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Every minute matters: Improving outcomes for penetrating trauma through prehospital advanced resuscitative care

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ABSTRACT

Introduction: Prehospital resuscitation with blood products is gaining popularity for patients with traumatic hemorrhage. The MEDEVAC trial demonstrated a survival benefit exclusively among patients who received blood or plasma within 15 minutes of air medical evacuation. In fast-paced urban EMS systems with a high incidence of penetrating trauma, mortality data based on the timing to first blood administration is scarce. We hypothesize a survival benefit in patients with severe hemorrhage when blood is administered within the first 15 minutes of EMS patient contact.

Methods: This was a retrospective analysis of a prospective database of prehospital blood (PHB) administration between 2021 and 2023 in an urban EMS system facing increasing rates of gun violence. PHB patients were compared to trauma registry controls from an era before prehospital blood utilization (2016-2019). Included were patients with penetrating injury and SBP ≤ 90mmHg at initial EMS evaluation that received at least one unit of blood product after injury. Excluded were isolated head trauma or prehospital cardiac arrest. Time to initiation of blood administration before and after PHB implementation and in-hospital mortality were the primary variables of interest.

Results: A total of 143 patients (PHB=61, controls=82) were included for analysis. Median age was 34 years with no difference in demographics. Median scene and transport intervals were longer in the PHB cohort, with a 5-minute increase in total prehospital time. Time to administration of first unit of blood was significantly lower in the PHB vs. control group (8min vs 27min; $p < 0.01$). In-hospital mortality was lower in the PHB vs. control group (7% vs 29%; $p < 0.01$). When controlling for patient age, NISS, tachycardia on EMS evaluation, and total prehospital time interval, multivariate regression revealed an independent increase in mortality by 11% with each minute delay to blood administration following injury (OR 1.11, 95%CI 1.04-1.19).

Conclusion: Compared to patients with penetrating trauma and hypotension who first received blood after hospital arrival, resuscitation with blood products was started 19 minutes earlier after initiation of a PHB program despite a 5-minute increase in prehospital time. A survival for early PHB use was demonstrated, with an 11% mortality increase for each minute delay to blood administration. Interventions such as PHB may improve patient outcomes by helping capture opportunities to improve trauma resuscitation closer to the point of injury.

Study Type: Prospective

Level of Evidence: Level IV

Keywords: advanced resuscitative care; mortality; penetrating injury; prehospital blood; time of transfusion

INTRODUCTION

Interest in the use of prehospital blood products for patients with traumatic hemorrhage has grown rapidly in recent years, though widespread implementation and data support its use have remained limited. While as many as 900,000 trauma patients each year may benefit from prehospital blood administration, few EMS agencies currently have the ability to provide transfusions and less than 1% of patient with hemorrhagic shock in the US currently receive prehospital blood products[1]. Several studies have shown encouraging improvements in vital signs and early mortality through the use of prehospital transfusion, though have not demonstrated a benefit in mortality at hospital discharge [2,3]. Recently, delivery of blood as part of a prehospital Advanced Resuscitative Care (ARC) bundle, including calcium and tranexamic acid (TXA), in patients with severe hemorrhage from penetrating trauma in a fast-paced urban setting has shown a survival benefit compared to those who received standard care without blood products [4,5].

In patients with traumatic shock, early hemorrhage control and effective volume resuscitation with blood products are essential interventions. The “Golden Hour” concept refers to the short window of opportunity following traumatic injury that has been considered the crucial time period which may determine a patient’s outcome [6]. Several studies suggest that this window is narrower and that the optimal time for resuscitation may actually be the “platinum 10 minutes” for patients suffering from severe hemorrhage [6,7,8,9].

If not treated rapidly, patients with severe hemorrhage are at risk for a condition known as “blood failure,” in which shock leads to oxygen debt, disrupted hemostasis, endothelial dysfunction, and ultimately multiple organ failure[10]. Prehospital blood transfusion allows EMS providers to initiate resuscitation earlier, thereby reversing shock and preventing blood failure. The results of the MEDEVAC trial support this approach, demonstrating a survival benefit exclusively among patients who received PRBCs or plasma within 15 minutes of air medical evacuation [11]. Deeb et al (2023) found that 30 day mortality increases 2% for every 1 minute delay in time to resuscitative intervention and Hosseinpour et al (2023) demonstrated that mortality increases 2% with every minute delay in whole blood transfusion [12,13]. Similarly, increased time to initiation of a massive transfusion protocol has been associated with increased mortality[14].

