Scientific Session III-A

Paper #12
January 11, 2018
10:30 am

THE ROLE OF 4-FACTOR PROTHROMBIN COMPLEX CONCENTRATE (4-PCC) IN COAGULOPATHY OF TRAUMA: A PROPENSITY MATCHED ANALYSIS

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Presenter: Hassan Aziz, MD

Discussant: Ryan A. Lawless, MD, Denver Health Medical Center

Objectives: Coagulopathy is a common complication after severe trauma. 3-factor PCC has shown to be effective in reversing coagulopathy of trauma (COT), however, the role of 4-factor PCC is still unclear. The aim of our study is to compare 4-PCC+FFP vs. FPP alone for the treatment of COT.

Methods: We reviewed all trauma patients >18y of age who received PCC+FFP or FFP alone at our Level I trauma center from 2014-16. We excluded patients on preinjury oral anticoagulants. Patients were divided into two groups (4-PCC+FFP: FFP alone) and were matched in a 1:2 ratio using propensity score matching (PSM) for demographics, vital and injury parameters, and initial INR. COT was defined as admission INR>1.5. Corrected INR was defined as INR<1.5. Outcome measures were time to correction of INR, pRBC units transfused, thromboembolic complications, and mortality.

Results: 516 patients analyzed, of which 120 patients (4-PCC+FFP: 40, FFP: 80) were matched. Mean age was 58+/-20 y; 60% were male, median ISS was 29 [14?38]. Mechanism of injury was blunt in 87% patients. 4-PCC+FFP was associated with an accelerated correction of INR (373 vs. 955 min; *p*=0.001), decrease in pRBC units (7 vs. 9 units; *p*=0.04), and FFP units (5 vs. 7 units; *p*=0.03) transfused as compared to FFP alone. 4-PCC+FFP was associated with lower mortality rate (25% vs. 33% *p*=0.04) as compared to FFP alone, however, there was no difference in the thromboembolic complications (2.5% vs. 1.2%, *p*=0.5) between the two groups. Administration of PCC+FFP led to an earlier correction of the INR compared to FFP alone (**Figure 1**).

Conclusions: Results of our study demonstrated that the use of 4-factor PCC in conjunction with FFP is associated with rapid reversal of INR and reduction in transfusion requirements as compared to FFP alone. 4-PCC is an effective therapy for the reversal of COT without increasing the risk of thromboembolic complications.

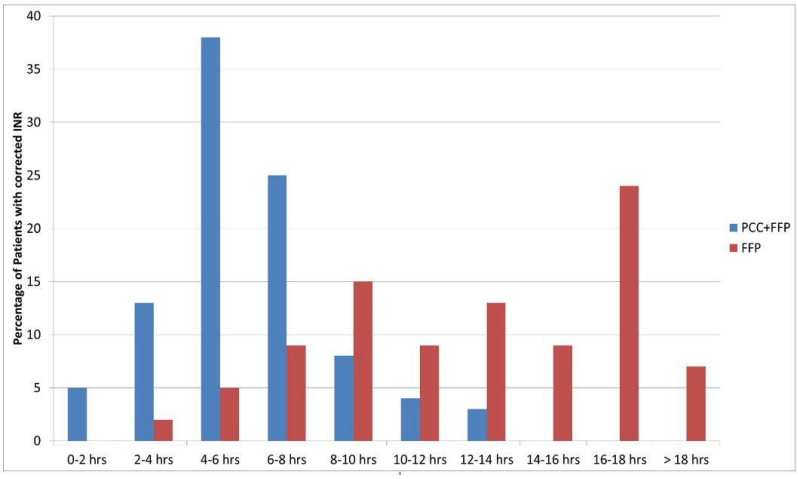

Figure 1. Proportion of patients with corrected INR and time to correction of INR

Scientific Session III-A

Paper #13
January 11, 2018
10:50 am

IN VITRO EFFECTS OF A KAOLIN BASED HEMOSTATIC DRESSING ON ANTICOAGULATED BLOOD

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Presenter: Michael W. Cripps, MD

Discussant: Andrew J. Dennis, DO, Cook County Hospital

Objectives: The use of kaolin coated dressings has become common in hemostatic treatment algorithms and have efficacy in normal patients, but their increased use will inevitably include patients on anticoagulants. We hypothesize that kaolin coating material (KCM) will improve clotting regardless of anticoagulation medication.

