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Meaningful viscoelastic abnormalities in abusive and non-abusive pediatric trauma☆

Ryan Phillips [a,b,*], Niti Shahi [a,b], Gabrielle Shirek [b], Jenny Stevens [a,c], Maxene Meier [d], John Recicar [a,e], Daniel M. Lindberg [f], John Kim [g], Steven Moulton [a,b]

[a] Division of Pediatric Surgery, Children's Hospital Colorado, Aurora, CO, USA
[b] Department of Surgery, University of Colorado School of Medicine, Aurora, CO, USA
[c] Department of Surgery, Louisiana State University School of Medicine, New Orleans, LA, USA
[d] The Center for Research in Outcomes for Children's Surgery, Center for Children's Surgery, University of Colorado School of Medicine, Aurora, CO, USA
[e] Division of Nursing, Children's Hospital Colorado, Aurora, CO, USA
[f] Department of Emergency Medicine, University of Colorado School of Medicine, Aurora, CO, USA
[g] Department of Pediatrics, Heart Institute, Children's Hospital Colorado, University of Colorado, School of Medicine, Aurora, CO, USA

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ABSTRACT

Background/Purpose: There remains a lack of data on the utility of viscoelastic tests in managing abused patients. We hypothesize that abnormalities on admission thrombelastography (TEG) will differ in abused patients compared to those accidentally injured.
Methods: Pediatric trauma patients (≤10 years old) who had an admission TEG at a Level I pediatric trauma center (2010–2020) were included and stratified into two cohorts: abuse versus accidental trauma. TEG abnormalities were based on the institution's normative values and compared between the groups.
Results: Of 41 children included, 21 sustained abuse. Five abused patients and three accidentally injured patients died. Abused children showed a hypercoagulable pattern on viscoelastic testing with TEG when compared to those accidentally injured, as demonstrated by a short R-time (67% vs. 30%, $p = 0.040$) and an increased alpha angle (47% vs. 0%, $p = 0.001$). There was no significant difference in the MA and LY30 values between the two groups. In a multivariable model, only an abnormal alpha angle remained associated with abuse [odds ratio (OR) 0.17 (confidence intervals (CI) 0.02–0.92)]. In a separate multivariable model, only an abnormal MA was associated with mortality [OR 18.97 (CI 1.93–475.47), $p = 0.025$].
Conclusions: Our data suggest that hemostasis is significantly different in abused children relative to those who are accidentally injured.
Type of Study: Retrospective Comparative Study.
Level of Evidence: Level III.

Child physical abuse is a devastating and prevalent public health issue in the pediatric population. It is defined as any act of commission or omission by a parent or caregiver that results in harm, the potential for harm, or threat of harm to a child [1]. According to the Centers for Disease Control and Prevention, in 2018, child protective services in the United States (U.S.) received 3.5 million referrals for abuse. Of these referrals, 686,000 children were found to have been victims of maltreatment. Child physical abuse makes up approximately 18% of child maltreatment in the US [2]. It is estimated that one in four children will experience abuse or neglect over their lifetime [3]. In 2018, the Centers for Disease Control and Prevention, estimated 1770 children died from physical abuse in the US, and data shows that each year one in seven children experience abuse or neglect [2]. Although child physical abuse is a leading cause of morbidity and mortality in the younger pediatric population, it can present a diagnostic challenge to physicians and other healthcare providers, leading to delays in diagnosis and even missed diagnoses [4].

There are many potential reasons that child physical abuse has important physiological differences relative to other forms of trauma. Even adjusting for disease severity, child physical abuse results in longer hospitalizations, increased costs, and increased morbidity and mortality compared to other forms of trauma [5]. In particular, abusive head trauma exhibits distinct differences compared to other forms of head trauma, with differences in imaging findings, seizure burden, and long-term outcomes [6]. The reasons

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* Corresponding author at: Division of Pediatric Surgery, Children's Hospital Colorado, 13213 E 16th Ave, Box 323, Anschutz Medical Campus, Aurora, CO 80045. Tel.: +1 704 578 9856.
E-mail address: ryan.phillips@ochsner.org (R. Phillips).

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for these physiological differences are unknown. They may, however, relate to an increased likelihood of repeated abuse, increased trauma severity, delays in seeking care, or mechanistic differences (i.e., shaking). Despite these known differences, abused children currently receive medical care using similar guidelines and procedures as non-abused children. Personalized, targeted care to reduce disparities in outcomes between abused and not abused children will require a better understanding of their physiological differences.

