




How can we better predict pulmonary blood clots in patients hospitalised for COVID-19?

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D-dimer threshold at 2590 ng·mL⁻¹ is able to predict pulmonary embolism in COVID-19 patients with clinical deterioration <https://bit.ly/3kYObc3>

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The emergence of coronavirus disease 2019 (COVID-19) has put pressure on health systems around the world [1, 2]. This coronavirus has also questioned much of our medical knowledge, with each day seeing the appearance of a new possible clinical expression of the virus [3]. Although its physiopathology is still poorly understood, the vascular tropism of the disease now seems to be a major pathway [4]. Recent studies highlight the development of a specific pulmonary vascular endothelialitis associated with thrombosis and angiogenesis [5].

A strong association between coronavirus infection and the risk of venous thromboembolism (VTE) was suggested by Chinese authors [6], who described an increase in the blood level of D-dimer (increase associated with an increased risk of death) [7]. A specific coagulopathy was evoked [8], as well as a possible increased risk of VTE. However, it also appeared that COVID-19 may also challenge our usual way to deal with VTE suspicion and management [9]. First, the respiratory impairment of COVID-19 directly impacts the usual modalities of suspicion of VTE. In patients admitted to the emergency department with a respiratory picture compatible with a COVID-19, the symptomatology close to that of pulmonary embolism (PE) may hinder the evocation of alternative diagnoses. The (now classic) secondary respiratory deterioration raises the same question of alternative diagnosis as PE. When VTE is suspected, the pandemic situation makes access to vascular and thoracic explorations more complex, requiring the development of parallel flows for contagious and non-contagious patients. In patients admitted to the intensive care unit (ICU), the issues are even more specific, with the difficulty of diagnosing VTE (and particularly PE) in sedated patients, and the technical difficulty of performing chest imaging in intubated patients with renal failure.

It is in this context in the current issue of the *European Respiratory Journal* that MOUHAT *et al.* [10] report their retrospective analysis concerning the suspicion of pulmonary embolism in COVID-19 patients admitted to a university hospital in a pandemic zone.

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The authors analysed the clinical and biological data of 349 COVID patients admitted in 1 month. Among the 162 patients who underwent a computed tomography pulmonary angiography (CTPA) because of a severe clinical presentation (respiratory rate ≥ 30 breaths·min⁻¹, oxygen saturation measured by pulse oximetry $\leq 93\%$, or rapid clinical worsening), PE was diagnosed in 44 (27.2%) patients, of which 20% were at hospital admission. Two factors were associated with the risk of PE: high D-dimer levels and lack of anticoagulant therapy. The association between PE and the lack of anticoagulant therapy was mainly supported by the inclusion of all PE patients (including PE diagnosed at admission). The authors propose a D-dimer threshold at 2590 ng·mL⁻¹ to predict CTPA-confirmed PE in severe COVID-19 patients, with high accuracy: AUC 0.88 (95% CI 0.809–0.932), $p < 0.001$. Patients with D-dimers above the cut-off of 2590 ng·mL⁻¹ accounted for 36.0% (95% CI 27.5–45.2) of the overall population, 42.6% (95% CI 30.7–55.2) of patients in ICU, and 15.9% (95% CI 9.2–24.9) of patients in conventional COVID wards. While their study is retrospective and as a result exposed patients to heterogeneous management, it gives us an interesting perspective.

Where do we go from here? First, we need to prospectively assess the frequency of PE at admission and the validation of the D-dimer cut-off of 2500 ng·mL⁻¹ to indicate PE to be present in COVID-19 patients. The current work suggests that only one in five PE was diagnosed at admission, which is lower than in another study [11], but in agreement with a recent retrospective study [12]. It also confirms that D-dimers still have a role in the stratification of a patient prognosis, being associated with an increased risk of death (>1000) but also PE (if >2500). The combination of D-dimer results with a clinical prediction rule (as the Geneva [13], the Wells [14], or the YEARS scores [15] proposed in the European guidelines [16]) is still under debate and this also needs prospective validation. Secondly, we need to determine factors associated with hospital-acquired VTE in COVID-19 patients. In the current work by MOUHAT *et al.* [10], most of the PE occurred after admission. Thromboprophylaxis is indicated in any patient admitted for COVID-19 [8], and many authors proposed to increase the dosage of usual parenteral drugs, with the hope to decrease the rate of venous and arterial complications [17], without increasing the bleeding risk. Hence, the risk and benefits of such modified thromboprophylaxis, as well as the potential of pharmacological agents targeting thromboinflammation [18], deserve further analysis.

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