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Safety Evaluation of Intravenous Heparin Protocol Following Alteplase Treatment in Patients with Suspected or Confirmed Pulmonary Embolism

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Beaumont

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Background

- Pulmonary embolism (PE) is a medical emergency requiring prompt intervention
- Guidelines recommend systemic thrombolysis in high-risk individuals presenting with hemodynamic compromise[1,2]
- IV alteplase 50-100 mg (0.5-0.6 mg/kg if < 50 kg) in non-cardiac arrest PE should be administered over 2 hours[2]
- IV alteplase during cardiac arrest should be administered as a 50 mg bolus that may be repeated once if return of spontaneous circulation (ROSC) is not obtained[1,3]
  - If ROSC is obtained after the first IV bolus, a subsequent IV alteplase 50 mg should be administered as an IV infusion
- Thrombolytics cause transient elevations in activated partial thromboplastin time (aPTT), thus parenteral anticoagulation should be held during its administration and resumed when aPTT is ≤ 2x ULN without a bolus[1,2,4]
- Transition from parenteral to oral anticoagulation should occur 2-3 days after thrombolytic administration to ensure patient stabilization[1]
- This organization introduced a new, system-wide, post-alteplase heparin workflow on September 13, 2021, which included changes such as aPTT collection times and pharmacist verification of every dose adjustment

Purpose

To assess adherence to a newly implemented health system protocol and safety of IV heparin therapy following alteplase administration for PE

Methods

Study Design: IRB approved, retrospective, 8 hospital health system chart review

Inclusion: Age ≥ 18 years who received IV alteplase for suspected or confirmed PE

Study Period: 9/14/2021 – 8/31/2022

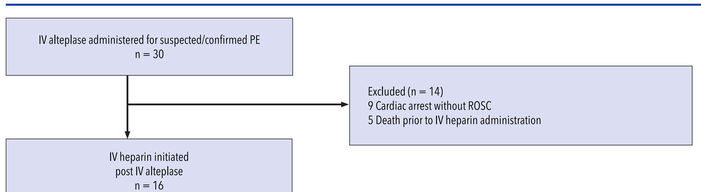
Exclusion: Patients who did not receive IV heparin therapy post IV alteplase

OUTCOMES	
Primary	Overall protocol adherence
Secondary	Time from post-thrombolytic aPTT to IV heparin initiation Accuracy of IV heparin dose modification based on approved protocol Transition time between IV heparin and oral anticoagulation Documentation of pharmacist interventions
Safety	Incidence of major bleeding defined by ISTH criteria[5]

Statistical analysis: mean, median, interquartile range (IQR), and standard deviation (SD) as appropriate

NOTE: Dosing strategies will also be described for excluded patients who did not receive IV heparin therapy post-alteplase

Results



Results cont'd

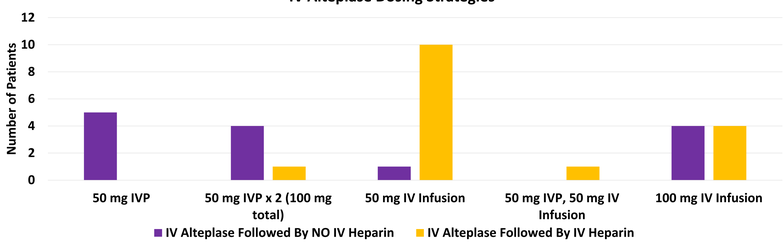


Table 1. IV Alteplase Followed By Heparin Administration

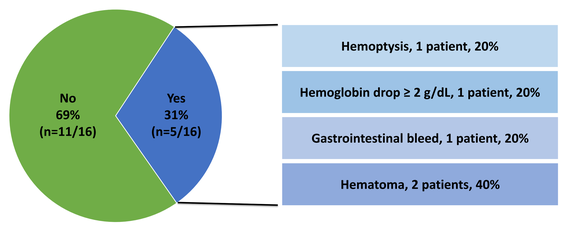
Demographics - IV Alteplase Followed By Heparin Administration	n=16
Male, n (%)	10 (63)
Age, years (SD)	64 (15)
Height, cm (SD)	174 (12)
Weight, kg (SD)	109 (22)
Outside facility transfer, n (%)	1 (6)
Massive PE, n (%)	10 (63)
Cardiac arrest, n (%)	2 (13)
aPTT obtained prior to IV alteplase, n (%)	12 (75)
aPTT, seconds [QR]	50 [27,61]
Heparin prior to alteplase, n (%)	7 (44)
Infusion stopped during alteplase administration, n (%)	7(100)
Heparin discontinuation to alteplase administration, minutes (SD)	43 (20)
Alteplase weight-based dosing, mg/kg (SD)	0.7 (0.3)