Trauma-induced coagulopathy (TIC) is well-established in the literature as a component of pediatric patient injuries; however, there is insufficient research or knowledge on the utilization of conventional coagulation tests and viscoelastic hemostatic assays as an evaluation tool in child physical abuse. Severely injured pediatric trauma patients exhibit dysregulation of their coagulation pathways leading to either a hypo or hypercoagulable state [7,8]. Researchers have studied the use of conventional coagulation tests [prothrombin time (PT), international normalized ratio (INR), partial thromboplastin time (PTT), fibrinogen, and platelet count] and viscoelastic hemostatic assays in an attempt to define and evaluate TIC in the pediatric population [9]. A 2014 systematic review found a wide range (10–77%) in the reported incidence of TIC in pediatric trauma patients [10]. Leeper et al. used INR levels to better define and establish TIC in pediatric trauma patients. They found that an INR ≥1.3 correlated with an increased mortality rate and was the most sensitive and specific conventional coagulation test in critically ill pediatric trauma patients [11].

Viscoelastic hemostatic assays include thrombelastography, or TEG, and rotational thrombelastometry (ROTEM). These are functional whole blood tests that use whole blood to evaluate aspects of the “life” of a blood clot, including clot formation time, strength, and degradation. Initial studies evaluating viscoelastic parameters found that activated clotting time, k-time, and alpha-angle correlate with aPTT, and that maximum amplitude (MA) correlates with platelet count [7]. TEG parameters have been used to accurately predict the need for blood products in pediatric trauma patients and define coagulation patterns in this cohort [7,8,10,11]. In a 2017 study, Leeper et al. were able to characterize fibrinolysis (LY30) phenotypes in injured children. They found that among their study cohort of pediatric trauma patients, 19% exhibited hyperfibrinolysis on admission TEG and 38% had fibrinolysis shutdown physiology [12].

Children with head trauma secondary to physical abuse have a higher risk for TIC [13], with one group finding 35% of head trauma patients having INR ≥ 1.3 [12]. Elucidating the differences in coagulopathy associated with child physical abuse compared to accidental trauma patients is important because abused children have worse outcomes [3,5]. With that in mind, we sought to determine if viscoelastic abnormalities measured via TEG differ between abuse vs. accidental trauma patients. We hypothesized that abnormalities on admission TEG would differ in abused children, when compared to accidentally injured children.

1. Methods

1.1. Study setting

The local Institutional Review Board approved this study. The study was performed at an American College of Surgeons verified Level I pediatric trauma center. Data was evaluated over a 10-year period (January 2010–December 2020). Abuse was defined by the designation in the trauma registry at our institution, using the methods described by Falcone et al. [14], in which ICD-9 and ICD-10 diagnostic codes were reviewed for abuse, followed by a confirmatory chart review. Patients were stratified into two cohorts: those with abuse versus accidental trauma. All indeterminate cases were a priori classified as accidental trauma patients. Exclusion criteria included a lack of TEG within 2 hours and any patient >10 years old.

1.2. Data collection

A prospectively maintained trauma registry was used to identify all ≤10 years old patients. Next, our bioinformatics team pulled all admission laboratory values on these patients, which allowed us to narrow the list to only those with an admission TEG. The following data points were also extracted: age, weight, gender, mechanism of injury (blunt vs. penetrating), Glasgow Coma Scale (GCS), and Injury Severity Score (ISS). Initial emergency department vital signs and laboratory values, including conventional coagulation tests [defined as Prothrombin time (PT), international normalized ratio (INR), partial thromboplastin time (PTT), platelet count, D-dimer, and fibrinogen] and other laboratory values [lactate and base deficit (BD)] were collected.

The primary outcome was identifying differences in patterns of TEG results and abnormalities between patients with abuse compared to patients with accidental trauma. Secondary outcomes of interest were the total number of ventilator days, intensive care unit (ICU) length of stay (LOS), hospital LOS, and mortality.

