Clinical Implications of the Impact of Serum Tissue Factor Levels after Trauma

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In the setting of trauma, patients are at significant risk for thromboembolic complications. Platelets release granules containing tissue factor, a pro-coagulant protein that binds to factor VII to initiate the extrinsic pathway of the coagulation cascade. Additionally, traumatic injury activates monocytes which in turn up-regulate expression of membrane-bound tissue factor within hours of the initial insult.[1-2] Without effective prophylaxis, the risk of developing deep vein thrombosis after trauma may be greater than 50%, and the risk of fatal posttraumatic pulmonary embolism may range from 5% to 50%.[3-5]

The presence of traumatic brain injury ~~in this setting~~ however, may alter the physiology of coagulation. Specifically, traumatic brain injury attenuates the expression of tissue factor by circulating activated monocytes. The consequences of this attenuation are not fully understood. Additionally, injury of brain tissue is associated with increased anti-thrombin activity,[6] decreased platelet function,[7] and possible consumptive coagulopathy.[8]

~~While previous studies have examined the relationship between tissue factor levels and thromboembolic complications,~~ The clinical implications of elevated levels of serum tissue factor in acute trauma are incompletely understood. Furthermore, the consequences of attenuation of these levels~~correlation~~ in the setting of traumatic brain injury have~~s~~ not been successfully demonstrated due to lack of specificity or insufficient power .[1-2] Our study would measure serum tissue factor levels in patients with isolated traumatic brain injury, in patients with concomitant traumatic brain injury and other injuries, and in trauma patients without traumatic brain injury. By correlating these levels with incidence of venous thromboembolic events, this study will provide further insight into the need for thromboprophylaxis in patients with traumatic brain injury.

Specific Aims

~~This study will determine if traumatic brain injury in the setting of severe trauma alters the relationship between serum tissue factor levels.~~

This study will define the relationship between serum tissue factor levels and thromboembolic events in the setting of severe trauma.

This study will further determine the implications o~~i~~f traumatic brain injury with respect to ~~in the setting of severe trauma alters~~ the relationship between serum tissue factor levels and thromboembolic events.

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Inclusion criteria

We will evaluate for inclusion all trauma patients aged 18-65 requiring critical care admission.

Exclusion Criteria

Criteria for exclusion will include pregnancy, state custody of the patient, age less than 18 years or over 65 years, lack of an initial blood draw, and death within 24 hours of arrival.

Therapeutic Interventions

The study will be a prospective observational study and will not involve specific therapeutic interventions. Patients will be managed according to the discretion of the responsible surgeon.

Primary Outcome

The primary outcome will be 30-day mortality.~~tissue factor expression.~~

Secondary outcomes

Secondary outcomes will include incidence of venous thromboembolic events including~~such as~~ pulmonary embolism and~~,~~ deep venous thrombosis~~., or cerebrovascular accident, and incidence of sepsis.~~.

Variables~~:~~

Measured variables will include demographic data (age, sex), injury data (Injury Severity Scoring~~Abbreviated Injury Score, presence of head injury, nature of head injury~~, mechanism of injury), admission physiology (initial GCS,~~ base deficit,~~ transfusion requirements for packed red blood cells, platelets, or fresh frozen plasma over the initial 72 hours), and management variables (pre-trauma anti-coagulation or anti-platelet medications, medications given to correct coagulopathy, anti-coagulation medications, mechanical DVT prophylaxis, length of stay, ICU length of stay, and performance of an operation within 72 hours of admission).

Data Collection and Statistical Analysis

Patients will be assessed for inclusion in the study on arrival. Consent will be obtained as described below.

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Blood draws will be performed at the time of admission, and subsequently at 24, 72, 120, and 168 hours. Briefly, blood will be drawn into a green top vacutainer tube with heparin. Samples will be de-identified and given an assigned code. Samples will have serum separated by microcentrifuge and the serum will then transfer to 12.5x40 mm cryovial, frozen, and shipped on dry ice for subsequent evaluation of tissue factor level by ELISA.

