Prehospital Blood Product and Crystalloid Resuscitation in the Severely Injured Patient

A Secondary Analysis of the Prehospital Air Medical Plasma Trial

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Objective: The aim of this study was to determine whether prehospital blood products reduce 30-day mortality in patients at risk for hemorrhagic shock compared with crystalloid only resuscitation.

Summary of Background Data: Hemorrhage is the primary cause of preventable death after injury. Large volume crystalloid resuscitation can be deleterious. The benefits of prehospital packed red blood cells (PRBCs), plasma, or transfusion of both products among trauma patients is unknown compared with crystalloid.

Methods: Secondary analysis of the multicenter PAMPer trial was performed on hypotensive injured patients from the scene. The trial randomized 27 helicopter bases to prehospital plasma or standard resuscitation. Standard resuscitation at the sites was equally divided between crystalloid and crystalloid + PRBC. This led to 4 prehospital resuscitation groups: crystalloid only; PRBC; plasma; and PRBC+plasma. Cox regression determined the association between resuscitation groups and risk-adjusted 30-day mortality. The dose effect of resuscitation fluids was also explored.

Results: Four hundred seven patients were included. PRBC+plasma had the greatest benefit [hazard ratio (HR) 0.38; 95% confidence interval (95% CI) 0.26–0.55, $P < 0.001$], followed by plasma (HR 0.57; 95% CI 0.36–0.91, $P = 0.017$) and PRBC (HR 0.68; 95% CI 0.49–0.95, $P = 0.025$) versus crystalloid only. Mortality was lower per-unit of PRBC (HR 0.69; 95% CI 0.52–0.92, p = 0.009) and plasma (HR 0.68; 95% CI 0.54–0.88, $P = 0.003$). Crystalloid volume was associated with increased mortality among patients receiving blood products (HR 1.65; 95% CI 1.17–2.32, $P = 0.004$).

Conclusion: Patients receiving prehospital PRBC+plasma had the greatest mortality benefit. Crystalloid only had the worst survival. Patients with hemorrhagic shock should receive prehospital blood products when available, preferably PRBC+plasma. Prehospital whole blood may be ideal in this population.

Keywords: air medical, blood, emergency, injury, medical services, plasma, prehospital, transfusion, trauma

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Hemorrhage remains the primary cause of preventable death in both civilian and military trauma.[1,2] A recent call for zero preventable deaths by the National Academies of Sciences, Engineering, and Medicine focuses on strategies to mitigate the physiologic consequences of severe hemorrhage.[3] Adoption of damage control resuscitation minimizes crystalloid volume while furthering transfusion of packed red blood cells (PRBCs), plasma, and platelets, or even whole blood. Use of balanced transfusion may lessen trauma-induced coagulopathy and endothelial injury.[4,5] However, these techniques have been primarily applied to the in-hospital setting. In areas that lack rapid access to trauma centers or with long transport times, severely injured patients may progress to irreversible shock without early intervention.

Informed by data suggesting significant benefits from prehospital transfusion, PRBC administration has now become the standard of care when available for wounded casualties.[6,7] Prehospital blood products (defined as PRBC, plasma, or both PRBC and plasma) are increasingly available through civilian helicopter emergency medical services (HEMS). Prehospital PRBC transfusion improves early mortality, reduces shock, and in-hospital transfusion requirements.[8–10] The Prehospital Air Medical Plasma (PAMPer)

trial demonstrated prehospital plasma resuscitation reduced 30-day mortality of severely injured patients at risk for hemorrhagic shock by nearly 10% compared with standard care resuscitation.[11] The optimal prehospital blood product for resuscitation of hemorrhagic shock from trauma is unknown. Using both prehospital PRBC and plasma may improve results from in-hospital damage control resuscitation compared with either product alone.

Our objective was to determine whether prehospital blood product resuscitation reduces 30-day mortality in patients at risk for hemorrhagic shock compared with crystalloid-only resuscitation. We hypothesized that either PRBC or plasma would be associated with lower mortality than crystalloid resuscitation alone. As a secondary hypothesis, we postulate that the combination of PRBC and plasma is associated with the greatest reduction in mortality.

