Published in final edited form as:

Shock. 2013 May ; 39(5): 421–426. doi:10.1097/SHK.0b013e31828e08cb.

Early coagulopathy is an independent predictor of mortality in children after severe trauma

Brent Whittaker^{1,*}, Sarah C. Christiaans^{2,*}, Jessica L. Altice², Mike K. Chen³, Alfred A. Bartolucci⁴, Charity J. Morgan⁴, Jeffrey D. Kerby³, and Jean-François Pittet^{2,3}

¹Department of Pediatrics, University of Alabama at Birmingham, AL

²Department of Anesthesiology, University of Alabama at Birmingham, AL

³Department of Surgery, University of Alabama at Birmingham, AL

⁴Department of Biostatistics, University of Alabama at Birmingham, AL

Abstract

To determine whether early coagulopathy affects the mortality associated with severe civilian pediatric trauma, trauma patients < 18 years of age admitted to a pediatric intensive care unit from 2001 to 2010 were evaluated. Patients with burns, primary asphyxiation, preexisting bleeding diathesis, lack of coagulation studies or transferred from other hospitals > 24 hours after injury were excluded. Age, gender, race, mechanism of injury, initial systolic blood pressure (SBP), Glasgow Coma Scale (GCS) score, Injury Severity Score (ISS), prothrombin time (PT), partial thromboplastin time (PTT), platelet count and International Normalized Ratio (INR) were recorded. An arterial or venous blood gas was performed, if clinically indicated. Coagulopathy was defined as an INR > 1.2. The primary outcome was in-hospital mortality. Secondary outcomes were lengths of ICU and hospital stay. Eight hundred three patients were included in the study. Overall mortality was 13.4%. The incidence of age-adjusted hypotension was 5.4%. Early coagulopathy was observed in 37.9% of patients. High ISS and/or hypotension were associated with early coagulopathy and higher mortality. Early coagulopathy was associated with a modest increase in mortality in pediatric trauma patients without traumatic brain injury (TBI). In contrast, the combination of TBI and early coagulopathy was associated with a four-fold increase in mortality in this patient population. Early coagulopathy is an independent predictor of mortality in civilian pediatric patients with severe trauma. The increase in mortality was particularly significant in patients with TBI either isolated or combined with other injuries, suggesting that a rapid correction of this coagulopathy could substantially decrease the mortality after TBI in pediatric trauma patients.

Keywords

Pediatric trauma; Coagulopathy; Traumatic brain injury; Tissue hypoperfusion; Mortality

INTRODUCTION

Trauma remains the leading cause of death and disability in adults and children age 1 – 44 years. Worldwide, one in seven deaths is due to injury, and this is expected to rise to one in five in the next 15 years despite continuing advances in resuscitation, trauma surgery, and

Address correspondence to: Jean-François Pittet, Department of Anesthesiology, University of Alabama at Birmingham, 619 South 19th Street, JT926, Birmingham AL 35249 [pittetj@uab.edu], 205-934-996-4755.

*Brent Whittaker and Sarah Christiaans contributed equally to this work.

critical care. Hemorrhage is the major mechanism responsible for death during the first 24 to 48 hours after trauma and efforts to control hemorrhage and restore circulatory homeostasis form the core of the early therapeutic approach to traumatic injuries (1, 2).

