Letter to the Editor

D-dimer cut-off value for pulmonary embolism diagnosis in COVID-19

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We appreciate the valuable comments by van Twist *et al.* (1). We propose an optimized D-dimer cut-off value of 750 ng/mL for diagnosing pulmonary embolism (PE) in acute coronavirus disease 2019 (COVID-19) patients upon hospital admission (2). We acknowledge the valid concerns raised by van Twist *et al.* regarding the methodological aspects of our findings, particularly due to the retrospective nature of our study. As we employed computed tomography pulmonary angiography (CTPA) as the gold standard for diagnosing acute PE, we limited our analysis to COVID-19 patients with documented D-dimer levels who underwent CTPA within 5 days of hospital admission. The 466 patients without a CTPA performed were not clinically diagnosed with PE within 5 days or treated accordingly, but since they did not have the golden standard examination for ruling out, they were not included in the analysis.

In our hospital, we implemented the routine determination of D-dimer levels for all confirmed COVID-19 patients presenting at the emergency ward very early in the pandemic, even preceding national guidelines. This proactive approach may account for the relatively low confirmed rate of PE in COVID patients with known D-dimer levels at 3.9% overall. However, it is noteworthy that among the patients in our study who underwent a CTPA due to elevated D-dimer levels, clinical symptoms, or both, the rate of acute PE diagnoses [29/142; 20.4% (2)] was even higher than those reported in the studies cited by van Twist *et al.* [26/169; 15.4% (3), and 47/333; 14.1% (4)]. This observation diminishes the likelihood of protocol violations, as mentioned by van Twist *et al.* While it is plausible that very severe COVID-19 patients may have passed away before undergoing a CTPA, it is improbable that their D-dimer levels would have fallen below 750 ng/mL, based on insights from other studies (5). Therefore, we believe that excluding these cases is unlikely to have adversely impacted our determination of the D-dimer cut-off value.

van Twist *et al.* advocate for the use of the YEARS algorithm in diagnosing PE among COVID-19 patients (1), suggesting a D-dimer cut-off value of 500 ng/mL in the presence of ≥1 YEARS item: clinical signs of deep vein thrombosis, hemoptysis, and/or if PE is the most likely diagnosis (6). While we also identified a lower cut-off value than the commonly used <1,000 ng/mL as optimal for acute PE diagnosis in COVID-19 patients, we have reservations about implementing the YEARS criteria, which prompted our study. First, we noted no PE diagnoses in the lower D-dimer range (500–750 ng/mL), potentially reducing the

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need for CTPA by 13% without compromising sensitivity, and lowering the risk of overtreatment with anticoagulants and subsequent sequelae (2). Second, although hemoptysis is relatively common in PE patients without COVID-19, it is rare in acute COVID-19 presentations (7). Combining this with another probable diagnosis for respiratory symptoms (acute COVID-19 infection) resulting in a YEARS score of zero, most COVID-19 patients should maintain a D-dimer cut-off value of <1,000 ng/mL. Our study demonstrated that this approach could potentially overlook 6.9% of PE cases (2). Therefore, while we acknowledge the importance of straightforward guidelines in clinical management, we believe that the unique pathophysiology of COVID-19 warrants distinct D-dimer cut-off values for PE diagnosis compared to non-COVID-19 patients.

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Footnote

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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