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Pulmonary embolism: a diagnostic challenge

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Pulmonary emobolism (PE) is a common and potentially fatal disease. It is still largely underdiagnosed because physicians often fail to raise timely the suspicion of the disease. The onset of sudden, unexplained dyspnea is by far the most frequent symptom of acute PE, followed by pleuritic chest pain and syncope [1]. Such symptoms, either singly or in combination, were recorded in 96% of the patients with proven PE [1, 2]. Even though they are nonspecific, their occurrence should alert clinicians to consider PE in differential diagnosis [1, 2].

Once the suspicion of PE has been raised, effort should be made to establish the likelihood of PE on clinical grounds. In fact, the results of broad prospective studies lend support to the concept that clinical probability assessment is an important step in the diagnosis of PE [3]. When considered individually, symptoms, signs, or common laboratory tests have limited diagnostic power. Jointly, however, they may provide accurate assessment of the clinical probability of PE [1, 2].

Clinical probability assessment can be accomplished empirically or by means of a prediction rule. The latter is preferable over empirical assessment, especially for less experienced clinicians. In recent years, structured prediction models for PE have been developed with the very purpose of improving and easing the diagnostic approach [1, 2, 4-7].

The Canadian model introduced by Wells at al. [4] is the most frequently used prediction rule for suspected PE. It includes seven variables of which three refer to well-recognized risk factors for pulmonary embolism. The model heavily depends on the subjective judgement as to whether an alternative diagnosis is less likely than PE and, as such, it can hardly be standardized. The Wells' model seems better suited to rule out rather than to rule in the diagnosis of PE [8], and its performance is likely to be better in clinical settings where the prevalence of the disease is expected to be low [8].

Recently, a more precise prediction model [7] was introduced which rests on 16 variables including older age, risk factors, pre-existing cardiopulmonary diseases, relevant clinical symptoms and signs, and the interpretation of the electrocardiogram. The area under the receiver operating characteristic curve was 0.90 in the derivation sample (N=1,100), and 0.88 in the validation sample (N=400). In contrast to other prediction rules, the model includes variables that are negatively associated with pulmonary embolism. This gives the model greater flexibility which may explain why it performs equally well in detecting and in ruling out pulmonary embolism. Also, instead of using a point-scale score proportional to the regression coefficients, typical of other approaches [4-6], the probability of pulmonary embolism is estimated directly from the algebraic sum of the regression coefficients [7]. This allows predicting the clinical probability as a continuous function and estimating precisely likelihood ratios for PE. To facilitate the applicability of the model in clinical settings, easy-to-use software is available for online computation of the clinical probability on palm computers and mobile phones [7].

Assessing the clinical probability of PE helps clinicians choose the more appropriate objective test for diagnosing or excluding PE.

The measurement of D-Dimer — a breakdown product of the cross-linked fibrin clot — is widely used in the investigative work-up of patients with suspected venous thromboembolism [9]. Quantitative assay of D-Dimer, based on rapid ELISA method, has a high sensitivity (in the region of 95%) for venous thromboembolism [9]. Yet, the test features a low specificity (40%) because D-dimer may be raised in a number of conditions other than venous thromboembolism such as acute myocardial infarction, stroke, inflammation, active cancer, and pregnancy. Because of the high sensitivity, a negative quantitative D-dimer test has a high negative predictive value for venous thromboembolism, particularly when associated with a low (<50%) clinical probability. On the other hand, due to the low specificity, a positive quantitative D-dimer test does not modify the pretest (clinical) probability and is, therefore, clinically useless.

Based on the above, if the clinical likelihood of PE is low and the quantitative D-dimer is negative, a diagnosis of PE is unlikely and further investigations are not required. If the clinical likelihood of PE is low and the quantitative D-dimer is positive, further investigations for a range of diagnoses including PE are required. If the clinical probability is other than low, it seems more appropriate to skip D-dimer test and refer the patient directly to the appropriate imaging technique. This may be lung scintigraphy (either ventilation-perfusion or perfusion scintigraphy), or multidetector computed tomography (MDCT) depending on the local availability, medical expertise, and patient's clinical condition. Lung scintigraphy has virtually no contraindications and yields a substantially lower radiation burden than MDCT. The latter is more widely and readily available.

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