METHODS

Trial Design

The details of the PAMPer trial have been published previously.[11,12] Briefly, PAMPer was a pragmatic, multicenter, cluster-randomized trial that enrolled patients at risk for hemorrhagic shock during HEMS transport. Patients received either standard care resuscitation or initial resuscitation with 2 units of thawed plasma. Randomization of the control and intervention arms was carried out at the level of the HEMS base, with each base randomly assigned to carry plasma or not for 1-month blocks (eFigure 1, http://links.lww.com/SLA/B641).

Nine trauma center sites comprising 27 HEMS bases participated in the trial. During the trial period, standard care in this pragmatic trial was defined by local protocol. Resuscitation included transfusion of up to 2 units of type O-PRBC at 13 bases, while standard care at the remaining 14 bases included only crystalloid for volume resuscitation. Table 1 describes the pre-existing protocol for transfusion of PRBC by HEMS services. A unit of plasma contained 250 cc of fluid volume and a unit of PRBC contained 300 cc of fluid volume.

This configuration led to 4 potential resuscitation possibilities. During control months, patients at half of the bases would receive crystalloid only, while patients at the remaining bases would receive PRBC with or without additional crystalloid. During intervention months, patients at half of the bases would receive plasma with or without additional crystalloid, while patients at the remaining bases would receive plasma and PRBC with or without additional crystalloid.

Study Population

Eligibility criteria for this study mirrored that of the PAMPer trial. Inclusion criteria included transport by a participating HEMS service to a PAMPer network trauma center, hypotension [systolic blood pressure (SBP) of 70 to 90 mm Hg and tachycardia (heart rate >108 bpm), or severe hypotension alone (SBP <70 mm Hg)] at any time before arrival at the trauma center. As the objective of this study was to evaluate prehospital resuscitation strategies, we excluded patients who were transferred from referring facilities from the originally reported trial population. These patients were excluded, as they could receive both crystalloid and blood products at the outside facility before HEMS transport and potentially bias the outcomes of the prehospital resuscitation groups, as pre-enrollment resuscitation volumes were not reliably available for model adjustment.

TABLE 1. Protocol for Prehospital PRBC Transfusion on Scene

PRBC transfusion should be administered after 1 L of crystalloid total has been received (including by another EMS agency before provider arrival) and any one of the following are present:
(1) Hypotension with systolic blood pressure <90 mm Hg
(2) Changes in mental status
(3) Changes in skin color (pallor, mottling, or cyanosis)
(4) Tachycardia with heart rate >120 beats per minute
(5) Capillary refill >2 s
(6) Lactate level ≥4 mmol/L
(7) Shock index (HR/SBP) >0.9

For patients with penetrating injury or evidence of active bleeding, prehospital providers should consult a medical command physician to obtain orders for immediate transfusion of PRBC.

HR indicates heart rate; PRBC, packed red blood cells; SBP, systolic blood pressure.

Missing Data

We performed multiple imputation to address missing data. Imputed variables included 30-day mortality, injury severity score (ISS), and head-abbreviated injury score. Multiple imputation using iterative fully conditional specification chained equations was performed to develop 20 imputed datasets. Predictor variables for the chained equations included age, sex, mechanism of injury, and in-hospital mortality. Outcome models for 30-day mortality were subsequently performed using multiple imputation estimation techniques that combine model coefficients and standard errors from each imputed dataset while adjusting for the variability between imputed datasets.[13] Missing data proportions for imputed variables were 6% for 30-day mortality, 2% for ISS, and 2% for head abbreviated injury score. Similar results were obtained between complete case and imputed dataset, thus imputed results are presented below.