1.3. TEG processing

Whole blood specimens are obtained at our trauma center during the primary or secondary survey at the request of the trauma team leader. The clinical laboratory uses a kaolin-based TEG 5000 analyzer (Haemonetics Corp, Braintree, MA). TEG parameters collected for each subject included the R-time, alpha-angle, maximum amplitude (MA), and lysis at 30 min (LY30). The institutional normative value ranges for TEG are an R-time of 4–9 min, alpha-angle of 59–74 degrees, MA of 55–74 mm, and LY30 of 0.9–3%. The definition of all normal and abnormal (decreased or increased) values are shown in Table 1. Standard TEG definitions were used to define physiologic fibrinolysis (LY30 = 0.9–2.9%), fibrinolysis shutdown (LY30 <0.9%), and hyperfibrinolysis (LY30 ≥3.0%) [8]. The significance of each TEG parameter has been described previously [15].

1.4. Statistical analysis

Patients were stratified into two cohorts, those who sustained abuse versus those who sustained accidental trauma. TEG abnormalities were defined based on the institution's normative values and these values were compared between the two groups. Data are reported as frequencies and percentages, means and standard deviations, or medians and first and third quartiles (IQR) depending on their distribution. Univariate testing was performed with Fisher's exact tests, Chi-squared tests, or Student's *t*-tests to assess demographic and clinical characteristic differences.

Two logistic regression models were performed to determine if any significantly abnormal TEG values were predictors of child abuse or mortality. For the logistic regression analyses, all TEG values were dichotomized as *abnormal* (values outside the normative range) or *normal* (within the normative range). Significance was set at $p < 0.05$ for all analyses. R version 3.6.1 software (R Foundation for Statistical Computing, Vienna, Austria, http://www.R-project.org/) was utilized for data cleaning, analysis, and visualization.

Table 1
Normal and abnormal (decreased and increased) TEG values.

	Normal range	Decreased values	Increased values
R-time	4–9 min	< 4 min	> 9 min
Angle, degrees	59–74°	< 59°	> 74°
MA, mm	55–74 mm	< 55 mm	> 74 mm
LY30, % of clot lysis	0.9–2.9%	< 0.9%	> 3%

Table 2
Demographics, injury characteristics, and clinical outcomes stratified by abuse and accidental trauma.

	Child Physical Abuse (n = 21)	No Child Physical Abuse (n = 20)	p-value
Demographics and Injury Characteristics			
Weight (kg)	7.4 (6.6, 10.7)	19.0 (13.3, 30.0)	< 0.001
Age, years	0.5 (0.4, 1.5)	6.0 (2.5, 8.0)	< 0.001
Blunt mechanism	21 (100.0%)	14 (70.0%)	0.009
ISS	17.0895 (9.5, 25.0)	28.5 (17.8, 45.8)	0.004
SIPA elevated	8 (38.1%)	12 (60.0%)	0.217
Initial GCS	12.0 (4.0, 15.0)	10 (3.0, 15.0)	0.763
INR	1.2 (1.0, 1.7)	1.5 (1.4, 1.8)	0.974
Lactate	7.4 (2.3, 9.0)	5.4 (4.3, 8.2)	0.909
Base deficit	−6.0 (−5.0, −13.0)	−10.0 (−7.0, −12.5)	0.884
Platelet count	348.0 (174.0, 482.0)	225.0 (156.0, 339.0)	0.093
Fibrinogen	161.429 (81.228)	156.143 (66.875)	0.875
Clinical outcomes			
Mortality	5 (23.8%)	3 (15.0%)	0.697
Ventilator days	3.0 (1.0, 5.0)	4.5 (3.0, 10.5)	0.074
ICU LOS, days	4.0 (2.0, 7.0)	5.0 (4.0, 13.8)	0.054
Hospital LOS, days	5.0 (3.0, 10.0)	14.5 (4.0, 20.8)	0.018

Data presented as mean (SD) for continuous variables and n (%) for categorical variables. All categorical testing was done using Fisher's Exact test using abuse as the stratifying variable and continuous testing was done using *t*-tests.
Abbreviations: kg, kilograms; ISS, Injury Severity Score; SIPA, Shock Index Pediatric Age-Adjusted; GCS, Glasgow Coma Score; INR, international normalized ratio; ICU, intensive care unit; LOS, length of stay.

2. Results

2.1. Patient admission characteristics

Forty-one children met inclusion criteria, of which 21 were in the abuse cohort. Demographics and injury characteristics are presented in Table 2. Abused patients were less likely to have an INR > 1.3 (33% vs. 77%, $p = 0.001$) compared to those accidentally injured. Abused children showed a hypercoagulable pattern on TEG relative to the accidental trauma population, demonstrated by more frequently having a decreased (<4 min) R-time (67% vs. 30%, $p = 0.040$) and increased (>74°) alpha angles (47% vs. 0%, $p = 0.001$). There were no differences in the rates of increased R-time (> 9 min) between the cohorts (14% vs. 15%, $p = 1.0$). Abused patients less frequently had decreased (< 59°) alpha angles (24% vs. 60%, $p = 0.040$) compared to those accidentally injured.