These studies support the proposal that early and effective resuscitation with blood products in a fast-paced urban setting could provide a mortality benefit for trauma patients with severe hemorrhage. However, no previous civilian prehospital studies within urban EMS systems have examined mortality data based on the exact timing to first blood product administration. The purpose of this analysis is to precisely examine the timing of transfusion and its effects on mortality for patients with penetrating trauma in the civilian setting. We hypothesize a survival benefit among patients with severe hemorrhage when blood is administered within the first 15 minutes of EMS patient contact.

METHODS

This was a retrospective analysis of a prospective database of prehospital blood (PHB) administration in an urban EMS system with roughly 70,000 annual responses. The study period was October 2021 through January 2023. PHB was delivered as part of the ARC bundle, which consisted of 2 units of packed red blood cells (PRBCs), 2 grams of calcium, and 2 grams of tranexamic acid (TXA). Administration criteria for the ARC bundle in our EMS agency include systolic blood pressure (SBP) ≤ 70 or SBP ≤ 90 coupled with a heart rate (HR) ≥ 110 beats per minute (bpm) following traumatic injury [4], though in some cases the ARC bundle may be administered at the paramedic's discretion to patients who had hypotension (SBP<90) without tachycardia. PHB patients included for analysis in this study were those with penetrating injury and SBP ≤ 90 mmHg at initial EMS evaluation who received at least one unit of packed red blood cells (PRBCs).

PHB patients were compared to patients in our institution's trauma registry from the era before prehospital blood utilization (2016-2019) who met the same criteria. These patients were labeled as controls since they only received blood products after presenting to the emergency department but may have been eligible for PHB administration based on presenting physiology. Control patients were identified through a query of our registry for all hypotensive patients following traumatic injury (EMS SBP ≤ 90 mmHg). All patients with a prehospital SBP listed as "unable to obtain" at initial EMS triage were presumed to have a SBP ≤ 90 mmHg and were thus included in the analysis. Patients with blunt injuries, isolated head injuries, EMS SBP > 90 mmHg, prehospital cardiac arrest, and/or those that did not receive at least one unit of blood prior to ED disposition were excluded from the study.

The primary outcome of interest was time to initiation of blood administration and the overall effect on time to initiation on in-hospital mortality. Secondary variables included prehospital response, scene, and transport time intervals, transport distance, EMS vital signs, emergency department (ED) vitals, ED procedures, utilization of blood products, length of stay in the intensive care unit (ICU), New Injury Severity Score (NISS), shock index, and hospital length of stay. Prehospital variables were obtained from the EMS run sheets.

Categorical variables were expressed as frequencies and percentages. Continuous variables were reported as median and interquartile range. These variables were compared using two-sided Chi-Square and independent sample Mann-Whitney U analysis, respectively. Sensitivity analysis was conducted to assess the impact of missingness of data on univariate results. This analysis consisted of imputing median, highest, and lowest values independently for missing values and repeating univariate analysis for each outcome.

Multivariate analysis began by assessing each available variable individually in univariate logistic regression. The purpose was to identify independent predictors of in-hospital mortality. For each variable, any patient with missing data was automatically excluded during this portion of analysis. Patient age, HR at EMS triage, SBP at EMS triage, NISS, shock index, and time to initiation of blood administration were all identified as independent predictors of in-hospital mortality. Patient SBP was excluded from multivariate analysis due to greater than 10% missing data at EMS triage. A multivariate logistic model was then constructed using the remaining variables. Odds ratios using 95% confidence intervals (CI) were calculated for the variables of time to blood administration, total prehospital interval, EMS heart rate, NISS, and age.

All data analysis was performed using IBM SPSS version 29 (Armonk, NY). A *p*-value less than 0.05 was considered statistically significant. We adhered to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines to ensure all necessary components of the study were included (Supplemental Digital Content, http://links.lww.com/TA/D746). Institutional Review Board approval was obtained prior to the commencement of this study.

