Form "EAST Multicenter Study Proposal"

Study Title	Efficacy and safety of aspirin administration in conjunction with factor inhibition for DVT prophylaxis
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Use this area to briefly (1-2 paragraphs only) outline the burden of the problem to be examined	Venothromboembolic phenomenon (VTE) are still a 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 are usually Xa, prothrombin, and fibrinogen. These measures have been shown to reduce fatal pulmonary emboli (PE) only 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 aims	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 > 18, trauma patients, ventilated patients > 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

List specific variables to be collected & analyzed

Age, sex, blunt vs. penetrating, ISS, positive long bone fractures, positive pelvic fractures, spine fractures, spinal cord injury, paralysis(none, partial, paraplegic, quadriplegic) ventilator days, ICU days, hospital days, positive prolonged extraction time, positive chest injury with AIS > 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.

Outline the data collection plan and statistical analysis plan succinctly

This study will prospectively recruit patients from multiple centers and assign them to one of two groups: Group 1 (experimental - 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.

Outline consent procedures here, if applicable

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 able 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.

Succinctly outline a 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.

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.

Include a brief listing of key references

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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