Perturbations in blood coagulation are common following major trauma in adults, and are associated with poor outcomes (3–5). Classically, coagulopathy associated with trauma was thought to be due to the consumption of coagulation factors, dilution from fluid therapy, and/or hypothermia. While advances in trauma resuscitation protocols have focused on limiting these exposures, the traditional post-injury resuscitative protocol accelerated coagulopathy due to large volumes of crystalloids (dilution), exposure of the patient (hypothermia), and prolonged surgery (more exposure, hypothermia and continued bleeding), all of which precipitated metabolic failure (acidosis) (1). However, it has recently been recognized that a quarter of the severely traumatized adult patients have coagulopathy on presentation to the emergency department that is physiologically and mechanistically distinct from the classical iatrogenic posttraumatic coagulopathy. Two studies have described this acute traumatic coagulopathy and have shown it to be associated with higher transfusion requirements, a greater incidence of multiple organ dysfunction syndrome (MODS), longer intensive care unit (ICU) and hospital stays and a four-fold increase in mortality in coagulopathic patients compared to those with normal coagulation (3, 6). Furthermore, we have recently shown that early traumatic coagulopathy is characterized by a significant activation of the anticoagulant protein C pathway and a derepression of fibrinolysis after severe trauma in humans (7). The mechanistic role of the protein C pathway in the development of the early coagulopathy after severe trauma was confirmed with our experimental mouse model of trauma- hemorrhage (8).

The effect of early coagulopathy on the outcome of pediatric trauma patients is less clear. A recent retrospective study including pediatric trauma patients from combat hospitals in Iraq and Afghanistan reported that coagulopathy and shock on admission was associated with an increased mortality (9, 10). However, whether early coagulopathy plays an important role in civilian pediatric trauma patients is still unknown. We found in the present retrospective study of 803 severely traumatized children from a level 1 pediatric trauma center that the presence of early coagulopathy (INR > 1.2) was an independent predictor of mortality. Although there was a modest, but significant increase in mortality in pediatric trauma patients without brain injury, a four-fold increase in mortality was seen in patients with traumatic brain injury, either isolated or combined with injuries to other organs.

MATERIAL AND METHODS

Patient selection

After Institutional Review Board approval, we retrospectively identified all pediatric trauma patients < 18 years of age admitted from 2001 to 2010 to the pediatric intensive care unit (PICU) of the Children's Hospital of Alabama, the only level 1 pediatric trauma center in the state of Alabama. Only patients with recorded coagulation studies were included. Burn patients, patients sustaining primary asphyxiation, patients with preexisting bleeding diathesis and patients transferred from other hospitals > 24 hours were excluded from the study.

Data collection

Demographic and clinical information that were collected included age, gender, race, mechanism of injury, transfer times, and systolic blood pressure (SBP) on arrival to the hospital. In addition, Glasgow Coma Scale (GCS) score was recorded on admission, and Injury Severity Score (ISS) and Abbreviated Injury Scale (AIS) for each body region (head/

neck, chest, abdomen, extremities, external and face) were calculated for each patient. Laboratory data collected on admission included prothrombin time (PT), partial thromboplastin time (PTT), platelet count and International Normalized Ratio (INR) values. Arterial blood gas (ABG) or venous blood gas (VBG) analyses were only performed when possible.

Outcome measures

Coagulopathy was defined retrospectively as an elevated INR > 1.2 in accordance with previously published adult studies (4, 11). The primary outcome was in-hospital mortality. Secondary outcomes were lengths of ICU and hospital stay (LOS).

The pediatric population was divided into two groups based on ISS values with a cutoff of 25 and then assessed for mortality and incidence of coagulopathy. Systolic blood pressure (SBP) measured on arrival to the hospital was stratified in age-specific reference points according to the 2010 Pediatric Advanced Life Support guidelines: neonates < 60 mm Hg, infants < 70 mmHg, children 1 to 10 years < 70 mm Hg + (age in years $\times 2$) mm Hg and children > 10 years < 90 mmHg. When possible an ABG or VBG was obtained immediately after hospital admission. The base deficit (BD) was used as a marker for tissue hypoperfusion. In adult trauma patients, an admission BD > 6 mmol/l has previously been identified as predictive of worse outcome in these patients (12–14).

The cohort was also assessed according to age and divided into four groups: infants and toddlers (2 years or younger), preschool age (3–7 years), school age (8–12 years) and adolescents (13–17 years). The mechanisms of injury within our trauma cohort were reviewed and stratified into four main categories: motor vehicle crash (MVC), fall, gunshot wound (GSW) and non-accidental trauma (NAT).