Statistical Analysis

The primary outcome was 30-day mortality. Patients were categorized into 4 treatment groups based on prehospital resuscitation received: crystalloid only; plasma; PRBC; PRBC and plasma (PRBC+plasma). We employed Cox proportional regression to evaluate the association between 30-day mortality and the prehospital resuscitation group, with the crystalloid-only group serving as the reference group. As the prehospital resuscitation groups were no longer randomized, the regression model was adjusted for age, mechanism of injury, ISS, severe prehospital hypotension (SBP <70 mm Hg), prehospital time, prehospital crystalloid volume (as each of the prehospital blood product groups could receive crystalloid as well), emergent procedure within 24 hours of admission, international normalized ratio, 24-hour total PRBC and plasma transfusion requirements, development of multiple organ failure, nosocomial infection, and abbreviated injury scores for the head, chest, and abdomen. Robust variance estimators were used to account for site clustering.

The above model was repeated using the volume of crystalloid in liters, PRBC in units, and plasma in units transfused to determine the association of 30-day mortality with the dose of PRBC, plasma, and crystalloid. The model was also performed separately in patients who received any prehospital blood product and patients who received crystalloid only. Finally, as an exploratory analysis, prehospital crystalloid volume was categorized into clinically relevant volume categories of no crystalloid, 1 to 500, 501 to 1000, and >1000 mL, and characteristics of these groups were compared.

Data analysis was conducted using Stata v15MP (StataCorp, College Station, TX). Continuous data are presented as median [interquartile range (IQR)]. Continuous data were compared using Wilcoxon rank-sum tests, and categorical data compared using Chi-square. Cox proportional hazard model discrimination was assessed using Harrell C-statistic and goodness-of-fit assessed using the Groennesby and Borgan test. A 2-tailed P value ≤0.05 was considered

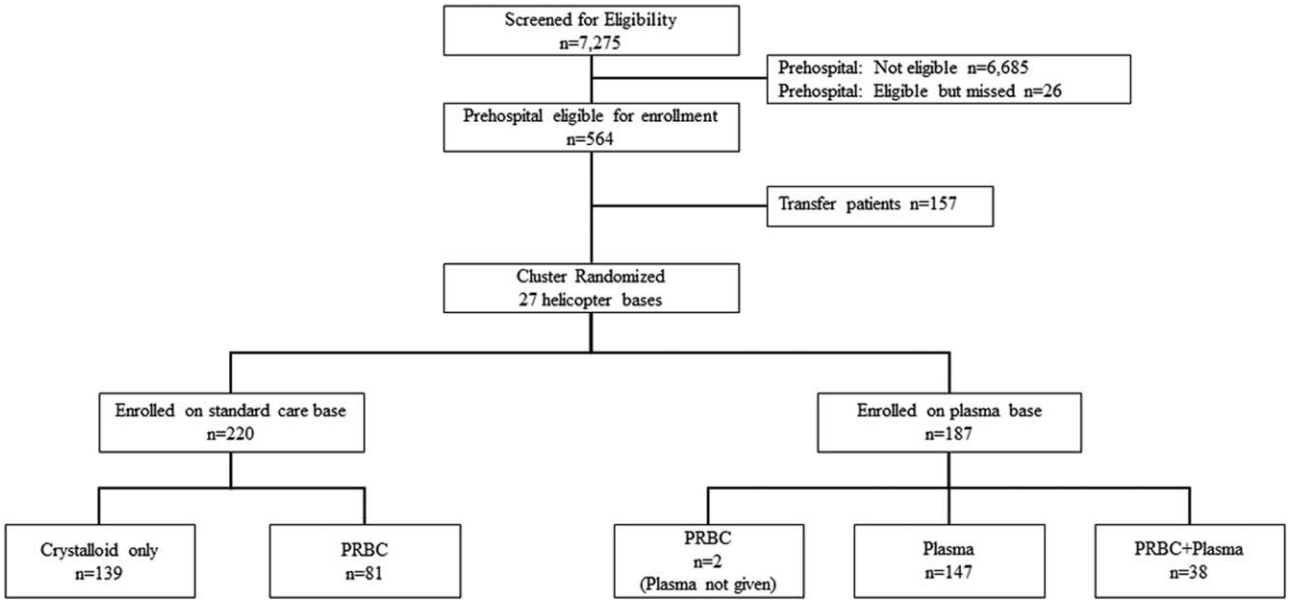

FIGURE 1. Study participant selection from the Prehospital Air Medical Plasma (PAMPer) trial.

significant. The University of Pittsburgh Institutional Review Board approved this study.