Data regarding the previously described variables and outcomes will be abstracted from the chart of the patient, de-identified, and coded to correspond with the blood samples. Secondary outcomes will be assessed based on clinical suspicion.

We will employ Fisher's exact test for nominal variables and Student's t test for continuous variables in statistical analysis of patient characteristics. We will perform repeated-measures analysis of variance in comparisons of serum tissue factor levels among the four time points.

Consent Procedures~~:~~

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This is a prospective observational study, designed to prospectively record data on patients who are managed according to institutional patient management protocols. This study will require collection of blood for analysis ~~by flow cytometry~~. Consent will be obtained either at the time of admission or retrospectively from the patient or a consenting family member or designated power of attorney. Data will be recorded on a data sheet and transferred to a secured database that is devoid of patient identifiers.

Risk/benefit analysis~~:~~

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A better understanding of the factors contributing to post-injury thrombotic events ~~-~~may lead to improved prevention of thromboembolic complications, improving outcomes in the entire patient population. The study is primarily observational and management is at the discretion of the treating physicians. Patient identity will be protected through de-identification of data. Risks are minimal and primarily due to the five necessary blood draws. The potential benefit of new knowledge justifies the risks inherent to this study.

Comment [JMG1]: Need to add risk benefit language

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Patient identity code _____

Clinical Implications of the Impact of Traumatic Brain Injury on Serum Tissue Factor Levels after Trauma

Data Collection Tool

Demographic Information

Age _____

Sex _____

Injury

Mechanism (blunt versus penetrating)
_____

Injury Severity Score [ISS] _____
AIS Head/Neck _____
AIS Face _____
AIS Thorax _____
AIS Abdomen _____
AIS Extremity _____
AIS External _____

Initial Glasgow Coma Scale score
Total Motor Eye Verbal .

Is the patient known to have been using anti-coagulant or anti-platelet medications prior to admission? _____

If so, which medication? _____
Indication? _____

Initial Management

Transfusion within 72 hours of admission?
PRBCs _____
FFP _____
Platelets _____
Cryo _____

Patient identity code _____

Use of tranexamic acid within 4 hours of admission? _____

Use of prothrombin complex concentrate within 72 hours of admission?
_____

Use of activated Factor VII within 72 hours of admission?
_____

Operative intervention within 72 hours of admission? _____
Dates of operative intervention? _____

Anti-coagulation? _____
Date of initiation? _____
Anti-coagulant agent? _____
Prophylactic or therapeutic? _____
Mechanical phrophylaxis? _____

Outcome

Vascular Thromboembolic Complications

DVT identification? _____
Location? _____
Date?_____
Management? _____

Pulmonary embolism identification? _____
Classification?_____
Date? _____
Management? _____

Renal Injury

Renal trauma present? _____
Nature of renal trauma, if present? _____
Oliguria or anuria (< 400 ml urine output over 24 hours) _____
New requirement for hemodialysis modalities? _____
Modality? _____

Respiratory Failure

Thoracic trauma present? _____
Intubation within 48 hours of admission? _____

Patient identity code _____

Lung Injury? (P:F ratio <300) _____

Hepatic Injury
Liver trauma present? _____
Nature of liver trauma, if present? _____
Hyperbilirubinemia with serum total bilirubin >2.5 mg/dL within 30 days of admission? _____

Length of stay
Length of ICU stay _____
Length of overall stay _____

Mortality
Did the patient survive 30 days from the date of injury? _____

For Lab Use

Serum Tissue Factor levels

Admission _____

24 hours _____

72 hours _____

120 hours _____

168 hours _____

Clinical Implications of the Impact of Traumatic Brain Injury on Serum Tissue Factor Levels after Trauma

Data Dictionary

Head Injury: Glasgow Coma Scale score of 9 or less, *and* Abbreviated Injury Scale (AIS) Head/Neck score of 3 or greater.

Hepatic injury: Hyperbilirubinemia with serum total bilirubin >2.5 mg/dL within 30 days of admission

Lung injury: PaO2/FIO2 ratio <300

Oliguria: less than 400 ml urine output over 24 hours