

## Scientific Session I - Raymond H. Alexander, MD Resident Paper Competition

Paper #1  
January 10, 2018  
8:00 am

### OVER RESUSCITATION WITH PLASMA IS ASSOCIATED WITH SUSTAINED FIBRINOLYSIS SHUTDOWN AND DEATH IN PEDIATRIC TBI

Christine M. Leeper, MD, Matthew Neal, Timothy Billiar, MD,  
Jason L. Sperry, MD, MPH\*, Barbara A. Gaines, MD\*  
University of Pittsburgh Medical Center

**Presenter:** Christine M. Leeper, MD

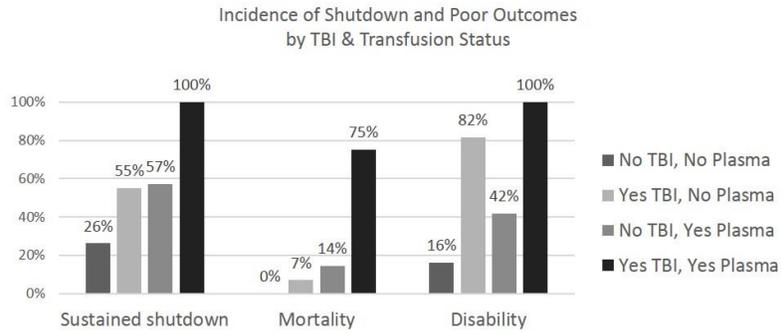
**Discussant:** Rachael Callcut, MD, University of California San Francisco

**Objectives:** Elevated INR is a marker of poor outcome, but not necessarily bleeding or clinical coagulopathy, in injured children. Conversely, children with traumatic brain injury (TBI) tend to be hypercoagulable based on thromboelastography(rTEG) parameters. Many clinicians continue to utilize INR as a treatment target.

**Methods:** Prospective observational study of children age<18 with rTEG on arrival and daily thereafter for 7 days. Standard TEG definitions of hyperfibrinolysis(HF; LY30=3) and fibrinolysis shutdown (SD; LY30=0.8) were applied. AIS score=3 defined severe traumatic brain injury. 24-hour blood product transfusion volumes were documented. Outcomes were death and disability.

**Results:** 101 patients were included: median (IQR) age=8(4-13), injury severity score=25(16-30), 47% severe TBI, 16% mortality, 45% discharge disability. Neither total volume nor any single product volume transfused (mL/kg; all  $p>0.1$ ) differed between TBI and non-TBI groups. On univariate analysis, transfusion of PRBC ( $p=0.016$ ), plasma ( $p<0.001$ ) and platelets ( $p=0.006$ ) were associated with sustained shutdown; however, in a regression model that included all products and controlled for TBI, only plasma remained an independent predictor of sustained SD (OR=1.15,  $p=0.033$ ). Every mL/kg plasma was associated with a 15% increased odds of sustained SD. Patients with both severe TBI and plasma transfusion had 100% sustained SD, 75% mortality, and 100% disability in survivors. Admission INR was elevated in TBI patients, but did not correlate with TEG-ACT( $p=NS$ ) and was associated with sustained SD( $p=0.006$ ).

**Conclusions:** Plasma transfusion is associated with sustained fibrinolysis SD and poor outcome, particularly in patients with severe TBI. This may be an indicator of over resuscitation; plasma transfusion should be directed by evidence of clinical bleeding or abnormalities in TEG-ACT, rather than an arbitrary INR threshold.



Patients with severe traumatic brain injury who received plasma have the highest incidence of sustained fibrinolysis shutdown and poor outcomes.

Logistic Regression Model to predict sustained shutdown			
Product (mL/kg)	Odds Ratio	95% Confidence Interval	p value
Plasma	1.15*	1.04-1.31	0.036
Platelets	1.16	0.74-1.82	0.518
Red Blood Cells	0.98	0.91-1.04	0.481
Traumatic Brain Injury	4.26	1.8-10.8	0.002

\*Every mL/kg plasma is associated with 15% increased odds of sustained SD

Plasma is the only blood product that independently predicts sustained shutdown after controlling for traumatic brain injury.