A subanalysis on mortality and coagulopathy was performed on patients with and without severe traumatic brain injury (TBI). Severe TBI was subdivided into isolated TBI (AIS head ≥ 3 and AIS extra cranial < 3) and non-isolated TBI (AIS head ≥ 3 and AIS extra cranial ≥ 3).

Statistical Analysis

Data analysis was performed using SAS software (SAS®; Cary North Carolina). Parametric data are presented as means $\pm$ SD. Nonparametric data are presented as median (interquartile range [IQR] and mean). Student's *t* test was used to compare two samples of parametric continuous data and Mann-Whitney *U* test for non parametric continuous data. For three groups comparison of continuous data, the Kruskal–Wallis one-way analysis of variance (if non parametric data) or ANOVA (for parametric data) was used. Fisher's protected least significant differences method was used to control for multiple comparisons. That is, only in cases of significance ($p < 0.05$), the Mann-Whitney *U* test (for non parametric data) or the Student *t*-test (for parametric data) was used to analyze specific sample pairs for significant differences. Categorical data were compared using χ^2 test or Fisher's exact test as appropriate. Multivariate logistic regression was used to determine which variables were independently associated with mortality and coagulopathy by initially including all variables with a $p < 0.1$. The Hosmer-Lemeshow goodness-of-fit test for the logistic regression model showed a $p > 0.2$ for both analyses, indicating that the fit was adequate. Receiver operating characteristic curves were calculated for mortality and coagulopathy. All tests are 2-sided, and the significance for all comparisons was set at $p = 0.05$.

RESULTS

Patient selection and demographics

During the study period (2001–2010) 1062 patients were admitted to the Children's Hospital of Alabama PICU after severe trauma. The majority of patients excluded did not have coagulation tests performed upon arrival to the hospital (n=221). In addition, patients were excluded for the following reasons: late transfer (n=2), age limit (n=2), death on arrival (n=10) and burns or asphyxiation (n=17). Table 1 shows the characteristics of the patients enrolled in the study. In all, 803 severely injured trauma patients were included in the study over a 10-year period. Sixty-two percent of patients were male and blunt trauma was the cause of injury in 92% of patients. Overall mortality was 13.4%. The incidence of age-adjusted hypotension was 5.4%. Finally, 37.9% of the patients presented with coagulopathy (defined as an INR > 1.2) measured on arrival to the hospital. In this patient group, there was a direct relationship between mortality rate and the initial INR value on arrival to the hospital (Figure 1).

Effect of injury severity and shock on early post-traumatic coagulopathy and mortality

High ISS or presence of hypotension on arrival to the hospital were associated with an increased incidence of early coagulopathy and higher mortality rate in pediatric trauma patients (Figure 2 **panels A–D**). Moreover, the combination of high ISS and hypotension was associated with the highest rate of coagulopathy and mortality in this patient population (Figure 2 **panels E&F**). These results were confirmed by measurement of the initial BD that indicated that a BD > 6, a marker of tissue hypoperfusion, is associated with an increased incidence of early posttraumatic coagulopathy and higher mortality rate in pediatric trauma patients (Figure 3).

Effect of age and mechanism of injury on the incidence of early coagulopathy and mortality

Mortality rate was higher in the patients who were less than 3 years old compared with the entire patient population (Figure 4A). Falls were associated with a lower incidence of early coagulopathy and lower mortality rate (Figure 4B). In contrast, patients who sustained a non-accidental trauma (NAT) were significantly more coagulopathic on arrival to the hospital and had a higher mortality rate (Figure 4B).

