

# Should you adjust your D-dimer?

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## INTRODUCTION

Testing for pulmonary embolism (PE) in the emergency department can be challenging. Estimates of the mortality risk from PE are high (and likely over-exaggerated), but they have led to the fear of missed diagnoses.<sup>1</sup> The presenting symptoms of PE vary, and even when emergency physicians feel that PE is an unlikely cause, PE testing is often ordered to provide objective evidence that it has been ruled out.<sup>2</sup>

Twenty years ago, Wells and colleagues demonstrated that patients with a low pretest probability of having PE who have a negative D-dimer test can have PE safely excluded at the bedside.<sup>3</sup> Since then, there has been a concerted effort among thrombosis researchers to increase the proportion of patients who have PE excluded with D-dimer testing, based on the premise that computed tomography (CT) scanning should be avoided to reduce cost, time, and radiation exposure. This has led to age-adjusted D-dimer,<sup>4</sup> clinical probability-adjusted D-dimer,<sup>5</sup> and pregnancy-adjusted D-dimer.<sup>6</sup>

In Canada, the prevalence of PE among those tested in emergency departments is low, around 5%, which is comparable to that found in the United States.<sup>7</sup> This is in contrast to European studies where the prevalence of PE is 15% to 20%.<sup>4,8</sup> In North America, a larger proportion of those tested have a low pretest probability; therefore, protocols that reduce the number of CT scans will have the greatest impact in Canada and the United States. The advantages include a shorter emergency department stay for a greater number of patients, fewer emergency department CT scans (which reduce the pressure on CT services), and fewer false-positive diagnoses of PE.

Age-adjusted D-dimer has generated much interest, discussion, and anxiety among emergency physicians, with variable adoption within Canadian emergency

departments. There has been reluctance to withhold CT pulmonary angiography in patients with a non-high pretest probability and negative age-adjusted D-dimer, in part, because Canadian evidence of safety was lacking. Furthermore, there is no Canada-wide emergency-focused guideline for PE testing, although Choosing Wisely Canada supports the use of D-dimer and pretest probability assessment to limit the use of CT angiography. A recent individual patient meta-analysis, including 7,268 patients from six PE diagnostic studies, reported a failure rate of 0.9% (95% confidence interval 0.6%-1.5%) when age-adjusted D-dimer was combined with a Wells score of  $\leq 4$ .<sup>9</sup> The American College of Emergency Physicians has published its own recommendations that age-adjusted D-dimer can be used to exclude PE in low- or intermediate-risk patients.<sup>10</sup>

In this edition, Senior and colleagues use administrative data to report on PE testing in 6,655 Canadian patients ages 50 and older, who presented to the emergency department with chest pain, breathlessness, or syncope and had D-dimer testing. The investigators are to be commended on the scale of this study, which combined data from four emergency departments in Calgary over a period of 18 months. The prevalence of PE was very low at 3.7%. Although only 66% of patients with a positive age-adjusted D-dimer underwent CT scanning, the reference standard included a diagnosis of PE at any of the four hospitals within the subsequent 30 days. The study group reported that the sensitivity of age-adjusted D-dimer was low, 90%. Despite a lower sensitivity, the false-negative rate was only 0.5%, which is well under the accepted 2% posttest probability threshold for a “rule-out” PE test.

How should we interpret these contradictory findings? Firstly, the investigators reported age-adjusted D-dimer as a stand-alone test without limiting its use to

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patients with low/moderate clinical probability, which is a reminder to us all that we should not age-adjust our D-dimers without having first calculated pretest probability. The sensitivity of the combined test will be higher. Secondly, the prevalence of PE in the tested population was so low to start with that even a test with a relatively poor sensitivity resulted in a low posttest prevalence.

What can we learn from this study? 1) Age-adjusted D-dimer should be applied to patients with a low or moderate pretest probability of PE, and 2) It is time to start a conversation around why we are testing for PE in places where it does not exist, instead of reserving testing for patients who need it. Over-testing has led to longer emergency stays, unnecessary CT and ventilation-perfusion scans, false-positive PE diagnoses, patient stress and misery, unnecessary long-term anticoagulation, and avoidable anticoagulant-associated bleeding. Perhaps instead of worrying about which tests to use, we should be focusing on whether to test for PE at all.

**Keywords:** Dimer, diagnosis, pulmonary embolism

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