**American Association for the Surgery of Trauma**

**Multi-Institutional Trial Committee**

**New Proposal Application Form**

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**Date:** 6/29/2019

**Title of Proposal:** When Is It Safe to Start VTE Prophylaxis After Blunt Solid Organ Injury?

**Hypothesis:** We hypothesize that venous thromboembolism (VTE) prophylaxis initiation within 48 hours of hospital admission for patients with blunt solid organ injury managed nonoperatively is both effective and safe, i.e. reduces VTE rates without an increase in failure of nonoperative management or need for blood transfusion.

**Type of Study: Prospective, Observational**

**Background-**

**Define the Knowledge Gap that Study Addresses:**

Trauma patients are at high risk for VTE and benefit from prompt initiation of VTE chemoprophylaxis (1). However, patients with blunt solid organ injury managed nonoperatively present a competing risk of ongoing bleeding, which theoretically may be further precipitated by early initiation of VTE prophylaxis. This could lead to additional blood transfusion requirement or failure of nonoperative management. Because the risks of VTE and bleeding must be balanced, the optimal time to initiate VTE prophylaxis in these patients is unclear. Previous retrospective work and one prospective study suggest that initiation within 48 hours of hospital admission is both safe and effective at preventing VTEs (2-6). Prospective multi-institutional validation of these findings is required.

**Study Aim(s)-**

**Primary Aim:** To determine if early VTE prophylaxis initiation, defined by ≤48h after hospital admission, among patients with blunt solid organ injury managed nonoperatively reduces the rates of VTE.

**Secondary Aim:**  To determine the impact of: early VTE prophylaxis initiation on the need for and volume of blood transfusion, need for delayed angioembolization, and failure of nonoperative management; missed doses of VTE prophylaxis on VTE events in this patient population; and routine screening for DVTs on the rate of VTE among patients with blunt solid organ injury.

**Proposed Study Population-**

**Inclusion Criteria:**

Patients who meet all of the following criteria will be enrolled:
Age >15 years
Blunt mechanism of injury
Solid organ injury (liver, spleen, and/or kidney)
Nonoperative management, defined by lack of exploratory laparotomy ≤4h from hospital admission

**Exclusion Criteria:**

Patients who meet any of the following criteria will be excluded:
Transfer to or from outside hospital
ED death
Pregnancy
Home antiplatelet or anticoagulant medication
Pre-existing bleeding disorder

**Outcome Measures-**

**Primary Outcome:** Rate of VTE (DVT and PE)

**Secondary Outcome(s):** Mortality, hospital length of stay (LOS), intensive care unit (ICU) LOS, ventilator days, volume of pre- and post-prophylaxis blood transfusion, need for delayed (>4h) angioembolization, failure of nonoperative management (defined by exploratory laparotomy >4h); number of missed doses of VTE prophylaxis.

**Data Collection Variables:**

Patient demographics (age, sex, comorbidities, home medications)
Clinical data (time of arrival to ED, initial ED vital signs and GCS)
Injury data (mechanism of injury, ISS, AIS by body region)
Solid organ injury data (type of solid organ(s) injured, AAST grade of injury)
Angioembolization with date/time
VTE chemoprophylaxis data (agent, dosing, time of first dose, reason for delay if initiated >48h)
Missed doses of VTE prophylaxis (number of missed doses [expected number of doses of VTE prophylaxis during hospitalization minus actual number of doses of VTE prophylaxis received during hospitalization]; reason for missed doses of VTE prophylaxis).
Other VTE prophylaxis (sequential compression devices, time to ambulation)
Center policy for VTE screening (routine vs. symptom-driven, imaging modalities used for diagnosis [venous duplex, CTPA, VQ scan, etc])
Blood transfusion data (need for and volume of pre- and post-prophylaxis blood transfusion)
Failure of nonoperative management, i.e. need for exploratory laparotomy >4h after hospital admission (indication, time from admission at which it occurred)
VTE data (development of DVT, PE, or both; hospital day at which it occurred)
Other secondary outcomes (mortality, hospital LOS, ICU LOS, ventilator days)