The combination of traumatic brain injury and early coagulopathy is associated with a statistically significant increase in mortality in pediatric trauma patients

Overall mortality was significantly higher in patients with TBI (either isolated or combined with other injuries) than in patients without TBI (Table 2). Furthermore, patients with combined injuries had a higher incidence of tissue hypoperfusion, as shown by an initial BD > 6, and of early post-traumatic coagulopathy than the two other groups of patients (Table 2). The presence of early coagulopathy was associated with a small increase in mortality in patients without TBI. However, in presence of TBI, there was a more than four-fold increase in mortality in patients with early coagulopathy who had an initial INR of more than 1.2 (Figure 5). Finally, the data summarized in Table 3 indicate that TBI patients with an INR between 1.2 and 1.4 at the admission to the hospital have a statistically significant increase in mortality, although their INR value was below the usual threshold for diagnosis of coagulopathy (> 1.5).

Outcome

Age < 3 and presence of early coagulopathy were associated with an increased odds ratio for mortality. Furthermore, higher ISS and lower GCS were also independent predictors for

mortality in this pediatric patient population (Table 4). In addition, higher ISS and the presence of arterial hypotension were both independent predictors of the development of early coagulopathy after severe trauma in pediatric patients (Table 4). ROC curve analysis showed an AUC of 0.94 for mortality and of 0.80 for coagulopathy (Figure 6). Finally, the presence of early coagulopathy was associated with a significantly longer ICU LOS (INR > 1.2: median ICU LOS 4 days, range 0–28 days vs INR ≤ 1.2: median ICU LOS 2 days, range 0–42 days, $p < 0.0001$) and hospital LOS (INR > 1.2: median hospital LOS 13 days, range 1–276 days vs INR ≤ 1.2: median ICU LOS 5 days, range 1–132 days, $p < 0.0001$) in survivors from severe trauma in pediatric patients.

DISCUSSION

The results of the present study indicate that early coagulopathy is an independent predictor of mortality in civilian pediatric trauma patients. Comparable findings have previously been reported in children admitted to combat support hospitals in Iraq and Afghanistan (9, 10). While major differences exist between the injured children in war zones and our civilian pediatric trauma patients with regard to mechanism of injury (penetrating vs. blunt) and definition of coagulopathy (INR 1.5 vs. 1.2) early coagulopathy was an independent predictor of mortality in both groups of pediatric patients. This important finding was confirmed by the results of a recently published smaller study that included transfused civilian pediatric trauma patients (15). In the present study, early posttraumatic coagulopathy was defined as an INR > 1.2. This is based on recent work showing that a PT ratio of > 1.2 is associated with an increased mortality in adult trauma patients (4). Previous trauma studies have defined posttraumatic coagulopathy as an INR > 1.5 that was originally adopted from international guidelines for initiating administration of fresh frozen plasma. This threshold was derived from correlations between clotting times and the incidence of microvascular bleeding in patients undergoing massive blood transfusions (16–18).

The second important finding of this study is that the combination of injury severity and tissue hypoperfusion (hypotension and/or increased BD on arrival to the hospital) were associated with a higher incidence of coagulopathy and mortality. A similar association between hypovolemic shock, severity of injury and development of coagulopathy has previously been reported in children suffering from penetrating trauma from middle East war zones (9, 10). Furthermore, we have previously reported comparable results in adult trauma patients and have shown that the severity of shock and traumatic injury directly correlated with the activation of the anticoagulant protein C pathway that may play an important role in the early posttraumatic coagulopathy (7, 19). In contrast to the results reported for children injured in the war zones (9), age and mechanism of injury did not significantly affect the incidence of early coagulopathy and mortality in our civilian pediatric trauma population with the exception of children less than 3 years of age who had an increased mortality rate compared with the entire pediatric trauma population. The likely explanation for the increased mortality in this very young age group is that the mechanism of trauma was mostly related to non-accidental trauma that has a higher mortality rate than accidental trauma (20).