HEPARIN

Table 2. Post IV Alteplase Heparin Administration

Post IV Alteplase Heparin Administration	n=16
Overall protocol adherence, n (%)	12 (75)
IV heparin stopped during alteplase administration, n (%)	7 (100)
Post IV alteplase aPTT correctly collected, n (%)	12 (75)
Correct post IV alteplase heparin order set used, n (%)	15 (94)
IV Heparin initiated without initial bolus, n (%)	16 (100)
aPTT obtained 6 hours after initiation of IV heparin, n (%)	16 (100)
IV heparin continuous infusion correctly adjusted per protocol, n (%)	16 (100)
Pharmacist documentation of IV heparin infusion assessment, n (%)	7 (44)
Correct documentation template used, n (%)	3 (43)
Time between IV alteplase completion and IV heparin start, minutes [IQR]	93 [64,155]
Post IV alteplase aPTT value, seconds (SD)	55 (44)
aPTT supratherapeutic, n (%)	2 (13)
IV heparin transitioned to oral or subcutaneous anticoagulation, n (%)	11 (69)
Time to transition, days [IQR]	4.7 [1.8, 5.0]

MAJOR BLEED EVENTS



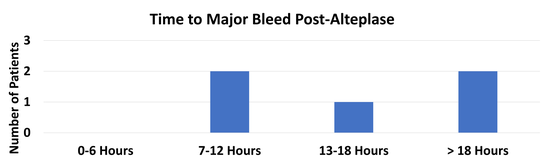


Table 3. Major Bleeding aPTT

Major Bleeding aPTT	n=5
Last documented aPTT prior to major bleed, seconds (SD)	107 (61)
aPTT supratherapeutic, n (%)	3 (60)

Discussion

- Post IV alteplase aPTT collection was found to be the primary area of improvement for overall protocol adherence
- Multidisciplinary education on post-alteplase STAT aPTT collection is necessary including emphasis that STAT aPTT is included in the post-alteplase workflow to ensure heparin is appropriately initiated or reinitiated post IV alteplase
- Supratherapeutic aPTT likely contributed to alteplase associated bleeding events
- Limitations: small sample size due to high thrombectomy rates, high mortality rate, retrospective chart review

References

1. Konstantinides SV, Meyer G, Becattini C, et al. 2019 ESC Guidelines for the diagnosis and management of acute pulmonary embolism developed in collaboration with the European Respiratory Society (ERS): The Task Force for the diagnosis and management of acute pulmonary embolism of the European Society of Cardiology (ESC). European Heart Journal. 2020;41(4):543-603.
2. Lavonas EJ, Drennan IR, Gabrielli A, et al. Part 10: Special Circumstances of Resuscitation: 2015 American Heart Association Guidelines Update for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care [published correction appears in Circulation. 2016 Aug 30;134(9):e122]. Circulation. 2015;132(18 Suppl 2):S501-S518.
3. Kearon C, Akl EA, Comerota AJ, et al. Antithrombotic therapy for VTE disease: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest. 2012;141(2 Suppl):e419S-e496S.
4. Granger CB, Hirsh J, Califf RM, et al. Activated Partial Thromboplastin Time and Outcome After Thrombolytic Therapy for Acute Myocardial Infarction. Circulation. 1996;93(5):870-878.
5. Schulman S, Kearon C, Scientific the SOCOAOT, Thrombosis SC of the ISO, Haemostasis. Definition of major bleeding in clinical investigations of antihemostatic medicinal products in non-surgical patients. Journal of Thrombosis and Haemostasis. 2005;3(4):692-694.

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