**Planned Duration of Study:** 1 year

**Center Participation Goal:** 12 **Patient Recruitment Goal:** 1200

**Power Analysis Performed: Yes** [x]  **No** [ ]

With an alpha of 0.05 and beta of 0.2, 579 patients are required in each study group (total n=1158) to detect the anticipated difference in primary outcome (VTE rate) based on existing literature (1.8% vs. 4.9% rate of VTE among patients with blunt solid organ injury initiated on VTE chemoprophylaxis ≤48h vs. >48h) (3-6).

**Plan for Statistical Analysis:** Patients will be dichotomized into study groups according to time of VTE chemoprophylaxis initiation: early (≤48h of hospital arrival) and late (>48h). Continuous variables will be presented as median [interquartile range] and categorical variables will be presented as number (percentage). Univariable analysis will compare demographics, clinical data, injury data, VTE chemoprophylaxis type, and outcomes between groups using the Mann Whitney U test or Fisher’s exact test, as appropriate. Multivariable analysis with logistic regression will be used to determine independent risk factors for VTE and factors associated with delayed initiation of VTE prophylaxis. Covariates will be selected a priori on the basis of existing literature and expert consensus. A ROC curve analysis will be performed to identify the inflection point for time-to-VTE chemoprophylaxis. Subgroup analysis of patients initiated on VTE prophylaxis <24h will be performed.

**Define How Findings from this Multi-Center Study Will Serve as the Foundation for Future Studies or Future Funded Research:**

Once the optimal time to VTE prophylaxis initiation after blunt solid organ injury is established in this prospective, multicenter, observational study, a randomized controlled trial would serve as the next step in delineating the safety and effectiveness of early VTE prophylaxis among this high risk subset of trauma patients.

**Does Study Require Informed Consent, Describe Rationale:**

Waived consent is appropriate for this prospective, observational study. Patients will not experience any changes in care as a result of study participation. Patient identifiers will be removed prior to data submission from each participating center and thus the data collection at the coordinating study institution will be deidentified.

**Database Development-**

**Do you have independent funding?: Yes** [ ]  **No** [x]

**Does your study require upload of imaging studies?: Yes** [ ]  **No** [x]

**If the cost of development of your database exceeds the allotted financial support from AAST, are you able/willing to fund the difference?: Yes** [ ]  **No** [x]

**Key References-**

1. Nathens AB, McMurray MK, Cuschieri J, Durr EA, Moore EE, Bankey PE, Freeman B, Harbrecht BG, Johnson JL, Minei JP, McKinley BA, Moore FA, Shapiro MB, West MA, Tompkins RG, Maier RV. The Practice of Venous Thromboembolism Prophylaxis in the Major Trauma Patient. J Trauma. 2007;62(3):557-62.
2. Schellenberg M, Inaba K, Biswas S, Heindel P, Benjamin E, Strumwasser A, Matsushima K, Lam L,
Demetriades D. When Is It Safe to Start VTE Prophylaxis after Blunt Solid Organ Injury? A Prospective Study from a Level I Trauma Center. World J Surg. 2019;Epub ahead of print.
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5. Rostas JW, Manley J, Gonzalez RP, Brevard SB, Ahmed N, Frotan MA, Mitchell E, Simmons JD. The safety of low molecular-weight heparin after blunt liver and spleen injuries. Am J Surg. 2015;210:31-4.
6. Datta I, Ball CG, Rudmik LR, Paton-Gay D, Bhayana D, Salat P, Schieman C, Smith DF, van Wijngaarden-Stephens M, Kortbeek JB (2009). A multicenter review of deep venous thrombosis prophylaxis practice patterns for blunt hepatic trauma. J Trauma Manag Outcomes. 2009;3:1-5.