Finally, in pediatric patients with isolated TBI or TBI combined with other injuries an INR > 1.2 was associated with a significant increase in mortality compared with patients without coagulopathy. Although 30% of patients without TBI were coagulopathic on admission to the hospital, the overall mortality was very low (2.2%) and none of the patients without coagulopathy died. In contrast, Patients with isolated TBI or TBI combined with other organ injuries had a sharp increase in the mortality when the initial INR was more than 1.2. Previously published studies have reported variable results about the value of coagulopathy as an independent predictor of mortality. A recently published European study reported that

early coagulopathy that was defined as a PT of twice the normal value was predictive of mortality in pediatric trauma patients with combined injuries that include TBI (21). Interestingly, coagulopathy was also present in patients who did not suffer from heavy bleeding because of their injuries. Comparable results were reported in a small study including pediatric patients with isolated TBI (22). Using the database of the German Trauma registry, another study reported that GCS is a predictor of coagulopathy after blunt pediatric TBI (23). In contrast, a study from University of Southern California (USC) that included children with isolated TBI, did not show that coagulopathy (defined as an INR > 1.2) was an independent predictor of mortality, although a large percentage of patients were coagulopathic (40%) (24). The difference between that study and those previously cited (including our study) could be related to the fact that the reported overall mortality was lower in the USC study. In addition, there are other factors that are also independent predictors of mortality in children with severe TBI, such as young age (< 3 years old), accidental hypothermia, and hyperglycemia (22) that may not have been present with the same prevalence in all cited studies. The results of the present study clearly demonstrate that a small increase in the initial INR value is associated with a large increase in mortality in children with TBI, but not in patients without TBI. However, despite the large number of patients included in our study, there are several limitations, the most important being the retrospective nature of data analysis. Second, the effect of therapeutic interventions on outcomes, such as transfusion of blood products could not be determined. Finally, data regarding long-term outcome were not available for analysis including the exact cause of death in each of the patients. Well-performed prospective clinical trials should be conducted to determine the potential beneficial effect of early treatment of acute TBI-associated coagulation abnormalities in children with severe trauma.

In summary, the results of the present retrospective study that includes 803 patients admitted over a 10 year period at the level 1 trauma center demonstrates that early coagulopathy defined as an INR > 1.2 is an independent predictor of mortality in pediatric patients with severe trauma. The increase in mortality was particularly significant in patients with TBI either isolated or combined with other injuries, suggesting that a rapid correction of this coagulopathy could substantially decrease the mortality after TBI in pediatric trauma patients.

Acknowledgments

Funding support: NIH RO1 GM086416 (JFP)

References

1. Gruen RL, Brohi K, Schreiber M, Balogh ZJ, Pitt V, Narayan M, Maier RV. Haemorrhage control in severely injured patients. *Lancet*. 2012; 380(9847):1099–108. [PubMed: 22998719]
2. Maegele M, Spinella PC, Schochl H. The Acute Coagulopathy of Trauma: Mechanisms and Tools for Risk Stratification. *Shock*. 2012; 38(5):450–458. [PubMed: 23042192]
3. Brohi K, Singh J, Heron M, Coats T. Acute traumatic coagulopathy. *J Trauma*. 2003; 54(6):1127–30. [PubMed: 12813333]
4. Frith D, Goslings JC, Gaarder C, Maegele M, Cohen MJ, Allard S, Johansson PI, Stanworth S, Thiemermann C, Brohi K. Definition and drivers of acute traumatic coagulopathy: clinical and experimental investigations. *J Thromb Haemost*. 2010; 8(9):1919–25. [PubMed: 20553376]
5. Mitra B, Cameron PA, Mori A, Fitzgerald M. Acute coagulopathy and early deaths post major trauma. *Injury*. 2012; 43(1):22–5. [PubMed: 21145056]
6. MacLeod JB, Lynn M, McKenney MG, Cohn SM, Murtha M. Early coagulopathy predicts mortality in trauma. *J Trauma*. 2003; 55(1):39–44. [PubMed: 12855879]

