Clinical Decision Rules For The Diagnostic Management Of Suspected Acute Pulmonary Embolism: The clinician… rules

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Key words:
- Pulmonary embolism
- D-Dimer
- Clinical decision rules

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Pulmonary embolism (PE) is a major health problem worldwide with an estimated incidence of 23-69 cases per 100,000 people annually[1,2]. The short-term mortality of the disease varies widely, ranging from less than 2% in patients with non-massive PE to more than 95% in patients with cardiorespiratory arrest[3,4], with an average case fatality rate within 2 weeks from diagnosis of approximately 11%[5]. Most patients present with non-specific symptoms (e.g. dyspnea or chest pain) and signs (e.g. tachypnea, tachycardia, or evidence of deep vein thrombosis) and most laboratory, electrocardiographic and radiological findings present low specificity and sensitivity. The complete evaluation of patients with suspected PE involves the performance of computed tomographic pulmonary angiography (CTPA) or ventilation-perfusion ($\dot{V}/\dot{Q}$) scans, both of which involve specialized facilities and the use of radiation and intravenous contrast or radioisotopes[5,6], with significant cost for the healthcare systems. Therefore, the safe exclusion of a diagnosis of PE, based on the evaluation of clinical probability based on clinical decision rules and plasma D-Dimer measurements in patients with low or intermediate clinical probability[6], represents a major clinical challenge[7].

Several clinical decision rules (CDR) have been developed for the evaluation of the pretest clinical probability of PE, the most popular being the Wells rule[8] and the Geneva score[9], that has been more recently revised[10] (Table 1). The major difference between the two CDRs is the presence of a subjective variable in the Wells score (the clinician must consider a possibility of a diagnosis other than PE), whereas the revised Geneva score comprises of objective variables, derived from the patient's history and clinical examination. However, the "classic" Wells and Geneva CDRs assign different points to different variables, providing a possibility for miscalculations from the busy clinician in the emergency department, and simplified scores have been also developed, showing similar performance to the original scores[11,12]. An additional simplification led from the original characterization of "low", "intermediate" and "high" clinical probability, to the dichotomous characterization of "PE likely" or "PE unlikely" (Table 1). A significant addition to the diagnostic management of patients with suspected PE is the use of

TABLE 1. Clinical Decision Rules for the Diagnostic Management of Pulmonary Embolism

Clinical Decision Rules	Points	
	Original version	Simplified version
Wells rule		
Previous PE or DVT	1.5	1
Heart rate >100 beats/min	1.5	1
Surgery or immobilization within 4 weeks	1.5	1
Haemoptysis	1	1
Active cancer	1	1
Clinical signs of DVT	3	1
Alternative diagnosis less likely than PE	3	1
Clinical probability		
PE unlikely	≤4	≤1
PE likely	>4	>1
Revised Geneva score		
Previous DVT or PE	3	1
Heart rate		
75–94 beats/min	3	1
≥95 beats/min	5	2
Surgery or fracture within 1 month	2	1
Haemoptysis	2	1
Active cancer	2	1
Unilateral lower limb pain	3	1
Pain on lower limb deep venous palpation and unilateral oedema	4	1
Age >65 y	1	1
Clinical probability		
PE unlikely	≤5	≤2
PE likely	>5	>2

DVT: deep venous thrombosis; PE: pulmonary embolism

a simple measurement of plasma D-dimer; a normal D-dimer result, measured by ELISA, may exclude PE with a sensitivity of 95%[13]. The combination of a score classifying a patient as "PE unlikely" with a normal D-dimer result can exclude a significant proportion of patients (20-40%) from further evaluation[14]. Computerized systems involving CDRs may further improve the diagnostic yield of CTPA for PE, but they do not tend to be widely accepted by the busy physicians in the emergency departments. Therefore, there is an increased need for simpler CDRs and the simplified Wells and Geneva scores had not been evaluated prospectively and the four scores presented in Table 1 had not been directly compared to each other until recently[15].

In a recent study, Douma and co-workers performed a prospective study aiming to directly compare the diagnostic performance of the 4 CDRs (Wells rule, revised Geneva score, simplified Wells rule, and simplified revised Geneva score)[14]. The authors included 708 consecutive patients (80% outpatients) evaluated in 7 centers in the Netherlands with a suspected first episode of acute PE (i.e. sudden onset of dyspnea, deterioration of existing dyspnea, or sudden onset of pleuritic chest pain) and all 4 CDRs were calculated by a computer-based program. When PE was considered unlikely according to all 4 CDRs in combination with a normal D-dimer result (cut-off <500 μcg/L), PE was excluded and no further testing was performed, whereas all the remaining patients (with at least 1 rule suggesting PE as likely or with increased D-dimer) were further evaluated by CTPA. All patients were followed-up for 3 months for the occurrence of venous thromboembolism [VTE: PE and/or deep venous

thrombosis (DVT)].

The prevalence of PE in this population was 23% (185 patients, of whom 184 had at least 1 positive CDR and/or increased D-dimer). In 169 patients (21%) PE was excluded on the basis of negative CDRs and normal D-dimer, with only 1 patient presenting with PE (0.6%) within the 3 months follow-up. In this patient, the attending physician ordered a CTPA scan despite the negative CDRs and D-dimer, based on clinical suspicion. From the 435 patients in whom PE was excluded by CTPA, seven patients (1.6%) presented with VTE in the 3-month follow-up (1 with PE and 6 with DVT).

The major finding of this study was that all 4 CDRs presented 99.5% sensitivity and 99.5% negative predictive value (NPV) for the exclusion of PE when combined with a normal D-dimer result, missing approximately only 0.5% of PE. However, when used alone, their diagnostic performance was lower, with NPVs ranging from 83% to 87%, suggesting a prevalence of PE of 13-17% in patients classified as «PE unlikely» by the CDRs. Moreover, despite a significant discordance between the CDRs in individual patients (approximately 29% of patients presented discordant results in the 4 rules), only 3.6% presented additionally normal D-dimer and PE was not missed in any of the patients with discordant results. Most importantly, the overall diagnostic performance of all 4 CDRs in characterizing PE as «unlikely» or «likely» was similar, especially in combination with a normal D-dimer assay.

What are the important implications of the evaluation of the 4 CDRs in the study by Douma et al. combined with the previous literature? First, all 4 CDRs performed similarly, practically excluding PE when combined with a normal D-dimer test. Second, clinical rules are no better than D-dimer alone, and may be used only complementary to a reliable (preferably measured by ELISA) D-dimer assay for the exclusion of PE. Third, the simplified rules may be preferred in clinical practice, since they perform similarly to the more demanding original Wells rule and revised Geneva score. Last, but by no means least, clinical judgment remains central in any decisions for further evaluation of patients with suspected PE, since even the very few cases that may be missed by CDRs and D-dimer measurements may be detected by careful physicians.

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