Clinical and Economic Outcomes of Warfarin Versus Direct Oral Anticoagulants (DOACs) Following Alteplase for the Treatment of Pulmonary Embolism (PE)

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Introduction

• The annual incidence of pulmonary embolism (PE) is estimated at 69 cases per 100,0009
• PE is associated with major complications including recurrent venous thromboembolism (VTE)
• Chronic thromboembolic pulmonary hypertension (CTEPH)
• Mortality rate of > 15% within the first 3 months3
• Therapy options for acute PE include:
  □ Parenteral anticoagulation alone
  □ Parenteral anticoagulation overlapped with vitamin K antagonists for a minimum of 5 days
  □ Direct oral anticoagulants (DOACs)
  □ Thrombolytic therapy in patients with acute massive or submassive PE without a high bleeding risk
• DOACs have gained popularity for PE treatment because of the reduction in therapeutic monitoring and favorable bleeding profiles
• Trials that evaluated DOACs for PE treatment excluded patients who received thrombolytic therapy3
• To date, the literature consists of only two observational studies addressing the use of DOACs following thrombolytic therapy4,5
  □ A recently published single-arm, single-center study suggests the use of rivaroxaban following alteplase 50 mg is safe and effective for the treatment of moderate to severe PE
  □ Use of alteplase 50 mg followed by rivanoxaban resulted in a length of stay (LOS) of 1.9 ± 0.2 days in patients who presented primarily with PE
  □ A retrospective study including patients who received apixaban or rivanoxaban following alteplase 50 mg reported similar results8
  □ No major bleeding events were observed with the use of rixanaxaban or following alteplase therapy9
• Both studies were conducted by the same investigators at a single medical center9,10
• The observed LOS in these trials is considerably shorter than observed LOS for PE treatment at Beaumont Hospital – Royal Oak:
  □ University HealthSystem Consortium (UHC) LOS data for PE treatment at Beaumont Hospital – Royal Oak: Mean LOS (Days): 9.82 Expected LOS (Days): 6.53
  □ A recent study by the University of Michigan reported similar results10
  □ In-hospital and 30 day mortality:

Objectives

• Characterize the use of oral anticoagulants following alteplase administration for PE treatment at Beaumont Health System
• Compare the hospital LOS in patients who received warfarin vs. DOAC post alteplase use
• Compare major or clinically relevant bleeds in patients who received warfarin vs. DOAC post alteplase use

Methods

• Retrospective, single health-system study
• Institutional Review Board (IRB) approved
• Inclusion Criteria:
  □ Age ≥18 years
  □ Received alteplase for indications of clinically overt bleeding
  □ Strong clinical suspicion or objective confirmation of PE by computed tomography (CTA) or ventilation and perfusion (VQ) scan

Data Collection

Patient Characteristics:

• Vitals
• Patient demographics
• Comorbidities
• Baseline labs

Safety:

• Documentation of clinically overt bleeding
• Hemoglobin values
• Diagnostic tests for blood management

Management of PE:

• Alteplase regimen
• Parenteral anticoagulation regimen
• Time to administration
• Transitions between anticoagulants
• Timing of transitions
• Oral anticoagulation regimen

Outcomes

Primary Outcomes

• Major or clinically relevant bleeds as defined by the International Society on Thrombosis and Haemostasis (ISTH)11

Secondary Outcomes

• Recurrent venous thromboembolism (VTE) in-hospital
• Readmissions for recurrent VTE or bled within 30 days
• In-hospital and 30 day mortality
• ICU LOS
• Cost of hospitalization
• Compliance with institutional guidelines

Statistical Analysis

• Data will be reported as mean ± standard deviation or percentage
• Descriptive statistics will be utilized to analyze the data
• Continuous variables with normal distribution will be compared using a two-sample t-test
• Continuous variables with non-normal distribution will be compared using a Wilcoxon two-sample rank-sum test
• Dichotomous variables will be compared by a Pearson’s chi-square test or a Fisher’s exact test, based on the cell sample size
• P-value < 0.05 for statistical significance

References


Disclosures

The following authors of this presentation have nothing to disclose concerning possible financial or personal relationships with commercial entities that might have a direct or indirect interest in the subject matter of this presentation: Lina Qasem, PharmD; Mona Ali, PharmD, BCPS; Terry Bowers, MD; Jenna Holzhausen, PharmD

The following author receives speaking from Janssen and Pfizer: Terry Bowers, MD

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The following author receives speaking honoraria from Bayer: Jenna Holzhausen, PharmD