There was no significant difference in the percentage of patients with either a decreased (<55 mm) or increased (>74 mm) MA values. Furthermore, there was no significant difference in the LY30 (lysis or shutdown) between the groups; however, two-thirds of the abused patients and all the accidental trauma patients presented with a fibrinolysis abnormality (either lysis or shutdown). All patients who died (8/41) presented in fibrinolysis shutdown (LY30 <0.9%) (Table 3).

2.2. Logistic regressions and clinical outcomes

On a multivariable logistic regression model, only an abnormal alpha angle was significantly associated with abuse [odds ratio (OR) 0.17 (confidence intervals (CI) 0.02–0.92), $p = 0.049$] (Table 4). From a separate multivariable logistic regression model, only an abnormal MA was significantly associated with mortality [OR 18.97 (CI 1.93–475.47), $p = 0.025$]. Patients who were abused had a significantly shorter hospital LOS, but no differences were found in ventilator or ICU LOS. Five of the abused patients and three of the accidentally injured patients died.

Table 3
Percentage of patients with abnormal TEG parameters by child abuse status.

	Child physical abuse (n = 21)	No child physical abuse (n = 20)	p-Value*
R-time			
Increased	3 (14%)	3 (15%)	1.0
Decreased	14 (67%)	6 (30%)	**0.04**
Angle, degrees			
Increased	10 (48%)	0 (0%)	**0.001**
Decreased	5 (24%)	12 (60%)	**0.04**
MA, mm			
Increased	2 (10%)	0 (0%)	0.49
Decreased	5 (24%)	8 (40%)	0.44
LY30, % of clot lysis			
Hyperfibrinolysis	4 (21%)[a]	3 (21%)[a]	1.0
Fibrinolysis Shutdown	9 (47%)[a]	11 (79%)[a]	0.14

* t-Test or chi-squared/fishers depending on the distribution.
[a] Nineteen out of the 21 child physical abuse patients had LY30 values. Fourteen out of 20 of the accidental trauma patients had LY30 values.

3. Discussion

In the present investigation, TEG abnormalities differed among pediatric patients who sustained abuse versus those who were accidentally injured. Child physical abuse patients, when compared to accidental trauma patients, were more likely to have a decreased R-time and an increased alpha-angle, suggesting a hypercoagulable pattern in abused trauma patients. Most notably, 48% of child physical abuse patients had an increased alpha angle, where none of the accidental trauma patients had an abnormal alpha angle ($p < 0.001$). On regression analysis, an abnormal alpha-angle was the only TEG parameter able to characterize abuse versus accidental trauma.

On a separate regression analysis, abnormal MA values were able to identify patients at risk for mortality. These findings are consistent with other research demonstrating that MA values are associated with mortality [8] and the likelihood of receiving massive transfusion (unpublished internal data, Phillips et al. 2020). Our findings of a hypercoagulable pattern (decreased R-time and increased alpha angle) in abused trauma patients indicate that abused trauma victims may require different blood product guidelines than other patients. For example, the abuse patients who present with a hypercoagulable pattern where their R-time is decreased may not benefit from coagulation factor repletion with fresh frozen plasma. If, however, an abused patient had a traumatic brain injury (i.e., a subdural hematoma) with an elevated INR, providers would historically treat this type of patient with fresh frozen plasma.

The treatment for a decreased R-time is to either administer anticoagulation therapy (which we would not recommend for a patient with a brain bleed) or monitor with serial TEG's to ensure normalization of their R-time. Data from Leeper et al. have eloquently shown that severe traumatic brain-injured patients who have abnormalities on their TEG and receive a plasma transfusion have significantly worse outcomes, including a 75% mortality rate [16]. They argue that plasma transfusions should not be targeted to INR thresholds, but guided by TEG values and evidence of clinical bleeding [16]. A growing body of research highlights the potential advantage of using viscoelastic tests, such as TEG, to provide a whole blood assessment of a patient's hemo-

Table 4
Logistic regression of abnormal TEG parameters to predict child abuse and mortality.