RESULTS

A total of 407 patients were included with the exclusion of transfer patients from the original trial population. There were 139 (34%) patients receiving crystalloid only, 83 (20%) receiving PRBC, 147 (36%) receiving plasma, and 38 (10%) receiving PRBC+plasma (Fig. 1). Table 2 demonstrates the baseline characteristics of the 4 prehospital resuscitation groups. Survival model diagnostics demonstrated excellent discrimination with Harrell C-statistic of 0.87, and acceptable calibration with nonsignificant Groennesby and Borgan test ($P = 0.239$).

Cox regression demonstrated that all prehospital blood product groups had a significantly lower hazard of 30-day mortality than crystalloid only resuscitation (Fig. 2). The PRBC+plasma group had the greatest mortality benefit with a 62% reduction in the hazards of mortality, followed by the plasma group with a 43% reduction in the hazards of mortality, and finally the PRBC group with a 32% reduction in the hazards of mortality (Table 3).

Hemorrhage was the most common cause of death in the PRBC, plasma, and PRBC+plasma groups, and the second most common in the crystalloid only group (Table 4). Traumatic brain

TABLE 2. Baseline Characteristics of Study Population by Prehospital Resuscitation Group

	Crystalloid only n = 139	PRBC n = 83	Plasma n = 147	PRBC+Plasma n = 38	*P*
Age, y	47 (28, 65)	40 (25, 55)	43 (30, 55)	45 (32, 58)	0.25
Sex, % male	100 (71.9%)	64 (77.1%)	108 (73.5%)	26 (68.4%)	0.75
Mechanism, % blunt	120 (86.3%)	71 (85.5%)	121 (82.3%)	30 (78.9%)	0.52
Prehospital time, min	35 (28, 44)	43 (37, 54)	38 (30, 46)	47 (41, 59)	<0.001
Prehospital crystalloid, mL	500 (0, 1000)	1000 (150, 1750)	200 (0, 1000)	675 (0, 1000)	<0.001
Prehospital SBP, mm Hg	72 (63, 81)	69 (60, 80)	72.5 (63, 81)	69 (61, 82)	0.79
Prehospital HR, bpm	115 (100, 127)	118 (100, 129)	118 (109, 130)	118.5 (101, 130)	0.64
Prehospital GCS	7 (3, 15)	13 (3, 15)	12 (3, 15)	12.5 (3, 15)	0.56
Prehospital intubation	74 (53.2%)	51 (61.4%)	75 (51.0%)	26 (68.4%)	0.16
Emergent procedure	84 (60.4%)	53 (63.9%)	75 (51.0%)	28 (73.7%)	0.04
PRBC first 24 h, mL	2 (0, 6)	6 (3, 11)	2 (0, 6)	6 (3, 12)	<0.001
Plasma first 24 h, mL	0 (0, 3)	1 (0, 5)	0 (0, 3)	2 (0, 5)	0.02
INR	1.2 (1.1, 1.4)	1.4 (1.2, 1.9)	1.17 (1.1, 1.3)	1.3 (1.1, 1.6)	<0.001
MOF	77 (55.4%)	44 (53.0%)	93 (63.3%)	24 (63.2%)	0.45
Nosocomial infection	21 (15.1%)	15 (18.1%)	28 (19.0%)	10 (26.3%)	0.35
ISS	21 (12, 33)	22 (16, 29)	22 (14, 34)	24 (17, 34)	0.57
Head AIS	2 (0, 3)	1.5 (0, 3)	2 (0, 3)	2 (0, 3)	0.85
Chest AIS	2 (0, 3)	2 (0, 3)	3 (0, 3)	3 (2, 4)	0.01
Abdomen AIS	2 (0, 2)	2 (0, 2)	2 (0, 3)	2 (0, 2)	0.56

Continuous variables presented as median (interquartile range); Categorical variables presented as N (%).