Methods: A prospective study was performed on blood from 45 patients on anticoagulation agents and 5 healthy controls. 10 patients were on a vitamin K antagonist (VKA), 10 on unfractionated heparin (UH), 10 on an anti-platelet (AP) agent, 10 on a Xa inhibitor (Xa), and 5 on a direct thrombin inhibitor (DTI). None were on more than one type of anticoagulation medication. Viscoelastic (VE) testing was performed with and without KCM. All p-values were adjusted for multiple comparisons.

Results: The addition of KCM significantly decreased the time for initial clot formation (CT) in all groups (Figure 1). The mean CT for controls was decreased from 692 to 190.8 sec($p<0.001$). KCM decreased the initial clot formation time by about 1.5 times in those on DTI ($p=0.043$) and 2.5 times in those taking AP medication ($p<0.001$). The most profound effect was seen in those on UH (No KCM 1602 secs vs KCM 440 secs;$p<0.001$), VKA (No KCM 1152 secs vs 232 secs;$p<0.01$), and Xa (No KCM 1342 secs vs 287 secs;$p<0.001$). Analysis of other clot formation parameters revealed that KCM significantly improved the clot formation kinetics (CFT) only in patients taking Xa ($p=0.03$). KCM improved maximum clot strength in patients on UH and Xa ($p=0.05$). Patients on UH had a larger effect size with an increase in clot strength from 24.35mm to 43.35mm while those on Xa had an increase of 38.7mm to 49.85mm.

Conclusions: In this in vitro analysis, the addition of KCM to the blood of patients taking any of these anticoagulation medications significantly improved the time to initial clot formation, indicating that kaolin based hemostatic dressings will be effective in initiating clot formation in patients on anticoagulants.

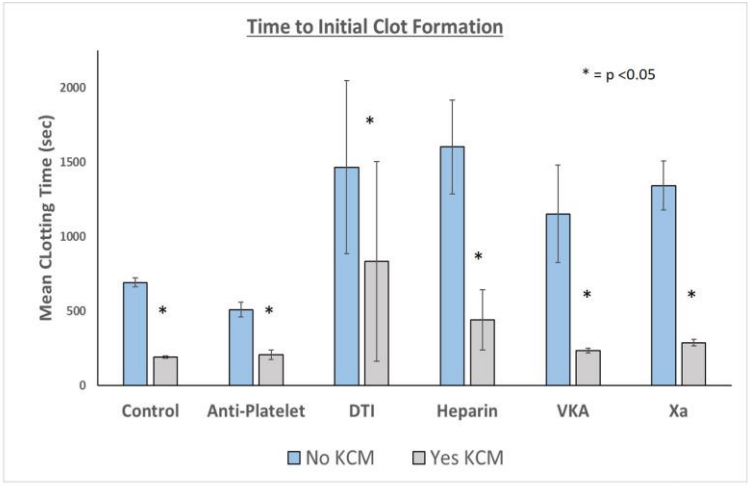

Figure 1. The addition of kaolin coating material (KCM) improved the time it takes to start forming a clot in all test groups.

Scientific Session III-A
Paper #14
January 11, 2018
11:10 am

MAR RATIO PREDICTS SHOCK VOLUME: TWO METRICS TO UNDERSTAND BURDEN OF INJURY

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Presenter: Brian L. Brewer, MD

Discussant: Franklin Lee Wright, MD, University of Colorado Denver

Objectives: Shock volume (SV) is a novel metric designed to quantify global oxygen debt over time. SV temporally integrates serial shock indices to reflect critical illness and hypoperfusion, as in increased base deficit and multisystem organ dysfunction following injury. Recent research has demonstrated that the ratio of MA to R on admission thromboelastography (TEG) not only reflects underlying coagulation dysfunction, it is an excellent predictor of mortality attributable to hemorrhage. We hypothesized that a relationship exists between admission MAR ratio and subsequent shock volume.