RESULTS

A total of 1,522 patients with EMS SBP triage SBP ≤ 90 mm Hg were evaluated. Among these patients, 949 were excluded for having non-penetrating injuries, 111 due to prehospital cardiac arrest, 304 due to missing data, and 15 due to isolated head injuries (**Figure 1**). The remaining 143 patients were included in the study. The study cohort was comprised primarily of African American (83.9%) adult males (83.5%). The median (IQR) total cohort age and NISS score were 34 (24-43) and 22 (14-30), respectively. Patient physiology at EMS triage, prehospital timing intervals, ED triage physiology, and time to first unit of PRBC initiation are summarized in **Table 1**.

The total cohort was subsequently divided into a PHB (n=61) and control group (n=82). No significant difference was observed in patient demographics or injury characteristics. Additionally, no significant difference was observed in prehospital vital signs between the two groups. The time intervals from 911 call to scene arrival and scene departure to hospital were similar between groups. Median time interval from EMS arrival to scene departure was longer in the PHB group compared to controls (8 vs 6 minutes, $p<0.001$). Additionally, the median total prehospital time interval was longer in the PHB group (24.5 vs 20 mins, $p<0.001$) (**Figure 2**).

Transport distance was similar for PHB compared to controls (3.8 (2.0-6.2) vs. 3.9 (2.3-6.5) miles, p=0.78). All 61 PHB patients received at least 1 unit of PRBCs prior to hospital arrival, with 60 of 61 (98%) receiving 2 units, 59 of 61 (97%) receiving 2 grams of calcium, and 45 of 61 (74%) receiving TXA.

Upon arrival to the hospital, the PHB group had a significantly higher median systolic blood pressure (116.5 vs 88 mm Hg; $p<0.001$) and lower median heart rate (79 vs 101 bpm, p=0.03). Time to administration of the first unit of blood was significantly shorter in the PHB group (8 vs 26 minutes; $p<0.001$). Overall, in-hospital mortality was lower in the PHB vs. control group (7% vs 29%; $p<0.001$) (**Figure 3**).

Multivariate logistic regression analysis was performed to assess the impact of time until initiation of the first unit of blood on patient mortality. The analysis included all 143 patients. When controlling for patient age, NISS, tachycardia on EMS evaluation, and total prehospital time interval, multivariate regression revealed an independent increase in mortality by 11% with each minute delay to blood administration following injury (OR 1.11, 95%CI 1.04-1.19)

(**Table 2**). Additionally, an increase in NISS was also associated with increased odds of mortality (OR 1.12, 95%CI 1.07-1.17, $p<0.001$). Patient age, tachycardia on EMS evaluation, and total prehospital time interval had no impact on patient mortality in the multivariate model.

DISCUSSION

Evidence for the benefit of early transfusion from military and civilian air medical trials has led to growing interest in deploying PHB within ground EMS agencies, yet two large studies of PHB in ground EMS services have yielded mixed results. The largest study to date noted improvements in physiology and early mortality but no difference in survival to hospital discharge[16]. The RePHILL trial, a large randomized controlled trial conducted in the UK, showed no advantage of blood products over crystalloid resuscitation in prehospital trauma patients with hypotension [17]. Recently, we demonstrated a survival benefit for prehospital transfusion in an urban EMS system among patients with penetrating trauma and hemorrhagic shock [5].

Our current analysis has also demonstrated improved survival at hospital discharge for prehospital transfusion and has revealed that each minute of delay in administration of blood was associated with an 11% increase in mortality. This survival benefit occurred despite a 4.5 minute longer prehospital time recorded for the PBH group. From the arrival of EMS personnel at the scene, patients received blood an average of 19 minutes earlier in the PHB group compared to controls. Our data suggest that while prehospital blood administration may modestly increase transport intervals, this cost is outweighed by the benefit of significantly earlier resuscitation in patients suffering from life-threatening hemorrhage.