AIS indicates abbreviated injury score; bpm, beats per minute; GCS, Glasgow Coma Scale; HR, heart rate; INR, international normalized ratio; ISS, injury severity score; MOF, multiple organ failure; PRBC, packed red blood cells; SBP, systolic blood pressure.

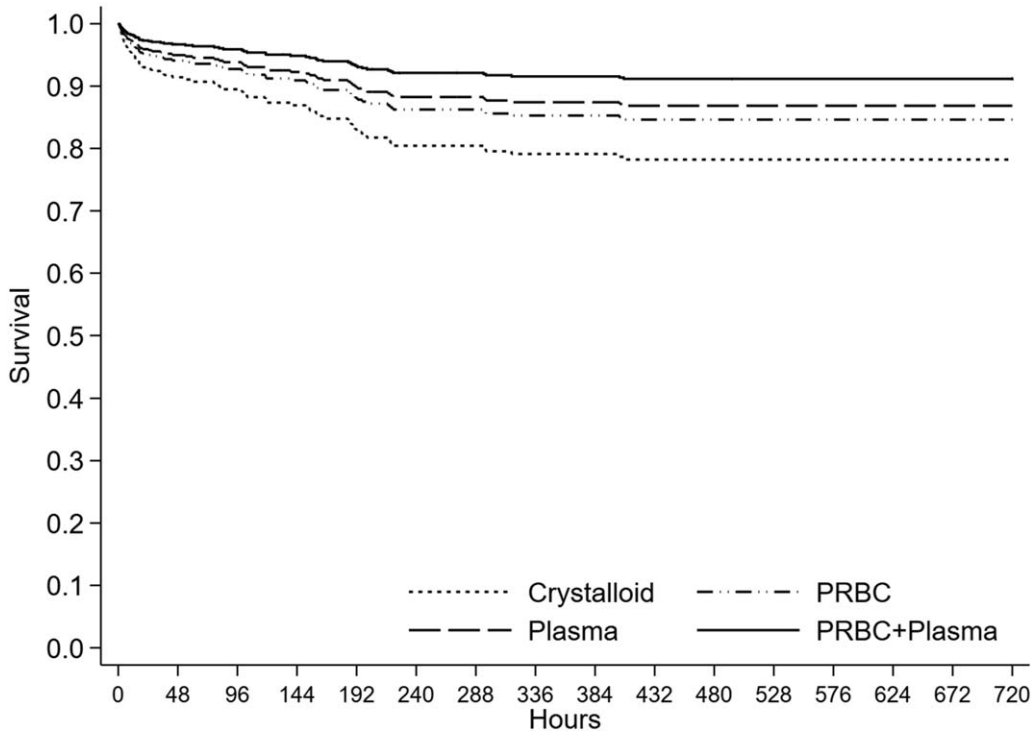

FIGURE 2. Cox proportional hazards regression adjusted survival curves based on prehospital resuscitation group. Time zero represents time of randomization in the original trial. PRBC indicates packed red blood cells.

injury was the most common cause of death in the crystalloid only group, and the second most common in the PRBC, plasma, and PRBC+plasma groups. There was no significant difference in the cause of death across resuscitation groups ($P = 0.180$).

When evaluating the dose effect of the resuscitation strategies among all patients, there was a significant reduction in the hazard of 30-day mortality per unit of prehospital PRBC [hazard ratio (HR) 0.69; 95% confidence interval (95% CI) 0.52–0.92, $P = 0.009$] and per unit of prehospital plasma (HR 0.68; 95% CI 0.54–0.88, $P = 0.003$) transfused, with no association between the dose of crystalloid and mortality (HR 1.20; 95% CI 0.81–1.77, $P = 0.372$).

When evaluating only patients who received a prehospital blood product, each liter of crystalloid was associated with a 65% increase in the hazards of 30-day mortality (HR 1.65; 95% CI 1.17–2.32, $P = 0.004$). However, among patients who received crystalloid only, the volume of crystalloid was not associated with 30-day mortality (HR 0.92; 95% CI 0.57–1.50, $P = 0.748$).