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Paper #2  
January 10, 2018  
8:20 am

### PLASMA CO-ADMINISTRATION IMPROVES RESUSCITATION WITH TRANEXAMIC ACID OR PROTHROMBIN COMPLEX IN A PORCINE HEMORRHAGIC SHOCK MODEL

John P. Kuckelman, DO, Morgan R. Barron, MD, Donald Moe, Michael S. Lallemand, MD, John McClellan, Shannon Marko, Matthew J. Eckert, MD\*, Matthew J. Martin, MD\*  
Madigan Army Medical Center

**Presenter:** John P. Kuckelman, DO

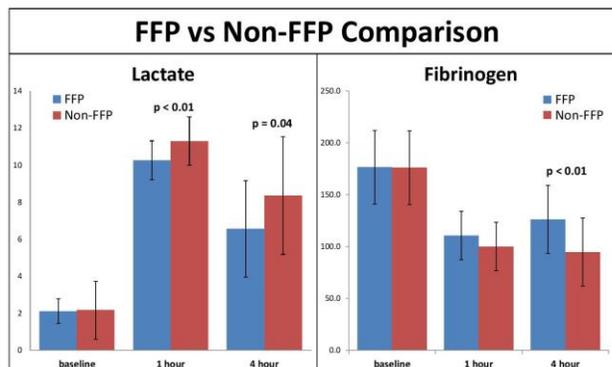
**Discussant:** Martin A. Schreiber, MD, Oregon Health and Science University

**Objectives:** Traumatic coagulopathy has been well characterized, but still carries high rates of mortality due to bleeding. A "factor-based" resuscitation strategy using pro-coagulant drugs and factor concentrates in lieu of plasma is being used, but with little evidentiary support. We sought to evaluate and compare resuscitation strategies using combinations of tranexamic acid (TXA), prothrombin complex concentrate (PCC), and fresh frozen plasma (FFP).

**Methods:** A 35% blood volume hemorrhage combined with a truncal ischemia-reperfusion injury was utilized in 60 adult swine to produce uniform shock and coagulopathy. Animals were randomized to control (N=12), a single agent group (TXA, N=10, PCC, N=8, or FFP, N=6) or combination groups (TXA-FFP, N=10, PCC-FFP, N=8, TXA-PCC, N=6). Resuscitation was continued to 6 hours. Outcomes included hemodynamics, lab values, and thromboelastometry (ROTEM). Results were compared between all groups, with additional comparisons between FFP and non-FFP groups.

**Results:** All 60 animals survived to 6 hours. Shock was seen in all animals, with hypotension (MAP 44mmHg), tachycardia (HR 145), acidosis (pH 7.18, lactate 11), anemia (HCT 17), and coagulopathy (Fibrinogen 107). There were clear differences between groups for mean pH ( $p=0.02$ ), INR ( $p<0.01$ ), clotting time (CT,  $p<0.01$ ), lactate ( $p=0.01$ ), creatinine ( $p<0.01$ ), and fibrinogen ( $p=0.02$ ). FFP groups had improved resuscitation and clotting parameters (Figures), with lower lactate 6.5 vs 8.4 ( $p=0.04$ ), and increased fibrinogen at 126 vs 95 ( $p<0.01$ ). ROTEM showed shortened CT at 60s in the FFP group vs 65s in the non-FFP group ( $p=0.04$ ).

**Conclusions:** When correcting traumatic coagulopathy, combinations of FFP with TXA or PCC were superior in improving acidosis, coagulopathy, and clotting time over these agents alone or in combo without plasma. Further validation of pure "factor-based" strategies is needed.



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Paper #3  
January 10, 2018  
8:40 am

### BLOOD PRODUCT AGE VERSUS MORTALITY: RESULTS FROM THE PRAGMATIC RANDOMIZED OPTIMAL PLATELET AND PLASMA RATIO (PROPPR) TRIAL

A. Cozette Kale, MD, MPH, Ronald Chang, MD, Erin Fox, Mohammad Rahbar, Rachel Mitchell, Stacia DeSantis, Eileen M. Bulger, MD, Mitchell J. Cohen, MD, FACS, Bryan A. Cotton, MD, MPH\*, Timothy C. Fabian, MD\*, Kenji Inaba, MD, Jeffrey D. Kerby, MD, PhD\*, Peter Muskat, Terence O'Keeffe, MD, MSPH\*, Sandro Rizoli, MD, PhD, FRCSC, FACS\*, Thomas M. Scalea, MD, FACS, FCCM\*, Martin A. Schreiber, MD, FACS\*, Karen Brasel, MD, MPH, Jeanette M. Podbielski, RN BSN, Michael Swartz, Charles E. Wade, PhD, John B. Holcomb, MD\*  
PROPPR Study Group  
University of Texas Health Science Center at Houston

