**Original Investigation** 

## Age-Adjusted D-Dimer Cutoff Levels to Rule Out Pulmonary Embolism The ADJUST-PE Study

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**IMPORTANCE** D-dimer measurement is an important step in the diagnostic strategy of clinically suspected acute pulmonary embolism (PE), but its clinical usefulness is limited in elderly patients.

**OBJECTIVE** To prospectively validate whether an age-adjusted D-dimer cutoff, defined as age × 10 in patients 50 years or older, is associated with an increased diagnostic yield of D-dimer in elderly patients with suspected PE.

**DESIGN, SETTINGS. AND PATIENTS** A multicenter, multinational, prospective management outcome study in 19 centers in Belgium, France, the Netherlands, and Switzerland between January 1, 2010, and February 28, 2013.

INTERVENTIONS All consecutive outpatients who presented to the emergency department with clinically suspected PE were assessed by a sequential diagnostic strategy based on the clinical probability assessed using either the simplified, revised Geneva score or the 2-level Wells score for PE; highly sensitive D-dimer measurement; and computed tomography pulmonary angiography (CTPA). Patients with a D-dimer value between the conventional cutoff of 500  $\mu$ g/L and their age-adjusted cutoff did not undergo CTPA and were left untreated and formally followed-up for a 3-month period.

**MAIN OUTCOMES AND MEASURES** The primary outcome was the failure rate of the diagnostic strategy, defined as adjudicated thromboembolic events during the 3-month follow-up period among patients not treated with anticoagulants on the basis of a negative age-adjusted D-dimer cutoff result.

**RESULTS** Of the 3346 patients with suspected PE included, the prevalence of PE was 19%. Among the 2898 patients with a nonhigh or an unlikely clinical probability, 817 patients (28.2%) had a D-dimer level lower than 500  $\mu$ g/L (95% CI, 26.6%-29.9%) and 337 patients (11.6%) had a D-dimer between 500  $\mu$ g/L and their age-adjusted cutoff (95% CI, 10.5%-12.9%). The 3-month failure rate in patients with a D-dimer level higher than 500  $\mu$ g/L but below the age-adjusted cutoff was 1 of 331 patients (0.3% [95% CI, 0.1%-1.7%]). Among the 766 patients 75 years or older, of whom 673 had a nonhigh clinical probability, using the age-adjusted cutoff instead of the 500  $\mu$ g/L cutoff increased the proportion of patients in whom PE could be excluded on the basis of D-dimer from 43 of 673 patients (6.4% [95% CI, 4.8%-8.5%) to 200 of 673 patients (29.7% [95% CI, 26.4%-33.3%), without any additional false-negative findings.

CONCLUSIONS AND RELEVANCE Compared with a fixed D-dimer cutoff of 500  $\mu$ g/L, the combination of pretest clinical probability assessment with age-adjusted D-dimer cutoff was associated with a larger number of patients in whom PE could be considered ruled out with a low likelihood of subsequent clinical venous thromboembolism.

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