TABLE 3. Cox Proportional Hazard Regression Treatment Effect Estimates by Prehospital Resuscitation Group for 30-day Mortality

	HR	95% CI	*P*
Crystalloid only	Reference	—	—
PRBC	0.68	0.49–0.95	0.025
Plasma	0.57	0.36–0.91	0.017
PRBC+Plasma	0.38	0.26–0.55	<0.001

95% CI indicates 95% confidence interval; HR, hazard ratio; PRBC, packed red blood cells.

TABLE 4. Unadjusted 30-day Mortality and Cause of Death by Prehospital Resuscitation Group

	Crystalloid Only n = 139	PRBC n = 83	Plasma n = 147	PRBC+Plasma n = 38	*P*
30-d mortality	47 (37)	30 (36)	31 (23)	10 (26)	0.05
Cause of death					0.18
Hemorrhage	10 (21)	15 (50)	9 (29)	4 (40)	—
Traumatic brain injury	17 (36)	9 (30)	8 (26)	2 (20)	—
MOF	3 (6)	1 (3)	0 (0)	0 (0)	—
Withdrawal of care	10 (21)	0 (0)	8 (26)	2 (20)	—
Cardiac dysfunction	5 (11)	3 (10)	1 (3)	2 (20)	—
Sepsis	0 (0)	0 (0)	2 (6)	0 (0)	—
Other	1 (2)	0 (0)	1 (3)	0 (0)	—
Unknown	1 (2)	2 (7)	2 (6)	0 (0)	—

Variables presented as N (%).
MOF indicates multiple organ failure; PRBC, packed red blood cells.

TABLE 5. Baseline Characteristics of Crystalloid only Resuscitation Group by Crystalloid Volume

	No Crystalloid n = 60	1–500 mL n = 16	501–1000 mL n = 31	>1000 mL n = 32
30-d mortality	24 (44)	3 (19)	9 (33)	11 (37)
Age, y	41.5 (26, 66)	47.5 (34, 51)	47 (29, 67)	50 (27, 67)
Sex, % male	46 (77)	10 (63)	22 (71)	22 (69)
Mechanism, % blunt	51 (85)	13 (81)	28 (90)	28 (88)
Prehospital time, min	35 (27, 43)	34 (28, 47)	33 (26, 39)	37.5 (30, 46)
Prehospital crystalloid, mL	0 (0, 0)	475 (300, 500)	900 (800, 1000)	1625 (1225, 2030)
Prehospital SBP, mm Hg	69.5 (60, 79)	75.5 (63, 86)	73 (64, 81)	78.5 (66, 83)
Prehospital HR, bpm	112 (85, 125)	115 (88, 142)	111.5 (106, 123)	120 (109, 130)
Prehospital GCS	8 (3, 15)	12.5 (3, 15)	6 (3, 15)	4 (3, 15)
Prehospital intubation	36 (60)	5 (31)	16 (52)	17 (53)
Emergent procedure	35 (58)	9 (56)	21 (68)	19 (59)
PRBC first 24 h, mL	3 (0, 7)	0 (0, 4)	2 (0, 3)	3 (0, 7)
Plasma first 24 h, mL	0 (0, 4)	0 (0, 0)	0 (0, 2)	0 (0, 2)
INR	1.2 (1.1, 1.4)	1.2 (1.1, 1.3)	1.2 (1.1, 1.6)	1.3 (1.1, 1.7)
MOF	30 (50)	11 (69)	17 (55)	19 (59)
Nosocomial infection	6 (10)	3 (19)	4 (13)	8 (25)
ISS	22 (14, 34)	20 (13, 32)	22 (9, 33)	18 (10, 29)
Head AIS	2 (0, 3)	2 (0, 4)	2 (0, 5)	0 (0, 3)
Chest AIS	2 (0, 3)	2 (1, 3)	2 (0, 3)	2 (0, 3)
Abdomen AIS	2 (0, 3)	0 (0, 2)	0 (0, 2)	2 (0, 2)

Continuous variables presented as median (interquartile range); Categorical variables presented as N (%).