7. Cohen MJ, Call M, Nelson M, Calfee CS, Esmon CT, Brohi K, Pittet JF. Critical role of activated protein C in early coagulopathy and later organ failure, infection and death in trauma patients. *Ann Surg.* 2012; 255(2):379–85. [PubMed: 22133894]
8. Chesebro BB, Rahn P, Carles M, Esmon CT, Xu J, Brohi K, Frith D, Pittet JF, Cohen MJ. Increase in activated protein C mediates acute traumatic coagulopathy in mice. *Shock.* 2009; 32(6):659–65. [PubMed: 19333141]
9. Matos RI, Holcomb JB, Callahan C, Spinella PC. Increased mortality rates of young children with traumatic injuries at a US army combat support hospital in Baghdad, Iraq, 2004. *Pediatrics.* 2008; 122(5):e959–66. [PubMed: 18977963]
10. Patregnani JT, Borgman MA, Maegele M, Wade CE, Blackburne LH, Spinella PC. Coagulopathy and shock on admission is associated with mortality for children with traumatic injuries at combat support hospitals. *Pediatr Crit Care Med.* 2012; 13(3):273–7. [PubMed: 21926654]
11. Davenport R, Manson J, De'Ath H, Platten S, Coates A, Allard S, Hart D, Pearce R, Pasi KJ, MacCallum P, Stanworth S, Brohi K. Functional definition and characterization of acute traumatic coagulopathy. *Crit Care Med.* 2011; 39(12):2652–8. [PubMed: 21765358]
12. Rutherford EJ, Morris JA Jr, Reed GW, Hall KS. Base deficit stratifies mortality and determines therapy. *J Trauma.* 1992; 33(3):417–23. [PubMed: 1404512]
13. Davis JW, Parks SN, Kaups KL, Gladen HE, O'Donnell-Nicol S. Admission base deficit predicts transfusion requirements and risk of complications. *J Trauma.* 1996; 41(5):769–74. [PubMed: 8913202]
14. Eberhard LW, Morabito DJ, Matthay MA, Mackersie RC, Campbell AR, Marks JD, Alonso JA, Pittet JF. Initial severity of metabolic acidosis predicts the development of acute lung injury in severely traumatized patients. *Crit Care Med.* 2000; 28(1):125–31. [PubMed: 10667511]
15. Hendrickson JE, Shaz BH, Pereira G, Atkins E, Johnson KK, Bao G, Easley KA, Josephson CD. Coagulopathy is prevalent and associated with adverse outcomes in transfused pediatric trauma patients. *J Pediatr.* 2012; 160(2):204–209. e3. [PubMed: 21925679]
16. Counts RB, Haisch C, Simon TL, Maxwell NG, Heimbach DM, Carrico CJ. Hemostasis in massively transfused trauma patients. *Ann Surg.* 1979; 190(1):91–9. [PubMed: 464685]
17. Ciavarella D, Reed RL, Counts RB, Baron L, Pavlin E, Heimbach DM, Carrico CJ. Clotting factor levels and the risk of diffuse microvascular bleeding in the massively transfused patient. *Br J Haematol.* 1987; 67(3):365–8. [PubMed: 3689699]
18. Murray DJ, Pennell BJ, Weinstein SL, Olson JD. Packed red cells in acute blood loss: dilutional coagulopathy as a cause of surgical bleeding. *Anesth Analg.* 1995; 80(2):336–42. [PubMed: 7818122]
19. Brohi K, Cohen MJ, Ganter MT, Matthay MA, Mackersie RC, Pittet JF. Acute traumatic coagulopathy: initiated by hypoperfusion: modulated through the protein C pathway? *Ann Surg.* 2007; 245(5):812–8. [PubMed: 17457176]
20. Stewart TC, Polgar D, Gilliland J, Tanner DA, Girotti MJ, Parry N, Fraser DD. Shaken baby syndrome and a triple-dose strategy for its prevention. *J Trauma.* 2011; 71(6):1801–7. [PubMed: 22182892]
21. Tude Melo JR, Di Rocco F, Blanot S, Oliveira-Filho J, Roujeau T, Sainte-Rose C, Duracher C, Vecchione A, Meyer P, Zerah M. Mortality in children with severe head trauma: predictive factors and proposal for a new predictive scale. *Neurosurgery.* 2010; 67(6):1542–7. [PubMed: 21107185]
22. Vavilala MS, Dunbar PJ, Rivara FP, Lam AM. Coagulopathy predicts poor outcome following head injury in children less than 16 years of age. *J Neurosurg Anesthesiol.* 2001; 13(1):13–8. [PubMed: 11145472]
23. Peiniger S, Nienaber U, Lefering R, Braun M, Wafaisade A, Borgman MA, Spinella PC, Maegele M. Glasgow Coma Scale as a predictor for hemocoagulative disorders after blunt pediatric traumatic brain injury. *Pediatr Crit Care Med.* 2012; 13(4):455–60. [PubMed: 22422166]
24. Talving P, Lustenberger T, Lam L, Inaba K, Mohseni S, Plurad D, Green DJ, Demetriades D. Coagulopathy after isolated severe traumatic brain injury in children. *J Trauma.* 2011; 71(5):1205–10. [PubMed: 21427617]

