**A Multi-Center Study on Early Trauma-Induced Coagulopathy: Defining Clinical and Biochemical Profiles**

**Summary**

Early trauma-induced coagulopathy (eTIC) has been shown to correlate with mortality in trauma patients. This study aims to better define the clinical profile of eTIC using a large dataset that includes prehospital and in-hospital data and to define the causes of mortality in affected patients. This is a prospective multicenter observational study that will require the collection of pre-hospital data (volume of crystalloid administered, units of whole blood, PRBC, and FFP administered, and tranexamic acid administration), routine admission labs, and cause of death. All other data will be collected from your trauma registry. The pre-hospital and trauma registry data will be compiled in a new dataset using the data collection tool provided by the study organizers. The information will then be uploaded to a REDCap database for analysis. All participating centers will need to obtain their own IRB (University of Maryland IRB and approval are attached) and complete a Data Use Agreement form prior to data collection.

**To participate**, we ask that you are willing to provide data for all admitted patients for at least one year, the requested prehospital fields are available, your admission labs include a PT and PTT, and you are willing to review all deaths for cause. Lastly please submit the attached DUA form.

**Background and Significance**

Uncontrolled hemorrhage remains a significant cause of potentially preventable deaths in individuals suffering from traumatic injuries in both civilian and military settings.1,2 The importance of hemorrhage and associated coagulopathy was highlighted by Kashuk et al3 in 1982 when they reported that over 50% of patients with major vascular injury who died of hemorrhage did so after hemorrhage control. These patients remained coagulopathic despite “adequate” resuscitation. Landmark studies in 2003 by MacLeod et al4 and Brohi et al5 showed that trauma-induced coagulopathy (defined as elevated prothrombin time or activated thromboplastin time) was present early after injury in up to 30% of trauma patients. In both studies, early trauma-induced coagulopathy (eTIC) was found to be an independent predictor of mortality. Over the last 20 years, there have been significant advances in the fundamental understanding of eTIC which has led to the institution of therapeutic interventions to reverse eTIC immediately upon arrival to trauma centers and, more recently, in the prehospital setting. Modern day prehosptial interventions include minimizing crystalloids, prevention of hypothermia, and the use of prehospital blood products and tranexamic acid.

We recently reported an update on the incidence of eTIC twenty years after its initial description.6 Our large retrospective study demonstrated that despite these advances in trauma care, the incidence of eTIC has not improved and remains an important risk factor for mortality even when adjusted for potentially confounding risk factors, especially in patients with low injury severity scores (ISS). While our cohort had a measurable reduction in mortality compared to the cohorts studied 20 years earlier, the degree of reduction was low and the prevalence of eTIC remained approximately 30% of patients. Importantly, our study was limited by the lack of data on prehospital interventions. Moreover, most of the patients in our cohort were not in hemorrhagic shock, suggesting that shock is not a prerequisite for trauma-induced coagulopathy.

This raises the important question of why coagulopathy may be associated with mortality in trauma patients who are not in hemorrhagic shock. Typically, PT, PTT, and other laboratory definitions of coagulopathy correlate poorly with clinical signs of coagulopathy and the need for transfusion.7 This is especially true in patients with low ISS and those without active hemorrhage. Yet, eTIC, as defined by abnormal PT and PTT, remains significantly associated with mortality in our recent study. It is possible that eTIC represents a biomarker for mortality by a yet-to-be-defined mechanism rather than a threshold for treatment.

Therefore, we are proposing a multicenter prospective observational study to address the limitations of our retrospective study. The objective of this prospective study is to better define the clinical profile of eTIC using large datasets to include prehospital and in-hospital data and to define the causes of mortality.

**Research Design and Methods**

Study Design

This study will employ a prospective, observational cohort design. It involves no therapeutic interventions.

Inclusion criteria: Sustain a traumatic injury, age between 18-89 years of age, hospital length of stay ≥ 24 hours or death at any time after hospital arrival.

Exclusion criteria: isolated hanging or drowning, age < 18 or > 89 years of age, hospital length of stay < 24 hours

Participating Centers

* Core Centers (University of Maryland and University of Pittsburgh)
* All participating centers are asked to obtain their own IRB. The University of Maryland IRB and approval are available to review.

Data Collection

* Prehospital Data: scene vital signs, prehospital cardiac arrest, prehospital intubation, transport mode, volume of crystalloid administered, units of whole blood, PRBC, and FFP administered, tranexamic acid administration
* In-hospital Clinical Data: age, sex, ethnicity, use of outpatient anticoagulation, injury characteristics (AIS, ISS, level of trauma activation, mechanism of injury), arrival vital signs, time from incident to hospital arrival, volume of whole blood, PRBC, FFP, cryoprecipitate, and platelets administered within first 24 hours, surgery for hemorrhage control, total ICU days, total vent days, hospital discharge disposition, length of stay, complications (TBI, DVT, PE, acute kidney injury, ARDS, and VAP as defined by the National Trauma Data Bank), and cause of death
* Laboratory values if collected for clinical care:
  + Hemoglobin count
  + Platelet count
  + Prothrombin time (PT)
  + Activated partial thromboplastin time (aPTT)
  + INR
  + Fibrinogen
  + Thromboelastography (TEG) parameters

Statistical Analysis

* Descriptive Statistics: To summarize patient demographics, injury characteristics, and clinical outcomes.
* Inferential Statistics: To compare coagulation profiles between patients with and without eTIC according to injury severity
* Case Matching: Various matching methods (e.g. propensity score, full exact, mahalanobis matching) to create comparable groups for robust analysis.
* Machine Learning Techniques: Supervised learning algorithms to develop predictive models for eTIC.

**Risks and Safety**

This study requires no therapeutic interventions and poses no more than minimal risk of breach of confidentiality and privacy of the patient. All study records will be kept in a secure area and confidentially maintained. Each patient will be assigned a unique identifier by each site. Pooled data will be compiled on a HIPAA-secure REDCap database maintained by the research teams at the University of Maryland. Only deidentified will be entered into REDCap, and the master list of participants will be password-protected on a secure server. Only members of the research team will have access to the data.

**For any questions and interested centers please contact us:**

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**References**

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