 [2.75, 12.25]	<0.001
Plasma in 24h (median [IQR])	1.50 [0.00, 5.25]	0.00 [0.00, 2.00]	4.00 [0.00, 6.00]	2.00 [0.00, 8.00]	<0.001

Variable	Unexpected Nonsurvivor (n=36)	Expected Survivor (n=276)	Expected Nonsurvivor (n=61)	Unexpected Survivor (36)	P Value
Platelets in 24h (median [IQR])	0.00 [0.00, 1.50]	0.00 [0.00, 0.00]	1.00 [0.00, 2.00]	1.00 [0.00, 2.00]	<0.001
Crystallloid in 24h (median [IQR])	4999.00 [3078.00, 7852.25]	4744.00 [3086.75, 6663.25]	4200.00 [2300.00, 5400.00]	6834.00 [3374.25, 9627.25]	0.021
Outcome					
MOF (%)	15 (41.7)	204 (73.9)	18 (29.5)	36 (100.0)	<0.001
ICU LOS [median [IQR]]	4.00 [1.75, 8.25]	5.00 [2.00, 12.00]	1.00 [0.00, 5.00]	16.00 [10.00, 24.00]	<0.001
Hospital LOS [median [IQR]]	4.00 [1.75, 8.25]	14.00 [7.00, 25.00]	1.00 [1.00, 5.00]	26.00 [18.00, 30.00]	<0.001
Ventilator Days [median [IQR]]	3.50 [1.00, 8.00]	2.00 [1.00, 8.00]	1.00 [1.00, 5.00]	12.00 [4.50, 18.50]	<0.001

Table 2:

A comparison of unexpected survivors (predicted mortality >50%) across randomized arms of the PAMPer trial. Probability (P) values for between-group comparisons determined by the Pearson's chi-square test for categorical variables and the Mann-Whitney test for nonparametric, continuous variables. GCS=Glasgow coma scale; ISS=Injury severity score; AIS=Abbreviated injury scale; TBI=Traumatic brain injury; PH=Prehospital; SBP=Systolic blood pressure; PRBC=Packed red blood cells; CPR=Cardiopulmonary resuscitation; INR=International normalized ratio; MOF=Multiple organ failure; ICU=Intensive care unit; LOS=Length of stay.

	Standard Care (n=12)	Plasma (n=24)	P Value
Predicted Mortality (median [IQR])	0.63 [0.57, 0.79]	0.73 [0.59, 0.89]	0.33
Age (median [IQR])	35.00 [20.75, 52.00]	33.00 [25.75, 46.75]	0.85
Sex (% male)	12 (100.0)	18 (75.0)	0.16
GCS (median [IQR])	3.00 [3.00, 3.75]	3.00 [3.00, 4.00]	0.90
ISS [median [IQR])	33.50 [23.50, 44.75]	34.00 [22.00, 50.00]	0.87
AIS Head [median [IQR])	4.00 [2.75, 5.00]	3.00 [2.00, 3.25]	0.18
TBI (%)	6 (50.0)	14 (58.3)	0.91
PH SBP<70 (%)	4 (33.3)	12 (50.0)	0.55
Blunt Injury (%)	11 (91.7)	19 (79.2)	0.64
PH Transport Time [median [IQR])	38.50 [28.00, 54.00]	41.00 [37.50, 50.75]	0.59
Transferred from Hospital (%)	2 (16.7)	4 (16.7)	1
PH Crystalloid [median [IQR])	300.00 [0.00, 975.00]	0.00 [0.00, 925.00]	0.74
PH Plasma Intervention (%)	0 (0.0)	24 (100.0)	<0.001
PH PRBC [median [IQR])	0.50 [0.00, 1.00]	0.00 [0.00, 0.00]	0.01
PH Intubation (%)	10 (83.3)	22 (91.7)	0.85
PH CPR (%)	1 (8.3)	3 (12.5)	1
INR (%)	1.43 [1.25, 1.68]	1.21 [1.10, 1.32]	0.01
Massive Transfusion (%)	6 (50.0)	8 (33.3)	0.546
PRBC in 24h (median [IQR])	9.00 [4.75, 12.50]	4.50 [0.75, 11.50]	0.15
Plasma in 24h (median [IQR])	5.00 [0.75, 8.50]	2.00 [0.00, 7.25]	0.44
Platelets in 24h (median [IQR])	1.50 [0.00, 3.25]	1.00 [0.00, 2.00]	0.24
Crystalloid in 24h (median [IQR])	9244.50 [6319.25, 10299.00]	5465.00 [2431.25, 7885.50]	0.065
MOF (%)	12 (100.0)	24 (100.0)	1
ICU LOS [median [IQR])	18.00 [12.50, 26.50]	14.00 [8.75, 19.25]	0.34
Hospital LOS [median [IQR])	28.00 [24.00, 30.00]	23.50 [16.00, 30.00]	0.27
Ventilator Days [median [IQR])	14.00 [10.50, 21.50]	11.00 [3.00, 16.75]	0.23

Table 3:

A comparison of (expected) nonsurvivors from the control arm and (unexpected) survivors from the plasma arm among patients with predicted mortality >50%. Probability (P) values for between-group comparisons determined by the Pearson's chi-square test for categorical variables and the Mann-Whitney test for nonparametric, continuous variables. GCS=Glasgow coma scale; ISS=Injury severity score; AIS=Abbreviated injury scale; TBI=Traumatic brain injury; PH=Prehospital; SBP=Systolic blood pressure; PRBC=Packed red blood cells; CPR=Cardiopulmonary resuscitation; INR=International normalized ratio; MOF=Multiple organ failure; ICU=Intensive care unit; LOS=Length of stay.

	Nonsurvivors (Control, n=43)	Survivors (Plasma, n=24)	P Value
Predicted Mortality (median [IQR])	0.78 [0.68, 0.92]	0.73 [0.59, 0.89]	0.14
Age (median [IQR])	46.00 [24.00, 68.50]	33.00 [25.75, 46.75]	0.13
Sex (% male)	34 (79.1)	18 (75.0)	0.94
GCS (median [IQR])	3.00 [3.00, 3.00]	3.00 [3.00, 4.00]	0.24
ISS [median [IQR])	34.00 [18.50, 43.00]	34.00 [22.00, 50.00]	0.34
AIS Head [median [IQR])	3.00 [2.00, 5.00]	3.00 [2.00, 3.25]	0.18
TBI (%)	32 (74.4)	14 (58.3)	0.28
PH SBP<70 (%)	24 (55.8)	12 (50.0)	0.84
Blunt Injury (%)	41 (95.3)	19 (79.2)	0.097
PH Transport Time [median [IQR])	43.00 [33.00, 50.50]	41.00 [37.50, 50.75]	0.64
Transferred from Hospital (%)	4 (9.8)	4 (16.7)	0.67
PH Crystalloid [median [IQR])	800.00 [0.00, 1350.00]	0.00 [0.00, 925.00]	0.14
PH Plasma Intervention (%)	0 (0.0)	24 (100.0)	<0.001
PH PRBC [median [IQR])	0.00 [0.00, 2.00]	0.00 [0.00, 0.00]	0.011
PH Intubation (%)	40 (93.0)	22 (91.7)	1
PH CPR (%)	9 (20.9)	3 (12.5)	0.52
INR (%)	1.70 [1.31, 2.06]	1.21 [1.10, 1.32]	<0.001