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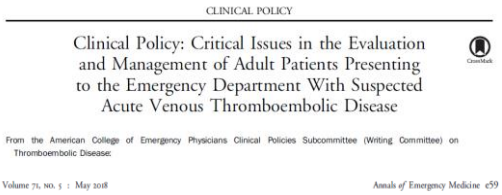
Some useful material to guide investigation and management of DVT/PE.



CLINICAL POLICY

Clinical Policy: Critical Issues in the Evaluation and Management of Adult Patients Presenting to the Emergency Department With Suspected Acute Venous Thromboembolic Disease

From the American College of Emergency Physicians Clinical Policies Subcommittee (Writing Committee) on Thromboembolic Disease:

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A challenge in evaluating patients for venous thromboembolic disease (VTE) lies in the variability of signs and symptoms of the disease that are related to the clot burden, location, and the individual patient's cardiopulmonary reserve. Workup is based on estimating a pre-test probability to interpret diagnostic evaluations and to generate post-test probability of disease. Structured clinical prediction rules are diagnostic (PERC, Wells criteria) or prognostic (e.g., Pulmonary Embolism Severity Index [PESI]) and can be incorporated with gestalt clinical assessment. Studies have supported a post-test probability threshold of < 2.0% to exclude the diagnosis; (i.e. it is not zero and never can be).

Treatment options as alternatives to heparin and warfarin include apixaban (Eliquis), dabigatran (Pradaxa), and rivaroxaban (Xarelto), and their role is being defined.

The 2011 ACEP clinical policy on VTE focused on 6 critical questions: pre-test probability and clinical assessment, utility of the PERC, the diagnostic role of highly sensitive D-dimer assays, CT-PA, CT venogram, and the therapeutic role of thrombolysis for PE. This revision will focus on 5 areas of interest.

CRITICAL QUESTIONS

1. **In adult patients with suspected acute PE, can a clinical prediction rule be used to identify a group of patients at very low risk for the diagnosis of PE for whom no additional diagnostic workup is required?**

Level B recommendations. For patients who are at low risk for acute PE, use the PERC to exclude the diagnosis without further diagnostic testing.

Existing literature supports the use of PERC to exclude PE in low-risk patients (generally estimated by clinical gestalt). Patient groups studied had an overall incidence of PE of about 8-10 %. However there is insufficient evidence to support the use of PERC in higher-risk populations. In studies of undifferentiated groups with 24% having VTE, the post-test probability of PE in PERC –ve patients was over 5%, which exceeds the 2% threshold considered safe.

2. **In adult patients with low to intermediate pretest probability for acute PE, does a negative age-adjusted D-dimer result identify a group of patients at very low risk for the diagnosis of PE for whom no additional diagnostic workup is required?**

Level B recommendations. In patients older than 50 years deemed to be low or intermediate risk for acute PE, clinicians may use a negative age-adjusted D-dimer* result to exclude the diagnosis of PE.

The literature refers to highly sensitive D-dimer assays with an upper range of 500 microgram/L and an aged adjusted cut off of age x10 microgram/L; the local assay is mg/L (upper range 0.5 mg/L; i.e. 500 microgram/L) For a 75 year old equivalent values are 750 mcg/L and 0.75 mg/L.

Accuracy is less defined in patients >80yr.

Available studies report the miss rate of the age-adjusted D-dimer was similar to a conventional D-dimer cutoff, and that the sensitivities were similar.

A prospective study of 3,324 ED patients with a 19% overall prevalence of PE reported 87% were at nonhigh risk. Not anticoagulating after a –ve age adjusted d-dimer was safe.

Studies varied, showing an absolute increase ranging from 5 – 12 % in those with a –ve d-dimer based on the age adjusted cut off. One study reported 40% were classified as –ve d-dimer with an age adjusted result compared to 28% with a standard cut off; another showed a smaller difference with 33% age adjusted -ve compared to 28%.

