

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 100,000¹
- PE is associated with major complications including:
 - Recurrent venous thromboembolism (VTE)
 - Chronic thromboembolic pulmonary hypertension (CTEPH)
 - Mortality rate of > 15% within the first 3 months²
- Therapy options for acute PE include^{3,4}:
 - 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 therapy⁵⁻⁸
- To date, the literature consists of only two observational studies addressing the use of DOACs following thrombolytics for PE treatment^{9,10}
 - 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 PE⁹
 - Use of alteplase 50 mg followed by rivaroxaban resulted in a length of stay (LOS) of 1.9 ± 0.2 days in patients who presented primarily with PE⁹
 - A retrospective study including patients who received apixaban or rivaroxaban following alteplase 50 mg reported similar results¹⁰
 - No major bleeding events were reported with the use of rivaroxaban or apixaban following alteplase therapy^{9,10}
 - Both studies were conducted by the same investigators at a single medical center^{9,10}
 - 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)	Expected LOS (Days)
Warfarin	9.82	7.01
DOAC	6.53	5.87

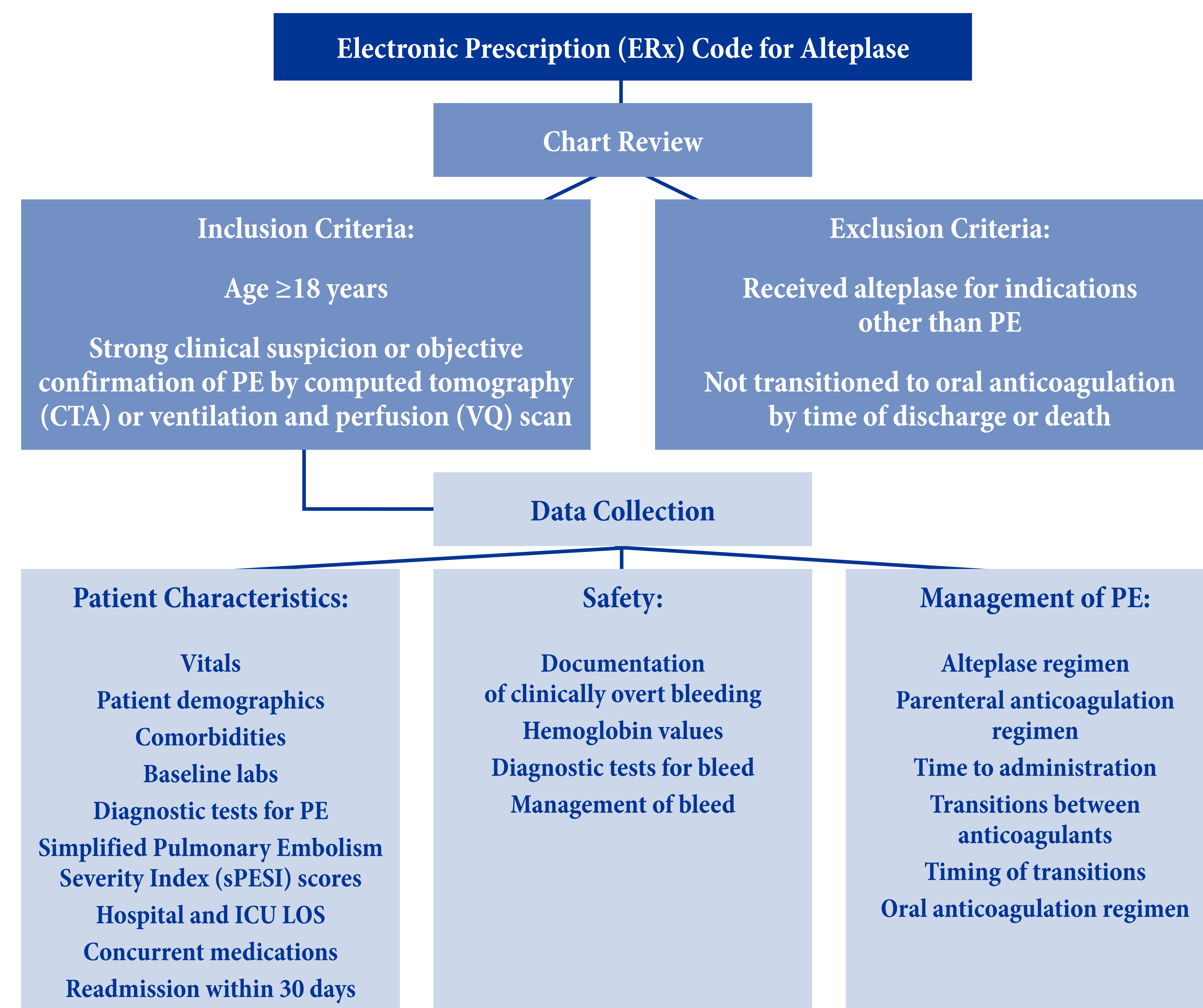
- An analysis of the EINSTEIN-DVT and EINSTEIN-PE trials suggest that DOACs may offer a potential to decrease hospital LOS¹¹
- It is unclear if this data translates into a reduction of LOS in patients who receive a DOAC following alteplase therapy
- Currently, there is a lack of standardized practice for transitioning to oral blood thinners following alteplase therapy at Beaumont Health and a lack of published data regarding how to transition in literature
 - Despite the lack of data, DOACs are utilized following thrombolytic therapy in clinical practice
 - Further data is needed to demonstrate this practice is safe and effective

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
- Patients who received systemic or catheter-directed alteplase for PE treatment between November 1, 2012 and August 31, 2015 will be identified



Outcomes

Primary Outcomes	Hospital LOS
	Major or clinically relevant bleeds as defined by the International Society on Thrombosis and Haemostasis (ISTH) ¹²
Secondary Outcomes	Recurrent venous thromboembolism (VTE) in-hospital
	Readmission for recurrent VTE or bleed 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 chi-square test or a Fisher's exact test, based on the cell sample sizes
- P-value < 0.05 for statistical significance

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Disclosures

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