Figure 1. High initial INR values are associated with increased mortality rate in pediatric trauma patients

Initial INR values were directly correlated with mortality rate in pediatric trauma patients; $p < 0.05$ from patients with normal INR values (0.9–1.2) at the admission to the hospital.

Figure 2. A combination of tissue injury and systemic arterial hypotension is associated with an increased incidence of early coagulopathy and higher mortality rate in pediatric trauma patients
Panels A–D. Patients were divided into groups using previously described definitions of injury severity based on Injury Severity Score and arterial hypotension corrected for age. High ISS or presence of systemic arterial hypotension at the admission to the hospital was associated with an increased incidence of early coagulopathy and higher mortality rate in pediatric trauma patients. **Panels E&F.** The combination of high ISS and arterial hypotension was associated with the highest rate of coagulopathy and mortality in this patient population. Panels A–D: * $p < 0.05$ from patients with low ISS or without arterial hypotension at the admission at the hospital. Panels E&F: * $p < 0.05$ from patients without arterial hypotension at the admission at the hospital.

Figure 3. High base deficit (> -6), a marker of tissue hypoperfusion, is associated with an increased incidence of early posttraumatic coagulopathy and higher mortality rate in pediatric trauma patients

Panels A&B. Patients were divided into two groups based on the initial base deficit (> -6) measured from the arterial or venous blood gas samples taken after admission to the hospital. Panels A&B: * $p < 0.05$ from patients with low base deficit (< -6).

Figure 4. Effect of age and mechanism of injury on the incidence of early coagulopathy and mortality in pediatric trauma patients

Panel A. Patients were divided in 4 groups based on the age range. The patients who are less than 2 year old had a significantly higher mortality than the other age groups. **Panel B.**

Patients were divided into 4 groups based on the mechanisms of injury. Patients with fall at a lower incidence of post-traumatic coagulopathy and mortality than the rest of the patient population. In contrast, patients with non-accidental trauma (NAT) had a significantly higher incidence of post-traumatic coagulopathy and mortality than the rest of the patient population; * $p < 0.05$ for comparison of mortality rate between falls and the other causes of injury; # $p < 0.05$ for comparison of the incidence of coagulopathy between falls and the other causes of injury; ** $p < 0.05$ for comparison of mortality rate between NAT and the other causes of injury; ## $p < 0.05$ for comparison of the incidence of coagulopathy between NAT and the other causes of injury.

