CJEM *Journal Club*

Diagnosis of pulmonary embolism with D-dimer adjusted to clinical probability

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INTRODUCTION

Background

Clinical diagnosis of pulmonary embolism (PE) can be challenging and relies on objective testing, but gold-standard testing with computed tomography (CT) pulmonary angiography or ventilation-perfusion scan ("chest imaging") exposes patients to potential harms. Thus, it is important to identify low-risk patients who can be discharged safely without the need for extensive testing.

Objectives

To assess whether a variable D-dimer threshold can be used based on clinical probability to exclude the diagnosis of PE safely without further imaging.

METHODS

Design

Prospective multi-centre cohort study.

Setting

Nine university-affiliated hospitals in Canada between 2015 and 2018.

Eligibility criteria

Outpatients (emergency department [ED] or outpatient clinics) with signs or symptoms of PE.

Intervention

Implementation of the Pulmonary Embolism Graduated D-Dimer (PEGeD) algorithm using three-tier clinical pre-test probability (C-PTP) risk stratification: low (Wells 0–4), moderate (Wells 4.5–6), or high (Wells >6), followed by D-dimer testing. Patients with low C-PTP and a D-dimer <1000 or moderate C-PTP and a D-dimer <500 did not undergo further diagnostic testing. All other patients underwent chest imaging and treatment for PE, if necessary.

Outcomes

Primary outcome was incidence of venous thromboembolism (VTE) at a 90-day clinical follow-up. Outcome assessors were unaware of the results of testing at initial presentation.

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MAIN RESULTS

Of 3,133 patients with signs or symptoms of PE, 2,017 were included. The mean age was 52, and two-thirds were women. On clinical assessment, 87% of patients had low, 11% had moderate, and 2% had high C-PTP. The overall incidence of PE was 7.4%. Further, 67% of patients with low (1,285 patients) or moderate (40 patients) C-PTP had a negative D-dimer and were discharged without further imaging. None of these patients had VTE on clinical follow-up at 90 days (95% confidence interval [CI] 0.00–0.29%). This included 315 patients who had a D-dimer level between 500 and 999 ng/mL. Only two patients were diagnosed with PE at follow-up, both of whom had positive initial D-dimers and subsequent negative imaging on initial presentation. Chest imaging was used in 34.3% of patients, a 17.6% reduction (95% CI −19.2 to −15.9), as compared with a strategy that rules out PE in patients with low C-PTP and a D-dimer level <500 ng/mL.

APPRAISAL

Strengths

- Clear, focused, and clinically important question
- Patient-centred outcome with an adequate follow-up period
- Applicable to an ED setting
- Uses Wells score for risk assessment, internationally used and recognized
- Multiple D-dimer assays improve external validity
- No industry funding
- Few patients lost to follow-up
- Blinded outcome assessment

Limitations

- Non-consecutive patient enrolment
- Inadequate sample size to reach conclusions on a moderate risk population
- Only 315 of 2,017 patients in the low C-PTP group had a D-dimer between 500 and999 ng/mL, limiting the strength of conclusions in this important subgroup. It did not assess how many of these patients might have been excluded using pulmonary embolism rule-out criteria (PERC; Kline 2008)
- No direct comparison to usual practice or alternate diagnostic strategy
- Cannot apply to inpatients, pregnant patients, or those who had recent major surgery
- The 7.4% incidence of PE is low compared with prior studies

CONTEXT

This study builds upon a strong body of evidence using clinical criteria and D-dimer testing to reduce advanced chest imaging in patients with a possible diagnosis of PE, including the Wells score with D-dimer, PERC rule,[1] YEARS criteria,[2] and age-adjusted D-dimer.[3] In particular, this study demonstrates the ability to exclude PE safely in patients with low C-PTP and a D-dimer level between 500 and 999 ng/mL.

BOTTOM LINE

The results of this study demonstrate a safe approach to exclude the diagnosis of PE using variable D-dimer thresholds based on C-PTP. Specifically, the evidence is strong for use of this method in patients with low C-PTP and a D-dimer <1000 ng/mL. Further studies with larger sample sizes are needed to validate the safety of this approach for patients with moderate C-PTP. This approach can be adopted by EDs to reduce chest imaging in the workup for PE.

Keywords: Pulmonary embolism, D-dimer, venous thromboembolism

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