	Abuse			Mortality		
Predictors	*Odds ratios*	*CI*	*p-Values*	*Odds ratios*	*CI*	*p-Values*
R-time	1.46	0.32–6.53	0.615	0.18	0.02–1.11	0.075
Alpha angle	0.17	0.02–0.92	**0.049**	0.18	0.01–1.96	0.192
MA	1.21	0.20–8.08	0.837	18.97	1.93–475.47	**0.025**

stasis, as opposed to conventional coagulation tests. Furthermore, if a clinician observes a hypercoagulable pattern on viscoelastic testing in a trauma patient, it might prompt them to consider abuse higher in their differential diagnosis.

Our results compare favorably to prior studies investigating the use of various coagulation assays in the diagnosis and evaluation of child physical abuse compared to accidental trauma [9,12,13]. In a two-center retrospective review, Paroskie et al. found that the hematologic evaluation of trauma patients in the setting of suspicion for abuse was inconsistent at best [17]. In their study, the most common hematologic laboratory test performed was a complete blood cell count (62.3% of the time). PT and PTT were ordered 55% and 53% of the time, respectively, and fibrinogen levels were only ordered 28%. Abnormal tests were not routinely reordered and evaluation for the most common bleeding disorder, von Willebrand disease, was rare.

Viscoelastic assays have only recently been used in the evaluation of coagulopathy of child physical abuse. In one of the few studies in the literature Lucisano et al. found that children who sustained abusive head trauma were more likely to have an elevated LY30 on admission – compared to patients with accidental head trauma–and this pattern was associated with abnormal blood clot strength and mortality [13]. Given the prevalence of child physical abuse and the knowledge that these patients are at high risk for TIC whereby they may exhibit a distinct coagulation pattern, viscoelastic assays offer the potential to better characterize trauma induced coagulopathy.

Current American Pediatric Surgical Association (APSA) child physical abuse screening and management guidelines recommend screening of suspected abuse patients with conventional coagulation tests, including CBC, PT, aPTT, and INR. They recommend repeating a CBC with reticulocyte count the following morning if hemoglobin levels are low or falling [18]. Our study reveals that there may be differences in initial TEG parameters in child abuse patients and that the use of viscoelastic assays in screening potential abuse patients may be valuable. Child physical abuse is a significant public health issue that can be challenging to diagnose. The stakes for these patients are too high for clinicians to miss this diagnosis, because victims of child abuse are at higher risk for repeat episodes of abuse [19].

We recognize some important limitations to our study. This is a retrospective study with a small sample size, as the total number of patients evaluated over 10-years was only 41. Future studies with larger sample sizes will be needed to validate our results. Another limitation is that we only examined one TEG value within 2 hours of admission. The only variable of interest that had missing data points was LY30. Therefore, the LY30 values were summarized as descriptive statistics only and were not included in our regression to prevent information from being lost. Since it would be very challenging to do, we were unable to stratify patients based on the chronicity of their abuse. Distinct coagulation patterns demonstrated on TEG may differ based on the frequency (i.e., number of times a child sustains abuse before they present) and the severity of the abuse (i.e., head injury plus multiple fractures versus a less severe injury).

Another limitation is that this was a single-institution study, which is at risk for bias given that TEG values were ordered at the discretion of the treating trauma team and not on all children admitted to our center. Therefore, the generalizability of our results to all trauma patients is still unknown. Our findings that abused children had a lower overall LOS was surprising compared to other studies, that typically find opposite results. A possible explanation for these findings is that in our cohort TEG's were ordered more often for abused children with more moderate injuries than the more severely injured accidental cohort. A multi-center evaluation of child physical abuse patients' viscoelastic parameters would allow for a broader generalization of our initial research.

4. Conclusion

The use of viscoelastic assays in screening child physical abuse patients may lead to a more accurate diagnosis of underlying coagulopathies and better resource utilization of resuscitative blood products. Child physical abuse patients may exhibit different viscoelastic assay parameters than accidental trauma patients, specifically a decreased R-time and increased alpha-angle on TEG. These findings suggest that this specific trauma patient population may not benefit from early plasma transfusion. Furthermore, for all patients (abused and accidental trauma patients), an abnormal MA is a marker of higher risk of mortality. The use of TEG should be considered for inclusion in the APSA guidelines for screening and managing this patient population. Based on these results, future work elucidating changes in TEG values over time is warranted, and essential to fully unlock the potential of viscoelastic tests in diagnosing abuse.

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