COVID-19 and Pulmonary Embolism: Diagnostic Imaging Trends

TO THE EDITOR: A recently published editorial by Zuckier et al. (*1*), titled "Diagnostic Evaluation of Pulmonary Embolism During the COVID-19 Pandemic," suggested reverting to a non-ventilation approach for the evaluation of pulmonary embolism (PE) to minimize potential exposure to aerosolized secretions in the nuclear medicine suite.

Although the authors have provided a novel approach to mitigate the risk of aerosolized transmission from coronavirus disease 2019 (COVID-19) patients, the diagnostic efficacy of the algorithm needs to improve. First, the authors have mentioned reducing the number of ventilation scans by rigorous assessment of pretest probability using well-known diagnostic scoring systems such as the Wells criteria, the PE rule-out criteria, and the Geneva scoring system. Although these scoring systems are commonly used to predict PE in the outpatient population, they might not be an appropriate and valid tool to predict the risk of PE in COVID-19 patients who are critically ill or admitted in the intensive care unit, which is attributed to the higher mortality rate (*2–4*). In this context, if not contraindicated, cardiothoracic pulmonary angiography is recommended as the instant diagnostic tool regardless of chest radiography findings (*5*). Consequently, it is crucial to consider patients' hemodynamic instability before approaching the mentioned algorithm.

In the setting of infection with severe acute respiratory syndrome coronavirus 2 and a contraindication to cardiothoracic pulmonary angiography, respiratory distress in COVID-19 patients may preclude an optimal ventilation–perfusion scan procedure. In such cases, we recommend reverting to perfusion-only scintigraphy or bedside critical-care ultrasound as a real-time point of care examination (if the availability of scintigraphy is limited), along with modified scoring system, clinical judgment, and D-dimer assay. Although a positive value for D-dimer does not significantly predict the risk of PE, a negative D-dimer test (<500 ng/mL) has a high negative predictive value when there is a low or intermediate pretest likelihood (*6–8*). A negative result for D-dimer test can reduce the number of imaging modalities, leading to minimized aerosolized secretions in ventilation–perfusion scans.

Marked increase in coagulation parameters including D-dimer level, fibrin degradation products, and fibrinogen are reportedly associated with a higher mortality rate in COVID-19 patients (*3,9*). With an increasing hypercoagulability state in COVID-19 patients in the absence of major predisposing factors (in scoring assessments), such as previous proven deep-vein thrombosis or PE, recent major surgery or trauma, pregnancy, or cancer (which result in a low risk-probability for PE as per the scoring systems), these patients can still probably have PE. According to the criteria of the Prospective Investigative Study of Acute PE Diagnosis, perfusion scintigraphy has inferior diagnostic value than combined ventilation–perfusion scintigraphy in patients with a low pretest probability for PE (*10*), which occurs and is expected more frequently in COVID-19 patients as explained earlier.

Ultimately, a negative perfusion-only scintigraphy result cannot reliably exclude PE in all COVID-19 patients. Other imaging techniques, clinical judgment, and laboratory evaluations are reconsidered to efficiently diagnose PE in these patients.

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REPLY: We wanted to thank Karimzadeh and colleagues for their thoughtful comments on our editorial entitled, "Diagnostic

Evaluation of Pulmonary Embolism During the COVID-19 Pandemic" (*1*). Perforce, any response to an evolving crisis will be based on incomplete data and best judgments. Certainly, in the case of the coronavirus disease 2019 (COVID-19) pandemic, decisions we made in real time were based on the best available information at hand. It is mandatory to stop, reevaluate, and adjust our approach as more information comes to light. We therefore appreciate the constructive comments furnished, as discussed below. By and large, we feel quite comfortable with many of the choices we made at the onset of the COVID-19 surge as they apply to the evaluation of pulmonary embolism.

We certainly agree with the authors that appropriate tools be applied to determine the pretest probability of pulmonary embolism, and we did not mean to be prescriptive in our suggestions, other than recommending that appropriate a priori assessment be performed. Hemodynamic stability is paramount, and no patient should undergo any diagnostic test for which the risk of ill effects would outweigh any potential benefit. We do, however, maintain that in a clinically stable patient, with minimal or no abnormalities on the chest radiograph, a perfusion study is an efficient and rapid method of eliminating the presence of macroscopic pulmonary emboli. Indeed, normal results on perfusion scans were seen in over 85% of patients we studied during the COVID-19 surge, thereby vindicating our approach. We do agree with Karimzadeh and colleagues that in different clinical scenarios, other solutions may become preferable. We must also keep in mind that acute kidney injury has emerged as a possible complication of COVID-19 (*2*); a potential limitation of CTPA is the nephrotoxicity of iodinated contrast medium, precluding its use in these patients.

The final consideration, that COVID-19 patients may have microscopic disease not picked up by perfusion scintigraphy (or CT pulmonary angiography) (*3*), is certainly salient and reinforces the authors' deference to D-dimer levels and clinical judgment. It is interesting that many seriously ill COVID-19 patients are placed on antithrombotic medications to counter their hypercoagulable state and prevent microembolic and microthrombotic phenomena, in and of itself altering the calculus of diagnosis and treatment.

The thrust of our initial editorial was to strongly recommend against use of ventilation scanning during the COVID-19 surge, especially when there are shortages of PCR testing reagents and personal protection equipment and where the status of the patients cannot be ascertained or protection of workers ensured. We suggested, and continue to support the thesis, that when testing for pulmonary embolism is indicated, perfusion scintigraphy alone can serve a useful purpose in screening patients for this disorder.

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