No statistically significant differences were present between crystalloid volume groups due to low numbers except for prehospital crystalloid volume as expected.

AIS indicates abbreviated injury score; bpm, beats per minute; GCS, Glasgow Coma Scale; HR, heart rate; INR, international normalized ratio; ISS, injury severity score; MOF, multiple organ failure; PRBC, packed red blood cells; SBP, systolic blood pressure.

Exploratory analysis of crystalloid volume categorization among patients receiving only crystalloid demonstrated that 30-day mortality among patients receiving no crystalloid was 44%; among patients receiving 1 to 500 mL of crystalloid was 19%; among patients receiving 501 to 1000 mL of crystalloid was 33%; and among patients receiving >1000 mL of crystalloid was 37%. Table 5 demonstrates the characteristics of crystalloid only patients across crystalloid volume categories.

DISCUSSION

These data confirm that any blood product resuscitation was associated with lower mortality than crystalloid only resuscitation. PRBC and plasma have similar reductions in mortality; however, PRBC+plasma had a much greater reduction in mortality than either PRBC or plasma alone. Both PRBC and plasma had a prehospital dose-response effect on mortality reduction. Among patients who met criteria for blood products, crystalloid increased mortality in dose-response manner. If only crystalloid was given, small volumes up to 500 mL had the lowest unadjusted mortality compared with no crystalloid or greater volumes; however, given the low numbers, no conclusions to guide therapy can be drawn, but invites further study.

Prehospital blood product resuscitation is not a new concept, administration of plasma in the field was introduced in World War II.[14] Since then, the military has led the investigation of prehospital blood product administration. Both UK and US medevac platforms have developed PRBC transfusion capabilities.[15,16] These interventions demonstrate greater than predicted survival, with a 37% reduction in mortality among severely injured patients at 30 days.[16,17] A matched cohort study of UK combatants demonstrated an 11% decrease in 30-day mortality among patients receiving either prehospital PRBC or plasma.[6] Similarly, a recent matched cohort of US service members in shock or with amputations by Shackelford et al[7] demonstrated a 14% reduction in 24-hour and 11% reduction in 30-day mortality for patients receiving prehospital blood product transfusion. Tactical Combat Casualty Care (TCCC) now recommends whole blood, PRBC and plasma, and plasma or PRBC in order of preference when available for field and tactical evacuation resuscitation.[18]

The promise of resuscitating with prehospital blood products in the military setting renewed interest in civilian prehospital transfusion. As PRBC administration became more practical, it was adopted by air medical transport agencies.[19] Broader utilization of PRBC administration is supported by evidence that large volume crystalloid resuscitation is associated with worse outcomes among injured patients.[20–23] Early reports demonstrated that use of prehospital PRBC was feasible and safe among HEMS providers.[24] A small observational series found physiologic differences, but no impact on mortality.[25] Our group evaluated pre-trauma center PRBC transfusion, demonstrating a reduction in mortality and coagulopathy.[8] We followed this with a larger examination of matched HEMS patients, demonstrating lower 24-hour mortality, PRBC requirements at the trauma center, and lower risk of shock.[9]

On the basis of this preliminary evidence and the outcomes of in-hospital damage control resuscitation, some programs began to develop prehospital plasma transfusion programs in addition to PRBC capabilities.[5,26,27] Kim et al[28] demonstrated improved coagulation parameters and better 1:1 matching of PRBC and plasma ratios in a small group of patients receiving both PRBC+plasma in the field. Holcomb et al[29] demonstrated a lower 6-hour mortality, lower transfusion requirement, and less shock among patients receiving PRBC+plasma in their HEMS program. A prospective multicenter observational cohort comparing patients receiving plasma and/or PRBC to resuscitation with crystalloid only did not identify a difference in mortality. The conclusions of that study were limited by significant differences in the groups, despite matching.[29]

Given these findings, the Department of Defense issued the Prehospital Use of Plasma for Traumatic Hemorrhage program announcement, which ultimately funded the PAMPer trial. This multicenter, cluster-randomized trial demonstrated a 9.8% reduction in absolute 30-day mortality for patients randomized to a plasma carrying air medical base.[11] Survival analysis demonstrated early separation of intervention and control groups at 3 hours from injury, with no differences in adverse events including transfusion reactions.