3. **In adult patients with subsegmental PE, is it safe to withhold anticoagulation?**

Level C recommendations. Given the lack of evidence, anticoagulation treatment decisions for patients with subsegmental PE without associated DVT should be guided by individual patient risk profiles and preferences. [Consensus recommendation]

Isolated subsegmental PEs refer to those without an associated DVT, whereas nonisolated subsegmental PEs are those with an associated DVT; the latter are typically anticoagulated because of the DVT.

A 2016 Cochrane review found no credible evidence to evaluate whether anticoagulation is useful in patients with isolated subsegmental PE.

Given the better prognosis of subsegmental PE , and increasing diagnosis of smaller PEs with better imaging, together with no apparent outcome benefit from treating them, it is reasonable to consider individual patient factors in deciding whether to anticoagulate, such as prior history of VTE, ongoing risk such as with malignancy or immobility, and bleeding risk, together with patient peference.

4. In adult patients diagnosed with acute PE, is initiation of anticoagulation and discharge from the ED safe?
Patient Management Recommendations

Level C recommendations. Selected patients with acute PE who are at low risk for adverse outcomes as determined by PESI, simplified PESI (sPESI), or the Hestia criteria may be safely discharged from the ED on anticoagulation, with close outpatient follow-up.

The Simplified PESI score is high risk if there is *any one* of: abnormal vital signs (O2 sats <90%, HR >110 bpm, SBP <100 mmHg), age >80, cancer and cardiopulmonary co-morbidity, e.g. CCF, COPD.

Simplified Pulmonary Embolism Severity Index

Age >80 years?
Cardiopulmonary co-morbidity?
History of cancer?
Arterial oxyhaemoglobin saturation level <90%?
Systolic blood pressure <100 mm Hg?
Pulse frequency ≥110 beats/min?

If one of the items is present the patient is regarded as high risk.

The full **PESI score** gives points for age (1 point per year); + 10 for male sex; + 30 for cancer, + 10 for heart failure; +10 for chronic lung disease; + 20 for HR >110, + 30 for SBP <110 mmHg; +20 for RR >30; + 20 for temp < 36° C; +60 for altered mental status; +20 for SaO2 <90%. Low risk is a score ≤85. It is more cumbersome than the sPESI, and may underestimate risk in young patients without comorbidities.

Patients have traditionally been hospitalised for monitoring and parenteral anticoagulant therapy. Low-molecular-weight heparins (LMWH) allow for safe outpatient treatment of uncomplicated DVT. NOACs (rivaroxaban, apixaban, dabigatran) have been approved for the treatment of both DVT and PE based on studies showing noninferiority to heparin and warfarin.

>95% diagnosed with acute PE are "haemodynamically stable" at presentation.

Nearly 50% of patients diagnosed with acute PE meet low-risk criteria. Outcome data shows outpatient care is safe with a rate of adverse events of about 1%, similar to if admitted.

Incorporating right ventricular dysfunction on imaging into decision making in regard to low risk is controversial. It is not a variable used in currently tested risk scores. Evidence indicates that presence of RV dysfunction takes about a third of otherwise low risk patients out of a low group with no improvement in outcome or safety.

Evidence supporting safe discharge from ED of low risk patients has limitations, and greater certainty would come from studies enrolling consecutive ED patients with symptomatic PE who are discharged within a reasonable timeframe (i.e. a typical ED length of stay). Available studies did not use NOACs for patients discharged for outpatient treatment, although they are presumed to be safe also.

5. In adult patients diagnosed with acute lower-extremity DVT who are discharged from the ED, is treatment with a NOAC safe and effective compared with treatment with LMWH and VKA?

Level B recommendations. In selected patients diagnosed with acute DVT, a NOAC may be used as a safe and effective treatment alternative to LMWH/VKA.
Level C recommendations. Selected patients with acute DVT may be safely treated with a NOAC and directly discharged from the ED.

Discharge of DVT on NOACs from ED is likely safe as compared to LMWH and warfarin though few studies look at that specifically, hence a low level recommendation.