Methods: Injured patients admitted to a Level 1 trauma center were included. Demographic data, injury characteristics and laboratory values were collected. The SV at 3, 6, 12 and 24 hours from admission was calculated from serial shock indices. The MAR ratio was calculated from admission TEG as follows:

MA/R = MAR ratio

Correlation analysis was used to determine the relationship between serial shock volumes and the admission MAR ratio.

Results: 80% of patients were male, mean age was 37 years(SD 12) and mean ISS was 29.4(SD 12.5). 32% had a positive critical administration threshold (CAT) within the first 24 hours and overall mortality was 7%. Correlation between the admission MAR ratio and the shock volume are displayed in Figure 1. There was a significant negative association with decreasing MAR ratio correlating with increased shock volumes (3 hours -0.3284, p=0.0046; 6 hours -0.4170, p=0.0002; 24 hours -0.3154, p=0.0066).

Conclusions: The true burden of injury is often difficult to anticipate immediately after injury. Shock volume quantifies cumulative volume of shock but utility is limited as it may take up to 24 hours to accurately calculate. The MAR ratio, which is calculated from the admission TEG, has a significant inverse relationship with shock volume at 3, 6 and 24 hours. The MAR ratio may serve as an immediate indicator of severity of shock and the potential downstream physiologic effects prior to other indicators.

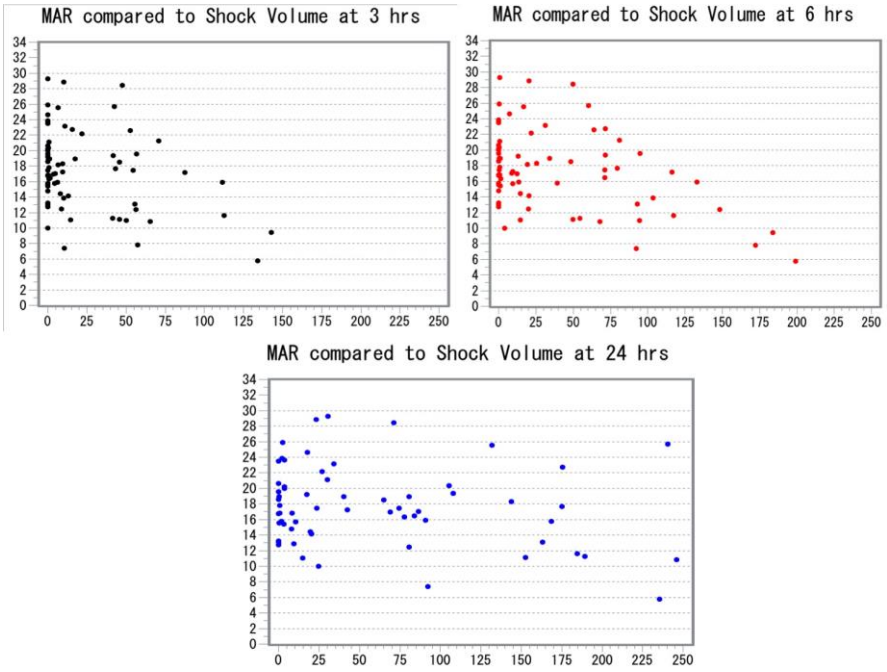

Figure 1 - Correlation between MAR ratio and Shock Volume at 3, 6 and 24 hours following admission.