These findings are consistent with study by Deeb et. al (2023), which found that every minute delay in administration of blood products or tranexamic acid was associated with a 2% increase in 30-day mortality[13]. Our finding of a larger 11% increase in mortality for every minute delay may be attributable to several factors. First, our population was sicker, with exclusively penetrating trauma mechanism and signs of more severe hemorrhagic shock at EMS arrival compared to other studies. Second, whereas our PHB patients received no prehospital crystalloid, in most previous studies patients were given 400-1000 mL crystalloid prior to blood transfusion. This unnecessary use of crystalloids could have contributed to traumatic coagulopathy and potentially obscured the positive effect of prehospital blood. Lastly, most of our patients received 2 grams of TXA and 2 grams of Calcium in addition to 2 units of PRBCs while enroute, which may have further enhanced the effectiveness of PHB. Our findings suggest that rapid resuscitation is possible and beneficial for patients with severe penetrating trauma, even in fast-paced urban EMS agencies with extremely short transport windows. These data may also suggest that the survival advantage is most dramatic in sicker patients.

The "Golden Hour" of trauma resuscitation, a term originally attributed to R. Adams Cowley at the Baltimore Shock Trauma Institute, has served as a guide to trauma providers since its introduction in the 1970's [18]. This golden hour refers to the critical time period during which resuscitation may be most successful. Subsequent decades of experience have shown that the window for survivability is often much narrower, particularly for patients with penetrating trauma experiencing hemorrhagic shock. As a result, new efforts to provide early effective resuscitation within the "Platinum 10" or even 5 minutes after patient contact are emerging in the civilian population [9,10]. Reflecting improved understanding of this concept among prehospital care providers, in 2019 the National Association of State EMS Officials (NASEMSO) guidelines recommend trauma scene times of less than 10 minutes [19]. Although this goal is rarely achieved, as shown in one recent study which documented scene times of less than 10 minutes in only 35% of trauma encounters, we have demonstrated that effective hemorrhagic shock resuscitation can be achieved at a fast-paced EMS settings[20].

While efforts to reduce scene and transport intervals should theoretically improve survival by delivering patients to definitive care as early as possible, faster transport time has not consistently been demonstrated to improve survival [21-26]. In our analysis, though we did observe an almost 5-minute increase in transport time for the PHB group when compared to the control group, every minute was properly used to provide effective therapy, thereby avoiding "dead zones" in patient care and increasing the likelihood of survival. The increase in transport interval is attributable to the time required to initiate the ARC interventions, including obtaining vascular access and beginning the administration of PRBCs, since distance from the scene of injury to the trauma center did not differ between groups[12].

Limitations

Our study has several limitations which are inherent to the study design, the most prominent of which are the relatively small sample size and the use of historical controls. Since data were not completely available for all variables, we imputed missing values using median, highest, and lowest values, which did not alter the conclusions drawn from the data. We also acknowledge the potential for selection bias introduced by excluding patients with a prehospital SBP > 90 or a prehospital arrest.

Next, we did observe that ARC bundle was not uniformly applied to all patients since compliance improved over time as EMS personnel became more familiar with these new interventions. In particular, we noted that use of TXA increased later in the study, which could have influence outcome and should be a topic of future study.

Lastly, it is important to note that our data do not provide information on the independent effects of blood, calcium, and TXA within the patients who received the ARC bundle. While TXA has been shown to improve outcomes in patients with hemorrhagic shock, TXA would not be expected to play a role in the improved physiology we observed within a short prehospital interval[27,28]. The anti-fibrinolytic properties of TXA likely provided benefit through improved hemostasis over many hours and may have impacted late mortality but could not be expected to result in the immediate improvements in blood pressure, perfusion, and oxygen delivery seen after effective resuscitation with blood products. Calcium can play a role in improving vascular tone and cardiac contractility, but in our patients calcium most likely exerted any beneficial effect through blunting of ionized hypocalcemia induced by citrated PRBCs rather than independently producing the beneficial hemodynamic effects noted in the PHB group. While further study of the independent effects of each ARC bundle element are certainly warranted, it appears that early resuscitation with PRBCs, providing volume expansion and increased oxygen-carrying capacity, was predominantly responsible for the mortality improvement seen in the PHB group.

CONCLUSION

For trauma patients with hemorrhagic shock, early hemorrhage control and effective resuscitation are essential elements of care. Urban EMS systems have traditionally sought to achieve optimal trauma care through a "scoop-and-run" approach to trauma care that delivers the patient to the trauma center as early as possible. Our data suggest that minutes truly do matter in trauma resuscitation, and that prioritization of prehospital transfusion improves survivability in patients with severe penetrating injury despite a modest increase in transport time. While appropriate emphasis should continue to be placed on prehospital hemorrhage control, basic airway interventions, and efforts to reduce unnecessary transport time delays, the priority of effective resuscitation with blood products represents a significant opportunity to improve trauma outcomes.

