EAST MULTICENTER STUDY
DATA DICTIONARY

Does the Addition of Daily Aspirin to Standard Deep Venous Thrombosis Prophylaxis Reduce the Rate of Venous Thromboembolic Events?

Data Entry Points and appropriate definitions / clarifications:

Entry space	Definition / Instructions
Demographics / Injury Variables:	
Admission Date	Admission date of the TBI patient
Admission Time	Admission time of the TBI patient
Age	Age of TBI patient
Gender	Gender of TBI patient
Admission systolic blood pressure	Systolic blood pressure of TBI patient upon admission
Mechanism of initial Injury:	
Blunt	Single choice for best description of blunt mechanism (if penetrating mechanism proceed to next data point) Options include: MVC, Auto vs. Peds (Pedestrian), Fall, Assault, MCC (Motorcycle Collision / Crash), Machinery, Other
Penetrating	Single choice for best description of penetrating mechanism. Options include: GSW (Gunshot wound) Shotgun (Shotgun wound) Stab (Stab Wound) Other
ISS	Numerical value for calculated ISS (ISS = Injury Severity Score)
AIS Chest	Numerical Value for AIS body region = Chest (AIS = Abbreviated Injury Score)
GCS	Numerical Value for GCS upon admission (GCS = Glasgow Coma Scale score)

Mechanism of initial Injury Continued:

Long bone fracture	Answer type: Yes / No. Lower extremity fracture to femur, tibia, fibula
Pelvic fracture	Answer type: Yes / No. Any fracture to ilium, ischium, pubic bone, sacrum, coccyx, and acetabulum
Spine fracture	Answer type: Yes / No. Any cervical, thoracic, or lumbar spinal body fracture
Spinal cord Injury	Answer type: Yes / No. Spinal cord injury leading to partial or full neurologic deficit
Prolonged extraction time:	Answer type: Yes / No. Prolonged extraction time = ≥ 20 minutes
Chest Injury (AIS≥3)	Answer type: Yes / No. Chest injury with an Abbreviated Injury Scale score coding ≥3

Admission TEG Values

AA MA	AA MA from admission TEG (AA MA = arachidonic acid maximum amplitude)
ADP MA	ADP MA from admission TEG (ADP MA = adenosine diphosphate maximum amplitude)
AA %inhibition	AA %inhibition from admission TEG (AA %inhibition = arachidonic acid percent inhibition)
ADP % inhibition	ADP %inhibition from admission TEG (ADP %inhibition = adenosine diphosphate percent inhibition)
R time	R time from admission TEG (R time = reaction time)
Alpha angle	Alpha angle from admission TEG
K time	K time from admission TEG (K time = time from the end of R until clot reaches 20mm – speed of clot formation)
LY 30	LY 30 from admission TEG (LY 30 = percentage of clot that has lysed after 30 minutes)
G value	G value from admission TEG (G value is a log-derivation of MA – represents clot strength)
MA	MA from admission TEG (MA = maximum amplitude – represents clot strength)

Management Variables

Aspirin Group	Experimental group – randomized to receive aspirin in addition to standard DVT prophylaxis

Non-aspirin Group	Control group – randomized to not receive aspirin in addition to standard DVT prophylaxis

Outcomes

Pulmonary embolism (PE)	Sudden blockage by clot in lung artery. Positive pulmonary embolism diagnosed by chest computed tomography scan during hospital stay. Answer type: Yes / No
Deep venous thrombosis (DVT)	Blood clot that forms in one or more of the deep veins. Positive deep venous thrombosis diagnosed based on ultrasound or based on venous phase pelvic CT or MRI. Answer type: Yes / No (Two responses: DVT based on ultrasound: YES / NO; DVT based on phase pelvic CT or MRI: YES / NO)
ICU days	Total number of days patient spent in intensive care unit during treatment (ICU = intensive care unit)
Hospital days	Total days patient spent in hospital during treatment
Ventilator days	Total days, if any, the patient was on a mechanical ventilator during treatment
Mortality	TBI patient discharge status: Dead or alive. If dead, answer yes. If alive, answer no. Answer type: Yes / No

EAST MULTICENTER STUDY
DATA COLLECTION TOOL

Multicenter Study: Does the Addition of Daily Aspirin to Standard Deep Venous Thrombosis Prophylaxis Reduce the Rate of Venous Thromboembolic Events?

Enrolling Center: _____
Enrolling Co-investigator: _____

Demographics / Injury Variables:
Age: _____ Gender: _____ Admission systolic blood pressure: _____

Admission date: _____ Admission time: _____

Mechanism of initial injury:

Blunt:	YES / NO
Penetrating:	YES / NO
Long bone fracture:	YES / NO
Pelvic fracture:	YES / NO
Spine fracture:	YES / NO
Spinal Cord Injury:	YES / NO
Prolonged extraction time:	YES / NO
Chest Injury (AIS≥3)	YES / NO

ISS: _____ AIS Chest: _____ GCS: _____

Admission TEG values:

AA MA: _____ ADP MA: _____ AA% inhibition: _____ ADP % inhibition: _____

R Time: _____ Alpha angle: _____ K time: _____ LY 30: _____ G value: _____

MA: _____

Management Variables:

Aspirin Group:	YES / NO
Control Group:	YES / NO

Outcome Measures:

Positive pulmonary embolism based on chest CT:	YES / NO
Positive deep venous thrombosis based on ultrasound:	YES / NO
Positive deep venous thrombosis based on venous phase pelvic CT or MRI:	YES / NO
Mortality (Dead)	YES / NO

Outcome Measures Continued:

ICU days: _____ Hospital days: _____ Ventilator days: _____

Does the Addition of Daily Aspirin to Standard Deep Venous Thrombosis Prophylaxis Reduce the Rate of Venous Thromboembolic Events?

