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Assessment of the Safety and Efficiency of Using an Age-Adjusted D-dimer Threshold to Exclude Suspected Pulmonary Embolism

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BACKGROUND: D-dimer levels increase with age, and research has suggested that using an age-adjusted D-dimer threshold may improve diagnostic efficiency without compromising safety. The objective of this study was to assess the safety of using an age-adjusted D-dimer threshold in the workup of patients with suspected pulmonary embolism (PE).

METHODS: We report the outcomes of 923 patients aged > 50 years presenting to our ED with suspected PE, a calculated Revised Geneva Score (RGS), and a D-dimer test. All patients underwent CT pulmonary angiography (CTPA). We compared the false-negative rate for PE of a conventional D-dimer threshold with an age-adjusted D-dimer threshold and report the proportion of patients for whom an age-adjusted D-dimer threshold would obviate the need for CTPA.

RESULTS: Among 104 patients with a negative conventional D-dimer test result and an RGS ≤ 10, no PE was observed within 90 days (false-negative rate, 0%; 95% CI, 0%-2.8%). Among 273 patients with a negative age-adjusted D-dimer result and an RGS ≤ 10, four PEs were observed within 90 days (false-negative rate, 1.5%; 95% CI, 0.4%-3.7%). We observed an 18.3% (95% CI, 15.9%-21.0%) absolute reduction in the proportion of patients aged > 50 years who would merit CTPA by using an age-adjusted D-dimer threshold compared with a conventional D-dimer threshold.

CONCLUSIONS: Use of an age-adjusted D-dimer threshold reduces imaging among patients aged > 50 years with an RGS ≤ 10. Although the adoption of an age-adjusted D-dimer threshold is probably safe, the CIs surrounding the additional 1.5% of PEs missed necessitate prospective study before this practice can be adopted into routine clinical care.

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The clinical presentation of pulmonary embolism (PE) is highly variable. Use of a formalized pretest probability clinical decision rule that characterizes patient risk for PE in conjunction with a simple blood test, the D-dimer, is prospectively validated and recommended to evaluate the suspected diagnosis of PE.[1-4] This is possible in large part because of the high sensitivity of D-dimer for VTE. However, the specificity of D-dimer is low, and, therefore, many patients with an elevated D-dimer level require imaging (CT pulmonary angiography [CTPA]) to confirm or exclude PE. D-dimer levels increase with age[5,6] and lead to a proportional increased use of CTPA to exclude PE in elderly patients. Derivation and validation analyses[7] and retrospective studies[8-10] suggested that the use of a D-dimer threshold based on age will exclude PE among a greater proportion of patients. Initial reports of using an age-adjusted D-dimer threshold to exclude a greater proportion of elderly patients with suspected PE

are promising,[11] and a prospective clinical study in North America is under way.[12] Yet, the safety of broadly adopting an age-adjusted D-dimer threshold remains uncertain. We report the safety and efficiency of applying an age-adjusted D-dimer threshold among 923 consecutive patients aged > 50 years with suspected PE and a Revised Geneva Score (RGS) ≤ 10 who presented to our ED.

Materials and Methods

A summary of the methods from our previous study are published elsewhere.[13] The study methodology was a retrospective review of records of patients who underwent CTPA, from which those with suspected PE and low RGS were identified, and D-dimer level was obtained (Fig 1). In brief, we reviewed an electronic medical record to identify consecutive patients who had a CTPA ordered in the ED of LDS Hospital or Intermountain Medical Center to investigate suspected PE. The emergency physician's report was reviewed manually by one investigator (D. M. A.) who used a data abstraction form to verify that each CTPA was performed to investigate suspected PE and capture elements necessary to calculate the RGS. Among the 3,500 consecutive CTPAs ordered to evaluate clinically suspected PE, 1,745 had a pretest probability of PE unlikely defined as an RGS ≤ 10,[4] and all had a D-dimer level obtained.

Of these 1,745 encounters, 923 were among patients aged > 50 years, who comprised the study cohort (Fig 1).