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Paper #15
January 11, 2018
11:30 am

ASSOCIATION OF FRESH WHOLE BLOOD AND SURVIVAL AT ROLE 2 MEDICAL TREATMENT FACILITIES IN AFGHANISTAN

Jennifer M. Gurney, MD*, Amanda M Staudt, PhD, MPH, Shawn C. Nessen, DO, FACS*, Tuan Le, MD, DrPH, Philip C. Spinella, MD, FCCM*, Andrew Cap, Zsolt T. Stockinger, MD, FACS*, Stacy A. Shackelford, MD*, Heather Pidcoke, Elizabeth A Mann-Salinas, PhD, RN
US Army Institute of Surgical Research

Presenter: Shawn C. Nessen, DO

Discussant: Matthew J. Martin, MD, Madigan Army Medical Center

Objectives: The objective of this study was to compare mortality in combat casualties who received fresh whole blood (FWB) as compared to those who received no FWB and partial or complete component therapy at forward deployed (Role 2) medical treatment facilities (MTFs) with surgical capability.

Methods: Patients were separated into two groups: 1) received FWB (n=215) and 2) did not receive FWB (n=896); moreover, both groups potentially received plasma, Red Blood Cells (RBCs), and occasionally platelets. Kaplan-Meier plot, log rank test, and multivariate cox regression were performed to compare survival of patients 8 hours after Role 2 admission. A subgroup analysis was conducted among patients requiring a massive transfusion (FWB n=132, no FWB n=98).

Results: In FWB patients, 30.5% of total median blood volume transfused was FWB. In the Kaplan-Meier plot, survival was similar between FWB (93.5%) and no FWB (94.6%) groups (p=0.6434); however, after controlling for combat mortality index (i.e. physiological injury severity), base deficit, casualty classification, patient affiliation, and volume of blood product and crystalloid, the risk of mortality was elevated in patients who did not receive FWB (HR=2.0, 95% CI 1.1-3.8) versus patients who received FWB. For massive transfusion patients, the Kaplan-Meier plot showed increased survival in patients who received FWB (89.4%) as compared to patients who did not (79.6%)(p=0.0385); although, after adjusting for covariates, the difference in mortality between the study groups was only marginally significant (HR=1.9, 95% CI 0.9-4.0).

Conclusions: These results corroborate previous studies demonstrating, in environments where platelets are largely unavailable, patients who received FWB had lower mortality. Further analysis is needed to elucidate other factors (e.g. traumatic brain injury, temperature) that may result in improved survival in patients who receive FWB.

Scientific Session III-A

Paper #16
January 11, 2018
11:50 am

A COMPARISON OF RESUSCITATION INTENSITY (RI) AND CRITICAL ADMINISTRATION THRESHOLD (CAT) IN PREDICTING EARLY MORTALITY AMONG BLEEDING PATIENTS: A MULTICENTER VALIDATION IN 680 MAJOR TRANSFUSION PATIENTS

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Presenter: David Meyer, MD

Discussant: Ronald B. Tesoriero, MD

Objectives: We sought to evaluate the performance of the Critical Administration Threshold (CAT) and Resuscitation Intensity (RI) as more appropriate replacements for massive transfusion (MT) in defining mortality risk in patients undergoing major transfusions.

Methods: Patients predicted to receive MT at 12 Level-1 trauma centers were randomized in the PROPPR trial. MT: ≥10 U RBC in 24 hours; CAT+: ≥3 U RBC in first hour; RI: total products in the first 30 minutes (1 U RBC, 1 U plasma, 1.0 L crystalloid, 0.5 L colloids each assigned 1 unit). RI was evaluated as a continuous variable as well as dichotomized at ≥4 units. Each of these models was evaluated for their ability to predict mortality at 3, 6, and 24 hours.

Results: Of 680 patients randomized, 301 patients met MT, 521 met CAT+, and 445 had RI ≥4. Of those that died, 23% never reached MT threshold, but were all captured by CAT+ and RI ≥4. Half of patients who were CAT+ or RI ≥4 met MT criteria. The 30-day mortality was similar between CAT+ (28%) and RI ≥4 patients (29%). Predictive values for 24-hour mortality are represented in the TABLE below. In addition, when RI was evaluated as a continuous variable, each unit increase was associated with a 20% increase in hemorrhage-related mortality (OR 1.20, 95% CI 1.15-1.29).