Given the fact that half of participating HEMS bases already carried PRBC as standard care, we were presented with an opportunity for a nested evaluation of prehospital blood products.

A recent detailed evaluation of preventable civilian deaths revealed more than half of preventable prehospital deaths were due to hemorrhage, and more than one-third of preventable deaths due to hemorrhage occurred in the field.[30] Given this, the current study has several implications for prehospital trauma care. Patients with signs of shock should receive prehospital blood products whenever available. Crystalloid alone appears to be inferior to blood products and has a dose-response increase in mortality in this setting. If both PRBC and plasma are available, patients should receive both, as this led to the greatest mortality reduction. If blood products are unavailable, the optimal crystalloid volume for patients in shock remains unclear. Current guidelines suggest only the volume of crystalloid necessary to maintain indicators of clinical perfusion (normal mental status, radial pulse presence), but definitive evidence of volume targets is lacking.[18,31] HEMS programs without blood product availability should evaluate the feasibility of adding PRBC and plasma to their capabilities given the weight of evidence suggests a mortality benefit. If only 1 product can be added, plasma should be favored, as there is level 1 evidence to support it.

The additive benefit of PRBC+plasma also suggests that there may be a benefit to the use of whole blood in the prehospital setting. Whole blood resuscitation demonstrates improved survival in the military setting, and more recently has been shown to be safe and feasible in civilian hospitals.[32,33] Because of this, our group is leading the Pragmatic Prehospital Group O Whole Blood Early Resuscitation (PPOWER) trial to evaluate outcomes of prehospital and early resuscitation with whole blood compared with fractionated blood products.[34] Further, whole blood may overcome some of the logistical challenges to HEMS programs storing and carrying both PRBC and plasma. Other developments such as freeze-dried plasma may also mitigate the costs and storage challenges of traditional cold-stored blood products.[35] This may also expand access of prehospital blood product resuscitation to ground EMS agencies as well as soldiers at the point of injury.[36]

This study does have several limitations. Although the data come from a multicenter randomized trial, this is a secondary observational analysis that limits data available for analysis; however, the original trial intervention was prehospital plasma which collected data that lent itself to this particular analysis. Further, the prehospital resuscitation groups were not evaluated across the trial randomization scheme, necessitating risk-adjustment methods to control for known confounders while unknown confounders may remain. The prehospital blood product groups all received some crystalloid, and the PRBC and PRBC+plasma received relatively significant volumes. Although we adjusted for this in our models, this may be a marker of severe shock either with requirement for blood products after no response to crystalloid or significant crystalloid volume after available blood products are exhausted during transport. Further, the protocols for PRBC transfusion in the control arm generally required 1 L of crystalloid infusion in the absence of medical command orders for immediate PRBC transfusion. There were missing data present in the study; however, this was mitigated through use of multiple imputation and complete case analysis demonstrated similar results. With evaluation of 4 treatment groups, some of the groups had small numbers leading to wide CIs of estimates for treatment effect. Further, crystalloid volume groups also had small numbers and bias by indication limiting definitive conclusions. It is unclear why a group of patients received no fluid with the enrollment criteria, and they may have been extremis already leading to the high mortality. Thus, the analysis of crystalloid-only volumes should be considered exploratory.

CONCLUSION

Patients in this trial receiving prehospital PRBC and plasma had the greatest mortality benefit, followed by plasma, and PRBC respectively compared with crystalloid only resuscitation. Injured patients at risk for hemorrhagic shock should receive resuscitation with prehospital blood products when available. Crystalloid resuscitation should be limited when prehospital blood products are not available. Prehospital whole blood resuscitation may offer significant benefits to this patient population.

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