



EDITORIAL COMMENT

Diagnostic prediction rules in acute pulmonary embolism: Is it acceptable to compromise safety?

Regras de predição diagnóstica no tromboembolismo pulmonar agudo – será admissível comprometer a segurança?

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Diagnostic and therapeutic management of acute pulmonary embolism (PE) poses a considerable challenge for clinicians.^{1,2} The non-specific nature of its signs and symptoms, combined with the potentially life-threatening consequences of missing a diagnosis of PE, lead to a generally low threshold for further testing using sensitive, specific, and widely available imaging tests such as computed tomography pulmonary angiography (CTPA) or ventilation-perfusion scanning. CTPA is not only considered the gold standard for diagnosing PE; it has the added benefit of predicting PE-related effects and can help in the differential diagnosis of the cause of a patient's symptoms. Due to these considerable advantages, there is emerging evidence indicating that CTPA is overused as a diagnostic tool in the clinical setting, the main reasons being the availability of scanners, ease of ordering processes, poor understanding of the clinical consequences of excessive imaging, and doctors' and patients' fears of missing the diagnosis of PE.³

In fact, these tests have their own disadvantages, including radiation exposure, particularly in vulnerable groups such as young children, young women, and pregnant women; risk of contrast reactions or nephropathy; overdiagnosis of clinically insignificant PE; and increased healthcare utilization and costs. In a study by Ong et al., an intervention emphasizing the use of clinical prediction rules led to sav-

ings of US\$61 710 by causing 121 fewer CTPA procedures to be performed over a seven-month period.⁴

In a move to minimize unnecessary imaging without compromising patient safety, the 2019 European Society of Cardiology (ESC) guidelines for the diagnosis and management of acute PE gave a class I recommendation for patients with suspected PE to the use of clinical prediction algorithms incorporating risk factors that are identified through a patient's clinical history, together with D-dimer testing.⁵ These tools assist in calculating the pretest probability of acute PE and categorizing patients, aiming to safely exclude the disease in individuals with low or intermediate clinical probability and a D-dimer level below a fixed or variable threshold, thus reducing the potential for excessive investigation and inappropriate use of imaging modalities.

The Wells and Geneva scores are examples of such clinical prediction rules.⁶ They are based on simple, non-invasive, readily available clinical parameters, have been extensively validated, and are widely used to determine the pretest probability of acute PE in patients with a suspicious clinical presentation. However, these algorithms have limitations, and a significant proportion of patients with suspected PE still undergo inappropriate imaging studies.⁷ There are also concerns regarding the applicability of these algorithms across different healthcare settings, given the variability in patient demographics and prevalence of PE.⁸ Furthermore, these algorithms provide an overall risk score rather than an individualized probability estimate.

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In this context, the study by Silva et al.⁹ published in this issue of the *Journal* aimed to compare the accuracy of the standard diagnostic prediction rules for acute PE, namely the Wells and Geneva scores combined with a fixed D-dimer threshold, with three alternate strategies (age-adjusted, and the YEARS and PEGeD algorithms) in patients admitted to the emergency department of a tertiary hospital. They performed a retrospective analysis of 1402 consecutive patients who underwent CTPA for suspected acute PE between April 2019 and January 2021, and calculated the performance of the four strategies by evaluating their efficiency and safety.

The study found some important results. The conventional approach based on the Wells or Geneva scores combined with a fixed D-dimer threshold of 500 ng/ml shows the highest sensitivity for detection of acute PE, making it very safe to avoid CTPA in low-risk patients, but presents the lowest specificity and positive predictive value, leading to excessive imaging tests. Secondly, age-adjusted D-dimer cutoffs lead to a gain in specificity, with only a non-significant loss in sensitivity in older age groups. The YEARS and PEGeD algorithms show the highest specificity, but at the cost of a significant decrease in safety by missing an unacceptable number of acute PE diagnoses. Finally, for all four strategies, sensitivity increases and specificity decreases significantly with age, in parallel with increasing disease incidence.

The authors conclude that the use of an age-adjusted D-dimer cut-off may better stratify patients for further investigation and imaging than the standard fixed D-dimer threshold, especially at older ages, with other strategies presenting an unacceptable number of missed diagnoses. Although it has the strength of a large sample, this study has some limitations: the single-center origin of the patients, the retrospective nature of the analysis, and difficulty in assessing whether the results can be generalized.

The study's main findings are in line with previous evidence and with current clinical recommendations, as the ESC guidelines establish as class IIa recommendations both the use of an age-adjusted D-dimer cut-off for patients aged >50 years, and the use of clinical probability-adapted D-dimer levels, as alternatives to the fixed D-dimer cut-off to exclude PE in patients with low or intermediate clinical probability.¹⁰ These strategies improve clinical and economic efficiency, saving unnecessary imaging tests, without compromising safety by missing a diagnosis of acute PE.

Several other prediction algorithms have been tested and validated, such as YEARS and PEGeD.¹¹ Although they have the virtues of being simple and fast tools and of high specificity, they do not demonstrate a net gain, as their safety performance is significantly lower than conventional tests. Furthermore, it should not be forgotten that in a potentially serious disease such as acute PE, a diagnostic prediction rule must above all be safe, as the risk of missing a diagnosis can mean the loss of a life. Other alternate models, such as that recently proposed by van Es et al.,¹² offer an absolute, individualized probability of the presence of PE rather than a dichotomized classification, and may act in

the future as complementary tools to facilitate modern, informed decision-making.

So, should we replace the recommended prediction scores with new models? Current algorithms are easy to use and have demonstrated efficiency and safety in a population with a broad risk profile. Only in higher-risk subgroups, such as elderly patients, may the adoption of models with greater specificity be recommended, but for now in most patients, and if there is any doubt, the focus should remain on the safe side.

Conflicts of interest

The author has no conflicts of interest to declare.

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