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FIGURE LEGENDS

Figure 1. Trauma inclusion flowgram

Figure 2. Median total prehospital time interval was longer in the PHB group (24.5 vs 20 mins, $p<0.001$).

Figure 3. Transfusion timing (8 vs 26 minutes; $p<0.001$) and mortality outcomes (7% vs 29%); $p<0.001$.

Figure 1

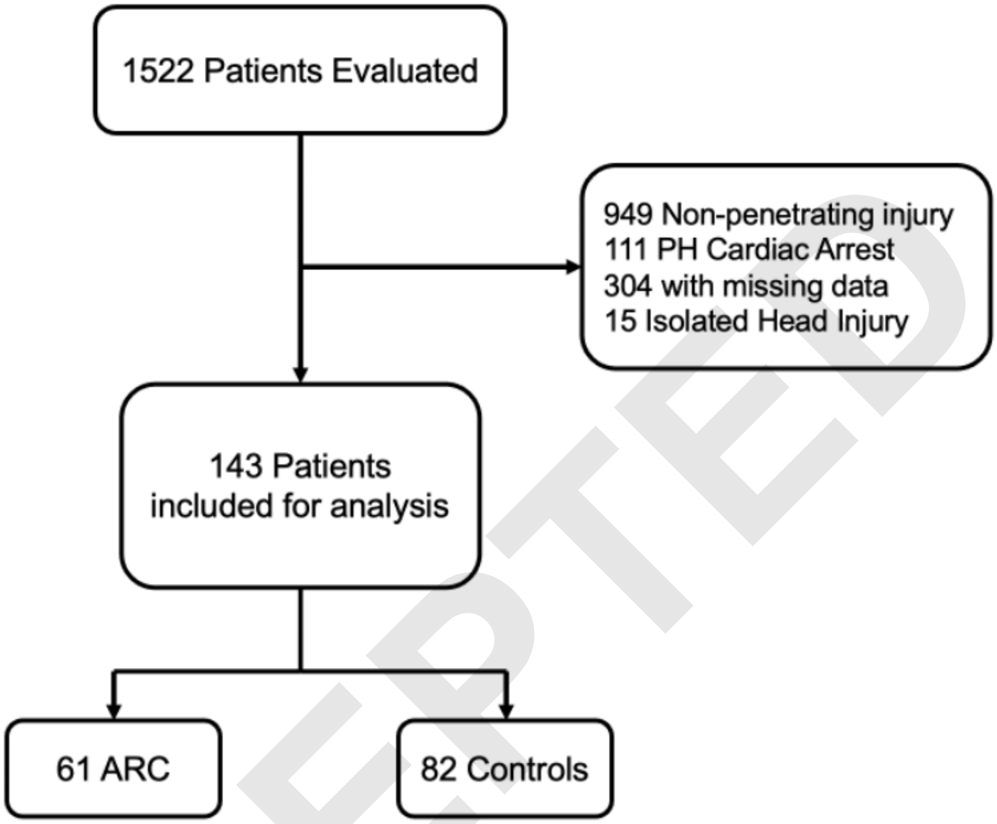

1522 Patients Evaluated
949 Non-penetrating injury
111 PH Cardiac Arrest
304 with missing data
15 Isolated Head Injury
143 Patients included for analysis
61 ARC
82 Controls