**Presenter:** A. Cozette Kale, MD, MPH

**Discussant:** Ali Salim, MD, Brigham & Women's Hospital

**Objectives:** The storage lesion of red blood cells (RBC), plasma (PLAS), and platelets (PLT) has been described. However, few studies have evaluated the independent effects of blood product age in seriously injured patients. We hypothesized that transfusion of older blood products was associated with increased mortality at 6hr, 24hr, and 30d in massively bleeding trauma patients.

**Methods:** Blood product and outcomes data prospectively collected during the PROPPR trial were analyzed. PLAS (FFP and thawed plasma) age was defined as days since thawing. "Old" was defined based on the median blood product age: RBC at least 20 days, PLAS at least 2 days, and PLT at least 4 days of storage. The total products and proportion of old RBC, PLAS, and PLT prior to the end of active resuscitation were calculated. We constructed a mixed-effects parametric survival model (Weibull distribution) controlling for age, ISS, mechanism, treatment arm, and total products transfused as fixed effects and study site as a random effect.

**Results:** There were 680 patients who received 7,776 RBC units (median 12 days, IQR [12, 27]), 4,489 PLAS units (median 2 days, IQR [1, 3]), and 940 PLT units (median 4 days, IQR [3, 5]). PLAS age significantly decreased with increasing units transfused while mortality increased (Figure). Conversely, there was no such change in the RBC or PLT age. Higher proportion of old RBC and young PLAS, but not old or young PLT, were associated with mortality (Table). Receiving any old RBC was associated with increased 6hr (HR 3.4, 95% CI 1.3-8.8) and 24hr (HR 2.2, 95% CI 1.1-4.5), but not 30d, mortality.

**Conclusions:** Transfusion of a higher proportion of old RBC, or receiving any RBC  $\geq 20$  days old, was associated with increased mortality. Young PLAS, but not old or young PLT, was associated with mortality. This finding is potentially confounded by decreasing PLAS age with increasing units transfused.

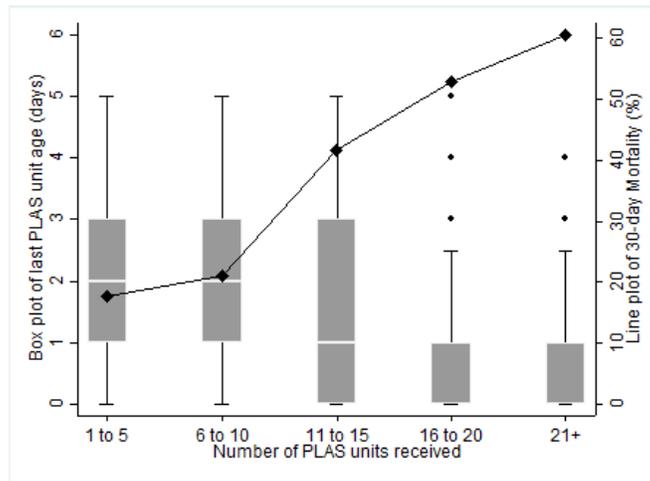


Figure. PLAS age decreased with increasing transfusions while mortality increased.

<b>6h mortality</b>	<b>HR*</b>	<b>95% CI</b>	<b>30d mortality</b>	<b>HR*</b>	<b>95% CI</b>
↑Old RBC	1.09	1.02 – 1.18	↑Old RBC	1.06	1.01 – 1.12
↑Old PLAS	0.91	0.85 – 0.98	↑Old PLAS	0.93	0.88 – 0.97
↑Old PLT	0.96	0.91 – 1.02	↑Old PLT	0.99	0.95 – 1.03
<b>24h mortality</b>	<b>HR*</b>	<b>95% CI</b>	* Hazard ratios for every 10% increase in proportion of old product		
↑Old RBC	1.08	1.01 – 1.16			
↑Old PLAS	0.91	0.86 – 0.98			
↑Old PLT	0.96	0.92 – 1.01			

Table. Increasing proportion of old RBC and young PLAS, but not old/young PLT, were associated with mortality at 6h, 24h, and 30 days.