Background and Significance

Venothromboembolic phenomenon (VTE) are still are significant source of morbidity and mortality in the critically ill patient. Mechanical ventilation when continued beyond two days is a significant contributor to an elevated rate of VTE. Trauma itself is known to be a contributor to elevated VTE rates. Standard treatment of prophylaxis involves a factor inhibition which ar usually Xa, prothrombin, and fibrinogen. These measures have been shown to reduce fatal pulmonary emboli (PE) by 50% and therefore VTE remains a significant problem. Thromboelastography has become a more widely used tool to measure the coagulation status of patients. It has also been used to gauge the propensity for patients to develop VTE. Recent literature has revealed administration of aspirin, an antiplatelet agent, reduces the risk of deep venous thrombosis (DVT) in critically ill mechanically ventilated patients. Even though the rate of DVT was lower in the aspirin alone group compared to standard prophylaxis, it did not reach significance. Other research has pointed to the fact that even with elevated anti-Xa activity, DVT rates may not change. Greater efficacy of VTE prevention may be achieved by attenuating the platelet arm of the clotting pathway along with the factor arm of the clotting pathway. TEG with platelet mapping (MP) allows for measurement of the platelet dysfunction and if possibly if the patient is not responsive to antiplatelet medications. These measurements would be crucial to this study.

Primary Aim

The primary aim of this study is to determine the efficacy of the addition of normal dose daily aspirin administration (325 mg) to standard DVT prophylaxis in the rate of VTE

Secondary Aim

Secondary aims of the study include examining the results of thromboelastography with platelet mapping between groups, rates of bleeding complications, mortality, ICU length of stay and hospital length of stay

Inclusion Criteria

Inclusion criteria include: Age $\geq$ 18, trauma patients, ventilated patients $\geq$ two days, capability of performing TEG with PM

Exclusion Criteria

Exclusion criteria include: Age < 18, intracranial hemorrhage, ventilation < 2 days, pregnancy, patients not on standard DVT prophylaxis

Therapeutic Interventions

This is a prospective randomized study. Patients will be randomized to receive standard daily aspirin therapy.

Primary Outcome

The primary outcome of the study is the difference between VTE rates between those that received additional regular dose aspirin and those that received just standard prophylaxis

Secondary Outcomes

The secondary outcome of the study include bleeding complication, acute coronary events, ventilation time, ICU stay, hospital length of stay, mortality, and destination for discharge

Variables

Age, sex, blunt vs. penetrating, ISS, positive long bone fractures, positive pelvic fractures, spine fractures, spinal cord injury (none, partial, paraplegic, quadriplegic) ventilator days, ICU days, hospital days, positive prolonged extraction time, positive chest injury with AIS $\geq$ 3, comorbidities, TEG values (R time, alpha angle, K time, MA, LY 30, ADP MA, G value, AA MA, ADP percent inhibition, AA and percent inhibition), positive PE based on chest CT, positive DVT based on US, positive DVT based on venous phase pelvic CT or MRI, positive acute coronary syndrome based on elevated troponin with initial normal troponin for the first 48 hours.

Data collection and Statistical analysis

This study will prospectively recruit patients from multiple centers and assign them to one of two groups: Group 1 (experi
mental - ASA) group; Group 2 (Control - No ASA). Rates of VTE will be calculated and compared between experimental and control groups in univariate analysis. Additionally, a multivariate logistic regression model will be implemented to determine whether ASA, as well as other collected variables, are significantly associated with VTE. Complications, particularly progression of bleed/onset of bleeding will be compared between groups.

Consent Procedures

This is a prospective randomized trial which will require a consent of the health care power of attorney as a critically injured intubated trauma patient. HCPOA that are not aboe to sign, due to lack of presence, or decline, may be entered into the non-therapeutic arm but this would violate the randomization process. However, the additional recruitment of patients may assist in obtaining more accurate results. This would still require a separate consent to be in the study even though not in the randomization process.

Risk/Benefit Analysis

The benefits of this intervention would potentially be decreased VTE and possibly decreased coronary events. This must be weighted against the potential increase in bleeding complications in the critically ill trauma patient. Other potential complications to this intervention include allergic reaction to aspirin, interaction with other medications, suppression of the inflammatory response including fever.

References

Gupta E, et al "Effect of aspirin on prevention of venous thromboembolism in critically ill mechanically ventilated patients" Chest 2015; DOI: 10.1378/chest.2243342.

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Louis SG, Van PY, Riha GM, Barton JS, Kunio NR, Underwood SJ, Differding JA, Rick E, Ginzburg E, Schreiber MA. Thromboelastogram-guided enoxaparin dosing does not confer protection from deep venous thrombosis: a randomized controlled pilot trial. J Trauma Acute Care Surg. 2014 Apr;76(4):937-42; discussion 942-3.

Van PY, Cho SD, Underwood SJ, Morris MS, Watters JM, Schreiber MA. Thrombelastography versus AntiFactor Xa levels in the assessment of prophylactic-dose enoxaparin in critically ill patients. J Trauma. 2009 Jun;66(6):1509-15; discussion 1515-7