Figure 2

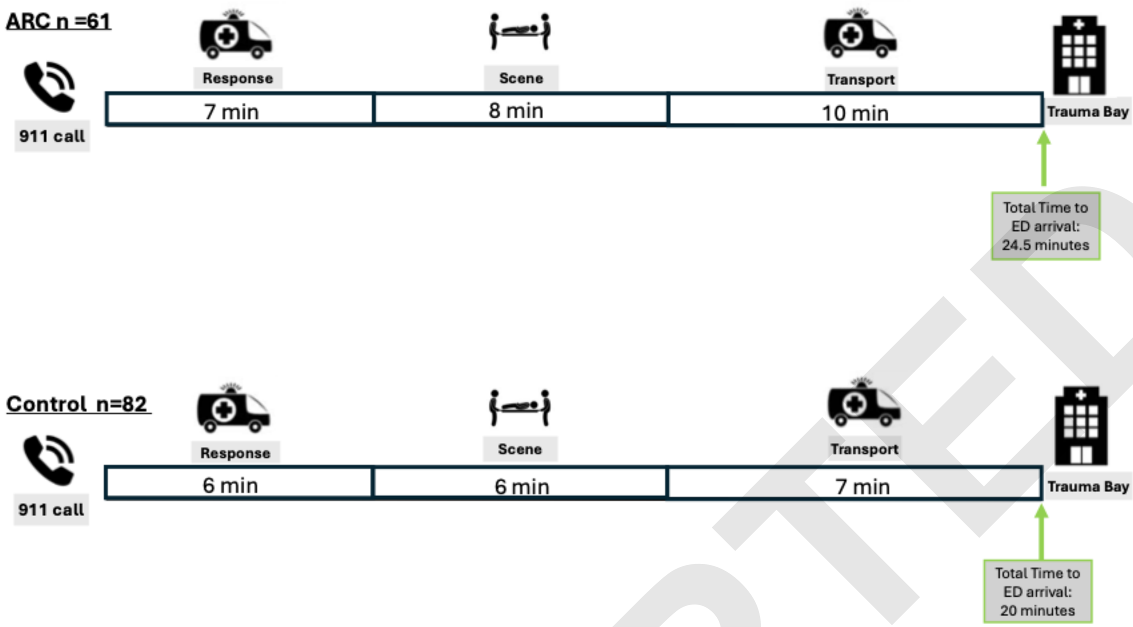

ARC n =61
Response
Scene
Transport
911 call
7 min
8 min
10 min
Trauma Bay
Total Time to ED arrival: 24.5 minutes
Control n=82
Response
Scene
Transport
911 call
6 min
6 min
7 min
Trauma Bay
Total Time to ED arrival: 20 minutes

