

THROMBOSIS

New D-dimer cut-off value helps rule out pulmonary embolism in the elderly

Researchers have determined an age-adjusted cut-off value that increases the specificity of the D-dimer test for excluding pulmonary embolism (PE) in patients older than 50 years of age.

The combination of a low clinical probability of having the disease and a blood D-dimer level $<500 \mu\text{g/l}$ safely excludes a diagnosis of PE. However, as patients age, D-dimer concentrations increase and, therefore, this test's efficacy decreases. Renée Douma and colleagues from five European medical centers have thus searched for a suitable cut-off value for D-dimer levels that increases gradually with age. The test should enable the safe exclusion of a PE diagnosis in more individuals, but not lead to an increase in false-negative test results. The investigators specified that the raised cut-off value would only be appropriate and safe in patients with an 'unlikely' or 'non-high' clinical probability of PE.

In their study, the researchers have pooled and analyzed data from two prospective cohort studies involving 1,721 patients with suspected PE. In this derivation set, they grouped patients by decade of age. "We used receiver operating characteristic curves to find the optimal cut-off of the D-dimer [levels] for each decade," explains Douma, "[that is,] the cut-off with a sensitivity of 100% and the highest possible specificity." Then, they calculated the increase in D-dimer cut-off level per year, which was approximately $10 \mu\text{g/l}$. On the basis of these findings, they concluded that the optimal D-dimer cut-off for patients older than 50 years of age would be calculated by multiplying $10 \mu\text{g/l}$ by the patient's age.



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The researchers applied the new age-adjusted D-dimer cut-off value to this data set and to two independent validation cohorts of patients with suspected PE (for a total of more than 5,000 patients). They compared the results with those obtained when using the conventional cut-off value. When the new cut-off value was used, the relative number of patients in whom the D-dimer test was negative increased considerably (20.1%, 11.2% and 18.2% in each data set), with only a modest increase in the rate of false-negative results (0.8%, 0.4% and 0.3%). The test's improved efficacy was particularly pronounced in patients older than 70 years of age; the proportion of these patients in whom PE was excluded was almost twice as high as that determined using the conventional cut-off value.

The increase in the proportion of patients for whom further diagnostic tests could potentially be avoided has considerable implications in clinical care. "Avoiding imaging tests would be of particular benefit for older patients," say the authors, owing to the high frequency of nonconclusive imaging results, the risks involved, and the increased length of hospital stay. Acknowledging that the study was retrospective, Douma comments that "the next step is to perform a large, prospective management study."

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Original article Douma, R.A. et al. Potential of an age adjusted D-dimer cut-off value to improve the exclusion of pulmonary embolism in older patients: a retrospective analysis of three large cohorts. *BMJ* 340, c1475 (2010)