Figure 5. The combination of traumatic brain injury and early coagulopathy is associated with a large increase in mortality in pediatric trauma patients

Patients were divided in three groups: Severe TBI was subdivided into isolated TBI (AIS head of 3 and AIS extra cranial < 3) and non-isolated TBI (AIS head 3 and AIS extra cranial > 2). The absence of traumatic brain injury was defined as AIS head 2. The association of an early post-traumatic coagulopathy and TBI increased the mortality by 3–4 fold compared with the patients without TBI; * $p < 0.05$ from patients without coagulopathy; # $p < 0.05$ from patients with coagulopathy but without TBI; ** $p < 0.05$ from patients without coagulopathy and without TBI.

Figure 6. Receiver operator characteristic curves for predictive models of mortality or coagulopathy in pediatric trauma patients

Panels A&B. The model includes all four clinical predictors for mortality and two clinical predictors for coagulopathy. AUC = area under the curve.

TABLE 1

Patient demographics

Variables	N=803
Age (yr), mean $\pm$ SD	8.7 $\pm$ 5.0
Gender male	62%
Race	
% Black	33.7%
% White	60.6%
% Hispanic	4.9%
% Other	0.7%
Mechanism blunt	92%
Mortality	13.4%
ISS median	22 (0–75)
% Arterial hypotension ^a	5.4 %
PT median/IQR	15.7 (14.6–17.5)
aPTT median/IQR	29.7 (26.7–34.0)
INR median/IQR	1.2 (1.1–1.4)
Coagulopathy	37.9%
Platelets	319 $\pm$ 114

ISS: Injury Severity Score (ISS); PT: Prothrombin Time;

aPTT: Activated Partial Thromboplastin Time

^aCorrected for age

Demographics, incidence of shock and coagulopathy including abnormal coagulation parameters according to different injury groups

Table 2

Characteristics	No TBI (n=267)	Isolated TBI (n=296)	Non-Isolated TBI (n=240)	P value
Age (yr), mean, $\pm$ SD	8.9 $\pm$ 4.9	8.6 $\pm$ 5.1	8.6 $\pm$ 4.9	NS
Gender male	62%	62%	62%	NS
Mechanism blunt	87.3%	91%	95%	<0.05 ^c
Mortality	2%	14%	25%	<0.05 ^{a c}
% Arterial Hypotension	4.9 %	3.4 %	8.3%	NS
% Base deficit $\geq$ -6	14.6%	17.6%	33.3%	<0.05 ^{a c}
% aPTT $\geq$ 36 s	14.2%	16%	30%	<0.05 ^{a c}
% INR $\geq$ 1.2	29.6%	27%	60%	<0.05 ^{ab c}
% platelets $<$ 150	2.6%	4%	7%	NS

TBI: Traumatic Brain Injury; aPTT: Activated Partial Thromboplastin Time; INR: International Normalized Ratio

^aNo TBI vs All Patients Statistically Significant

^bIsolated TBI vs All Patients Statistically Significant

^cNon-Isolated TBI vs all patients statistically significant

Table 3

Mortality is related to INR and presence of traumatic brain injury

INR	Non-TBI (n=267)	Isolated TBI (n=296)	Non-Isolated TBI (n=240)
<1.3	0% (0/188)	2.3% (5/215)	8.3% (8/96) *
1.3-1.4	2.5% (1/40)	20.9% (9/43) *	16.7% (11/66) *
1.5-1.6	4.8% (1/21)	27.3% (3/11)	20% (6/30)
1.7-1.8	33.3% (3/9)	100% (4/4)	56.3% (9/16)
>1.8	11.1% (1/9)	87% (20/23) *	84.4% (27/32) *

INR: International Normalized Ratio; TBI: Traumatic Brain Injury

* *p* value <0.05 compared to Non-TBI Group.

Table 4

Multivariate comparison for all pediatric trauma patients

Mortality:	Odds Ratio	p value
• Age <3	4.2	<.0001
• Coagulopathy	4.0	0.0008
• ISS	1.1	<.0001
• GCS	0.7	<.0001
Coagulopathy:		
• ISS	1.1	<.0001
• Arterial Hypotension	3.3	0.0057

ISS: Injury Severity Score; GCS: Glasgow Coma Scale