Original Investigation

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Effect of a Diagnostic Strategy Using an Elevated and Age-Adjusted D-Dimer Threshold on Thromboembolic Events in Emergency Department Patients With Suspected Pulmonary Embolism

A Randomized Clinical Trial

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Visual Abstract | Editorial Comment

Key Points

Question Among emergency department patients with suspicion of pulmonary embolism (PE) not ruled out by the pulmonary embolism rule-out criteria (PERC) rule, does use of a diagnostic strategy that combines the YEARS rule and age-adjusted D-dimer threshold safely exclude the diagnosis of venous thromboembolism?

Findings In this cluster-randomized, crossover, noninferiority trial that included 1414 patients with a suspicion of PE in France and Spain, the 3-month risk of a missed thromboembolic event using the intervention diagnostic strategy, compared with a conventional strategy, was 0.15% vs 0.80%; the confidence interval of this difference did not cross the noninferiority margin of 1.35%.

Meaning Among emergency department patients with suspected PE who were PERC positive, the

Abstract

Importance Uncontrolled studies suggest that pulmonary embolism (PE) can be safely ruled out using the YEARS rule, a diagnostic strategy that uses varying D-dimer thresholds.

Objective To prospectively validate the safety of a strategy that combines the YEARS rule with the pulmonary embolism rule-out criteria (PERC) rule and an age-adjusted D-dimer threshold.

Design, Settings, and Participants A cluster-randomized, crossover, noninferiority trial in 18 emergency departments (EDs) in France and Spain. Patients (N=1414) who had a low clinical risk of PE not excluded by the PERC rule or a subjective clinical intermediate risk of PE were included from October 2019 to June 2020, and followed up until October 2020.

Interventions Each center was randomized for the sequence of intervention periods. In the intervention period (726 patients), PE was excluded without chest imaging in patients with no YEARS criteria and a D-dimer level less than 1000 ng/mL and in patients with 1 or more YEARS criteria and a D-dimer level less than the age-adjusted threshold (500 ng/mL if age <50 years or age in years × 10 in patients ≥50 years). In the control period (688 patients), PE was excluded without chest imaging if the D-dimer level was less than the age-adjusted threshold.

Main Outcomes and Measures The primary end point was venous thromboembolism (VTE) at 3 months. The noninferiority margin was set at 1.35%. There were 8 secondary end points, including chest imaging, ED length of stay, hospital admission, nonindicated anticoagulation treatment, all-cause death, and all-cause readmission at 3 months.

Results Of the 1414 included patients (mean age, 55 years; 58% female), 1217 (86%) were analyzed in the per-protocol analysis. PE was diagnosed in the ED in 100 patients (7.1%). At 3 months, VTE was diagnosed in 1 patient in the intervention group (0.15% [95% CI, 0.0% to 0.86%]) vs 5 patients in the control group (0.80% [95% CI, 0.26% to 1.86%]) (adjusted difference, −0.64% [1-sided 97.5% CI, −∞ to 0.21%], within the noninferiority margin). Of the 6 analyzed secondary end points, only 2 showed a statistically significant difference in the intervention group compared with the control group: chest imaging (30.4% vs 40.0%; adjusted difference, −8.7% [95% CI, −13.8% to −3.5%]) and ED median length of stay (6 hours [IQR, 4 to 8 hours] vs 6 hours [IQR, 5 to 9 hours]; adjusted difference, −1.6 hours [95% CI, −2.3 to −0.9]).

Conclusions and Relevance Among ED patients with suspected PE, the use of the YEARS rule combined with the age-adjusted D-dimer threshold in PERC-positive patients, compared with a conventional diagnostic strategy, did not result in an inferior rate of thromboembolic events.

Trial Registration ClinicalTrials.gov Identifier: NCT04032769