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Diagnosing Pulmonary Thromboembolism in COVID-19: A Stepwise Clinical and Imaging Approach

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The full spectrum for manifestations of novel coronavirus disease 2019 (COVID-19) are still emerging; however; it seems the patients infected by severe acute respiratory syndrome of novel coronavirus 2 are at high risk for developing pulmonary thromboembolism (PTE) (1). Immobilization due to prolonged intensive care unit admission in severely ill patients as well as a hypercoagulable state may play a role. The latter one has been previously described to occur in other severe infections and thought to be triggered by an acute inflammatory state, hypoxia and endothelial cell dysfunction (2). The hypercoagulable state in COVID-19 has been confirmed in a study by Han et al, which revealed higher levels of D-dimer, fibrinogen, and fibrinogen degradation products in comparison to control group. Indeed, PTE has been reported in patients suffering from COVID-19 (2). Moreover, postmortem examination of lungs has revealed occlusion and microthrombosis of small pulmonary vessels (1).

Diagnosis of PTE is challenging in patients with COVID-19. Clinical symptoms and signs including low grade fever, cough and dyspnea are non-specific for PTE. Although raised D-dimer levels have been reported in several articles specially in intensive care unit admitted patients with COVID-19 pneumonia (3), the role of D-dimer in diagnosis of PTE is controversial (1,4,5). Furthermore, findings of unenhanced computed tomography (CT) of lungs, the widely applied modality with high sensitivity(6), are nonspecific for COVID-19. Similarly, manifestations of PTE are nonspecific in an unenhanced CT scan. On the other hand, the increased risk of acute kidney injury in patients suffering from COVID-19 (7), limits the liberal administration of contrast agents and acquisition of the CT angiography of pulmonary arteries. In a large retrospective study of patients admitted with COVID-19, 43.9% of patients had proteinuria and 26.7% had hematuria. The prevalence of elevated serum creatinine, elevated blood urea nitrogen and estimated glomerular filtration rate under 60 ml/min/1.73m2 were 14.4, 13.1 and 13.1%, respectively, with acute kidney injury occurring in 5.1% patients (7). The risk of contrast-induced nephropathy (CIN) may thus be higher in shocked patients with severe COVID-19 since multiple risk factors, including dehydration, acute tubular necrosis, direct invasion of renal tissue by severe acute respiratory syndrome of novel coronavirus 2, and cytokine storm (8) may exacerbate the effects of contrast on renal function.

Thus, a rational and stepwise clinical and radiologic evaluation is necessary for early detection of PTE while limiting the risk of CIN. Clinically, it is important to identify potential manifestations of PTE complicating the COVID-19 course, such as hemoptysis, respiratory deterioration and acute onset unexplained tachycardia and hypotension. Electrocardiography may also be helpful, especially when findings suggestive of PTE are present such as S1Q3T3 pattern.

A stepwise imaging approach is recommended to limit the risk of CIN. Color Doppler ultrasound of both lower extremities may be the first imaging step. Several cases of deep vein thrombosis on Doppler ultrasound have been reported in patients with COVID-19 (4). In the presence of hemodynamic compromise with clinical suspicion for PTE, signs of right ventricular pressure overload and dysfunction on echocardiography combined with measurement of markers of right ventricular stretch such as raised levels of brain natriuretic peptide or N-terminal-pro brain natriuretic peptide and elevated plasma troponin concentrations may be useful for diagnosis of large PTEs (9).

The perfusion-ventilation scan seems to have limited role. Several studies have indicated that the ground glass opacities and consolidation are detected in majority of the patients with COVID-19 (10,11). On the other hand, a lung scintigraphy is considered nondiagnostic in the presence of a pathologic chest imaging and concurrent ventilation defect according to PIOPED criteria (12).

CT angiography should be preserved for patients with high index of suspicion and negative sonography. To perform CT angiography in patients with COVID-19, it is advisable that established strategies to reduce the risk of CIN including hydration with normal saline before and after contrast injection, selection of a non-ionic, low or iso-osmolar contrast agent and limiting the dose and volume of the injected contrast medium are undertaken.

In conclusion, hospitalized patients with severe COVID-19 are at high risk of PTE. Performing CT angiography to diagnose PTE is limited by an overall high propensity for CIN in patients admitted with severe COVID-19. Careful, detailed evaluation of the clinical course to identify signs and symptoms suggestive of PTE complicating the course of the disease, assessment with electrocardiography and laboratory tests suggestive of myocardial injury and stretch, followed by a stepwise imaging approach would aid in the diagnosis of PTE while reducing the risk of CIN.

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