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Paper #4  
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9:00 am

### DO ALL HEAD INJURED PATIENTS ON ANTIPLATELET DRUGS REALLY NEED PLATELETS?

Christopher Bell, MD, Carlos Pelaez, MD\*, Sarah K Spilman, MA, Darla Eastman,  
Richard A. Sidwell, MD, FACS\*, Joseph Sherrill  
Iowa Methodist Medical Center

**Presenter:** Christopher Bell, MD

**Discussant:** Jose L. Pascual, MD, PhD, University of Pennsylvania

**Objectives:** It is common for patients with traumatic intracranial hemorrhage (ICH) taking antiplatelet medications to receive platelet transfusion after the ICH is identified. There is no high-quality evidence to guide platelet transfusion for these types of patients. In an effort to standardize the approach to platelet transfusion, a Level I trauma center adopted a targeted platelet transfusion guideline. Platelet reactivity test (PRT) results (Accriva Diagnostics, San Diego, CA) were used to determine need for transfusion, and patients who were non-therapeutic on antiplatelet medication (Aspirin or P2Y12 inhibitors) were not transfused, regardless of severity of head injury.

**Methods:** The protocol was analyzed retrospectively to evaluate outcomes during the study period (June 2014–December 2016). All patients had moderate to severe ICH (head abbreviated injury score > 1), received a PRT for known or suspected antiplatelet medication use, and had at least two head CT scans. Differences were assessed with Kruskal-Wallis and chi-square tests.

**Results:** 167 patients met study inclusion criteria and 49 patients (29%) had non-therapeutic PRT results. The groups did not differ by injury severity score and approximately 40% of patients in each group had a severe to critical ICH (head AIS>3). Regardless of ICH type or severity, 92% of patients with a non-therapeutic PRT were not transfused, and only 2 patients (4%) had clinically significant progression of the bleed. Implementation of this protocol reduced platelet transfusions by 56% and associated healthcare costs by 50%.

**Conclusions:** Using a targeted platelet transfusion protocol for ICH patients with non-therapeutic platelet reactivity significantly reduced platelet usage, particularly for patients with known or suspected antiplatelet medication use and unreconciled home medications. Results demonstrate that not all head injured patients taking antiplatelet drugs need to be transfused.

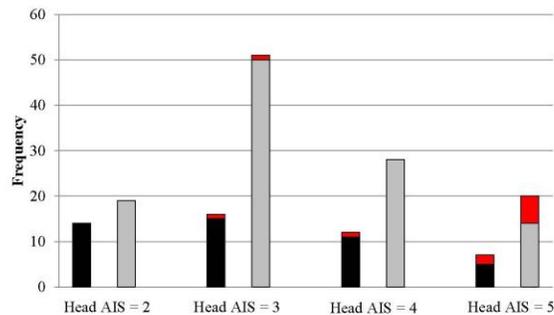
**Table 1. Patients with intracranial hemorrhage (ICH), broken down by platelet reactivity test (PRT) result, June 2014 to December 2016 (N=167)**

	Non-Therapeutic PRT N=49	Therapeutic PRT N=118	p-value
Age, median (IQR)	69 (57, 86)	79 (67, 84)	.06
Unstable physiology in emergency department (ED), n (%)	13 (27%)	13 (11%)	.02
Severe or critical head bleed, n (%)	19 (39%)	48 (41%)	.87
Injury severity score (ISS), median (IQR)	14 (10, 22)	14 (9, 21)	.46
Antiplatelet therapy home medication, n (%)	24 (49%)	108 (92%)	<.001
Received platelet transfusion, n (%)	4 (8%)	94 (80%)	<.001
ICU days, median (IQR)	3 (2, 5)	3 (2, 4)	.32
Hospital length of stay, median (IQR)	5 (3, 7)	4 (2, 7)	.28
Mortality, n (%)	6 (12%)	10 (9%)	.56
Clinically significant worsening of ICH, n (%)	4 (8%)	7 (6%)	.73

**Table 1. Patients with intracranial hemorrhage (ICH), broken down by platelet reactivity test (PRT) result, June 2014 to December 2016 (N=167)**

**Figure 1. Clinically significant worsening of intracranial hemorrhage (ICH), compared by head abbreviated injury severity score (AIS) and initial platelet reactivity test (PRT) result.**

Key: Black bars denote patients with non-therapeutic PRT. Gray bars denote patients with therapeutic PRT. In the stacked bars, red indicates clinically significant worsening.