Figure 3

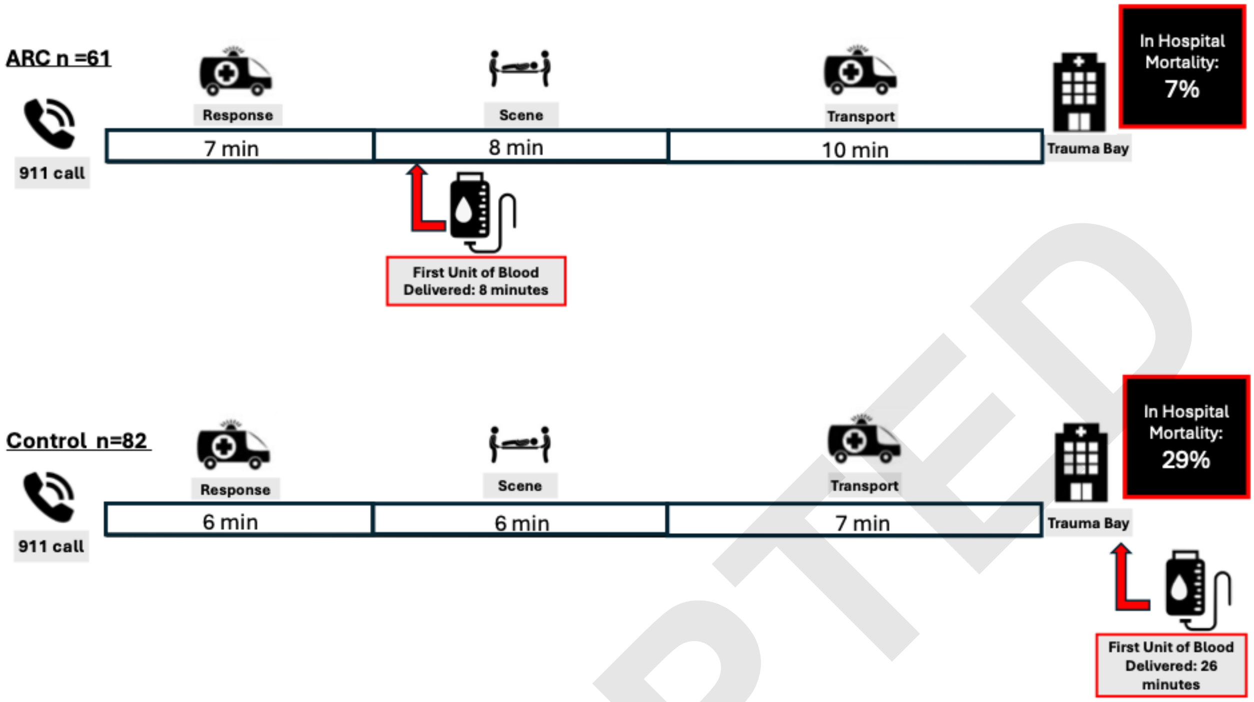

ARC n =61
911 call
Response
7 min
Scene
8 min
Transport
10 min
Trauma Bay
In Hospital Mortality: 7%
First Unit of Blood Delivered: 8 minutes
Control n=82
911 call
Response
6 min
Scene
6 min
Transport
7 min
Trauma Bay
In Hospital Mortality: 29%
First Unit of Blood Delivered: 26 minutes

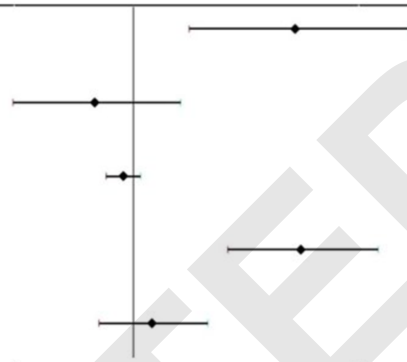
Table 1. Patients' outcomes

Parameter, median (IQR)	PHB (n=61)	Control (n=82)	p-value
Demographics			
Age, yr	35 (25-47)	30 (24-40.5)	0.214
Male, n (%)	55 (90)	75 (90)	0.51
African American, n (%)	51 (83.6)	69 (84.1)	<.001
Initial EMS Characteristics			
PH Systolic BP (mmHg)	70 (62-86.5)	78 (58-86)	0.83
PH Heart Rate (bpm)	110 (87-136)	112 (74.8-137)	0.8
PH Shock Index	1.4 (1.0-1.9)	1.41 (1.1-1.7)	0.79
PH Glasgow Coma Scale	14 (10-15)	15 (6-15)	0.45
Prehospital Timing Intervals (min)			
911 call to arrive scene	7 (5-11)	6 (4.0-9.0)	0.11
Arrive scene to depart scene	8 (6.0-9.5)	6 (4.0-7.0)	<.001
Depart scene to arrive hospital	9.5 (6.25-12)	7 (4.8-10)	0.10
911 call to arrive hospital	24.5 (20-30.5)	20 (14-23.5)	<.001
Distance to Hospital (miles)	3.9 (2.3-6.5)	3.8 (2.0-6.2)	0.78
ED Characteristics			
ED Systolic BP (mmHg)	116.5 (88-140)	88 (68-111)	<.001
ED Heart Rate (bpm)	79 (62-102)	101 (68-128)	<0.001
ED Shock Index	0.73 (0.50-0.73)	1.14 (0.85-1.52)	<0.001
ED Glasgow Coma Scale	15 (13-15)	14 (3.0-15)	0.33
New Injury Severity Scale	18 (9.5-31)	22 (16-31)	0.13
Head AIS	0 (0-1)	0 (0-1)	0.89
Chest AIS	3 (3-5)	3(3-4)	0.23
Abdomen AIS	3 (3-4)	3 (3-4)	0.58
Extremity AIS	2 (2-3)	2 (1-3)	0.22

Transfusion			
Time to Blood Transfusion (min)	8 (6.0-9.0)	26 (24-30)	<.001
Outcomes			
In-Hospital Mortality (%)	11 (7)	35 (29)	<.001

Table 2. Multivariable logistic regression. A survival for early PHB use was demonstrated, with an 11% mortality increase for each minute delay to blood administration.

Variable	OR (95% CI)	P-value
Time to Blood Administration	1.11 (1.04-1.19)	<0.01
Total Prehospital Interval	0.97 (0.98-1.03)	0.40
EMS Heart Rate	0.99 (0.98-1.01)	0.23
NISS	1.12 (1.07-1.17)	<0.01
Age	1.01 (0.98-1.05)	0.49



Odds Ratio (OR), 95% Confidence Interval (95%CI) derived from multivariate logistic regression