Pretest probability for PE was assessed with the RGS. Prior VTE information was collected through a computer program developed at Intermountain Healthcare with high sensitivity and specificity for the identification of prior VTE.[14,15] Recent surgery was extracted from the Operating Room Management Information System. Recent fracture and cancer were identified by *International Classification of Diseases, Ninth Revision* (ICD-9) codes. These electronically identified elements were verified during manual record review and were included if present in the medical record but not collected electronically. Unilateral leg pain and hemoptysis were recorded manually from the emergency physician's report. If these were not described in the emergency physician's report, we concluded that they were absent by using a strategy previously
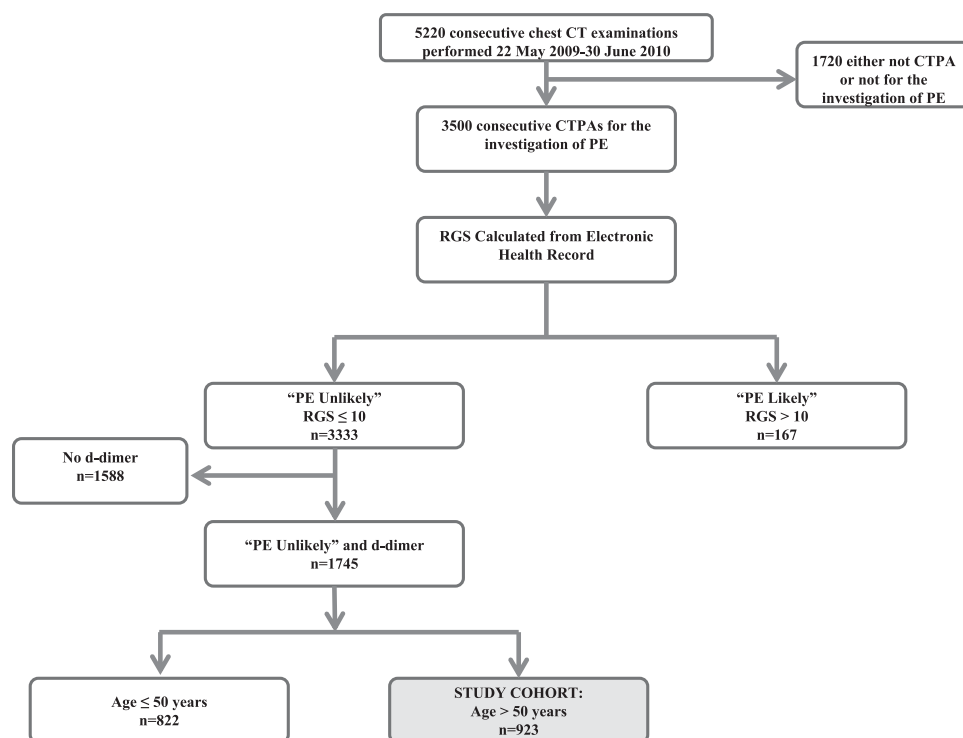


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┌──────────────────────────────────────────┐
│ 5220 consecutive chest CT examinations    │      ┌──────────────────────┐
│ performed 22 May 2009-30 June 2010        │─────▶│ 1720 either not CTPA │
└──────────────────────────────────────────┘      │ or not for the       │
                    │                              │ investigation of PE  │
                    ▼                              └──────────────────────┘
        ┌──────────────────────────┐
        │ 3500 consecutive CTPAs for│
        │ the investigation of PE   │
        └──────────────────────────┘
                    │
                    ▼
        ┌──────────────────────────┐
        │ RGS Calculated from       │
        │ Electronic Health Record  │
        └──────────────────────────┘
            │                    │
            ▼                    ▼
    ┌───────────────┐      ┌───────────────┐
    │ "PE Unlikely" │      │ "PE Likely"   │
    │ RGS ≤ 10      │      │ RGS > 10      │
    │ n=3333        │      │ n=167         │
    └───────────────┘      └───────────────┘
        │
   ┌────────────┐
   │ No d-dimer │◀───┐
   │ n=1588     │    │
   └────────────┘    │
            ▼
    ┌───────────────────┐
    │ "PE Unlikely" and │
    │ d-dimer           │
    │ n=1745            │
    └───────────────────┘
        │            │
        ▼            ▼
  ┌──────────┐  ┌──────────────┐
  │ Age ≤ 50 │  │ STUDY COHORT:│
  │ years    │  │ Age > 50 yrs │
  │ n=822    │  │ n=923        │
  └──────────┘  └──────────────┘
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Figure 1 – *CONSORT (Consolidated Standards of Reporting Trials) diagram of the study design. CTPA = CT pulmonary angiography; PE = pulmonary embolism; RGS = Revised Geneva Score.*