**Figure 1. Clinically significant worsening of intracranial hemorrhage (ICH), compared by head abbreviated injury severity score (AIS) and initial platelet reactivity test (PRT) result.**

Key: Black bars denote patients with non-therapeutic PRT. Gray bars denote patients with therapeutic PRT. In the stacked bars, red indicates clinically significant worsening.

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Paper #5  
January 10, 2018  
9:20 am

**EARLY PREDICTION OF HEMODYNAMIC INSTABILITY IN CRITICALLY ILL PATIENTS: A PROSPECTIVE STUDY**

Jarot Guerra, MD, Asif Rahman, Larry Eshelman, Szymon Bieganski, Brian Gross,  
Kelly Bochicchio, Minnan Xu-Wilson, Grant V. Bochicchio, MD, MPH\*  
Washington University in St. Louis

**Presenter:** Jarot Guerra, MD

**Discussant:** Robert D. Winfield, MD, University of Kansas Medical Center

**Objectives:** Earlier identification of patients at risk of hemodynamic instability has the potential to improve outcome. We previously developed a real time risk score, the hemodynamic instability indicator (HII), which predicts the need for cardiovascular support in ICU patients. We set out to validate this score in a trauma/surgical ICU.

**Methods:** We prospectively enrolled patients who were expected to stay in the ICU for at least 24 hours, hemodynamically stable, and expected to survive at least 48 hours and not DNI/DNR. HII was continuously calculated in real time by integrating risk factors such as vitals and laboratory values using a previously developed machine learning algorithm. All hemodynamic interventions were collected. The 24 hours before intervention is labeled as the pre-intervention true positive region. The region following resuscitation and until ICU discharge is considered the stable or false positive region. For each intervention segment, we evaluated how well our score predicted that episode of hemodynamic instability in the pre-intervention segment

**Results:** 126 patients were enrolled. The majority (64%) were male and acute care surgery patients (55%) with a median age of 60. 49% were eventually started on inotropes/pressors. ICU mortality was 9.4% and median ICU length of stay was 5.8 days. Of the enrollees, 60 patients (with sufficient data to calculate the pre-intervention score) were included for further analysis of HII performance. HII significantly predicted the need for pressors/inotropes within 24 hours of the event with sensitivity of 0.56, specificity of 0.76, ( $p < 0.01$ ) with increasing probability as time approached intervention initiation.

**Conclusions:** HII strongly predicted the need for pressor/inotrope use with increasing predictability as time approached pressor/inotrope initiation. Earlier identification of instability could potentially initiate earlier intervention and improve outcome.

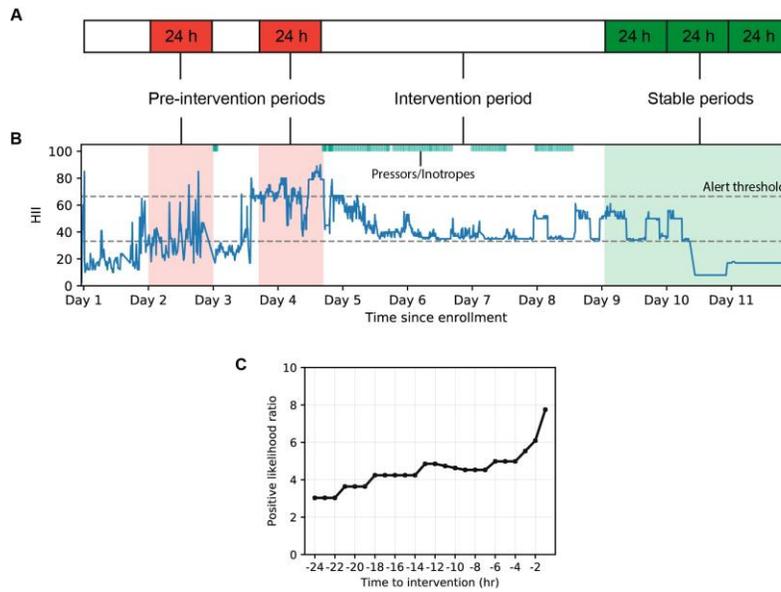


Figure 1. A) Pre-intervention, Intervention and stable periods. B) HII tracks therapy response. C) The positive likelihood ratio shows that the index predicts episodes of hemodynamic instability with increasing likelihood approaching the time of intervention.