Conclusions: Both RI and CAT may serve as valid surrogates for early mortality in severely injured patients undergoing major transfusion, capturing patients who be lost using MT definition. While CAT+ showed the best sensitivity overall, RI ≥4 consistently demonstrated better specificity and similar PPV and NPV. While CAT+ may better capture those patients receiving a RBC-dominant resuscitation, RI≥4 captures other resuscitation fluids and blood products, and can be used as a continuous variable to provide quantitative as well qualitative risk of death.

3-hour mortality				
	PPV	NPV	Sensitivity	Specificity
MT	9%	92%	51%	56%
CAT+	9%	97%	92%	25%
RI ≥4	9%	95%	77%	36%
6-hour mortality				
MT	16%	92%	64%	58%
CAT+	13%	96%	91%	25%
RI ≥4	14%	93%	78%	36%
24-hour mortality				
MT	21%	90%	63%	59%
CAT+	17%	94%	90%	26%
RI ≥4	18%	92%	80%	37%

A comparison of early mortality prediction by MT, RI and CAT

Scientific Session III-A

Paper #17
January 11, 2018
12:16 pm

BLEEDING AND THROMBOEMBOLISM AFTER TBI IN THE ELDERLY: A REAL CONUNDRUM

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Stephanie Bonne, MD*, Sri Ram Pentakota, Peter Yonclas,
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Presenter: Nina Glass, MD

Discussant: Catherine Velopulos, MD, MHS, University of Colorado Anschutz

Objectives: Studies suggest that up to 50% of elderly traumatic brain injury (TBI) patients are on anticoagulant therapy at the time of injury. Both trauma surgeons and neurosurgeons question whether anticoagulation should be stopped to prevent bleeding or recurrent TBI or continued to prevent thromboembolic (TE) events. Our objectives were 1) to evaluate the risks of bleeding and recurrent TBI vs. TE events following an initial TBI in older adults, and 2) to identify risk factors for TBI, bleeding, and TE events in this setting.

Methods: A retrospective analysis of 52,228 Medicare beneficiaries hospitalized with TBI from 2006 to 2010 was performed. We calculated unadjusted risk of post-injury TBI, GI bleeding, or hemorrhagic stroke (bleeding events) and TE events (stroke or MI) over twelve months of follow-up and identified risk factors for these events.

Results: Among beneficiaries with TBI, risk of TE events (4.9 events/100 person-years; 95% confidence interval (CI) 4.7, 5.1) was significantly higher than bleeding events (4.0 events/100 person-years; CI 3.8, 4.2). Several common risk factors (liver disease, COPD) predisposed to all of these complications (Table). Atrial fibrillation and coagulopathy were risk factors for thromboembolic events. Alcohol use and previous history of bleeding were associated with higher risk of bleeding events after TBI. In addition, depression and previous stroke were associated specifically with recurrent TBI.

Conclusions: For elderly patients admitted with TBI, the incidence of thromboembolism is significantly higher than that of bleeding and caution regarding restarting anticoagulation in high-risk patients may be detrimental. Specific risk factors for bleeding and TE events were identified and can help guide care of older adults following TBI. Further studies are needed to establish the optimal management of elderly TBI patients, in particular with respect to anticoagulation.

Risk Factor	Any Bleed	Thromboembolic Events
Race (Black/Other)	X	
Male	X	
Cataracts	X	
Alcohol dependence	X	
Pre-TBI history of bleeding	X	
Disability/End Stage Renal Disease	X	
Discharge to a nursing facility	X	
COPD	X	X
Hyperlipidemia	X	
Liver disease	X	X
Coagulation defect		X
Ischemic heart disease		X
Neurologic disease		X
Rheumatoid arthritis		X
Atrial fibrillation		X

Risk Factors for Adverse Events among Medicare beneficiaries following Traumatic Brain Injury