“Mosaic Perfusion Pattern” on Dual-Energy CT in COVID-19 Pneumonia: Pulmonary Vasoplegia or Vasoconstriction?

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Editor:
Finding dilated subsegmental vessels at dual-energy CT (DECT), Dr Lang and colleagues (1) proposed inflammatory-mediated impaired hypoxic pulmonary vasoconstriction (HPV) with overactive regional vasodilation to explain coronavirus disease 2019 (COVID-19) hypoxemia in their article in the June issue of Radiology: Cardiothoracic Imaging. However, this was not associated with increased pulmonary blood volume (PBV) in consolidated areas; instead, most (96%) patients had decreased peripheral perfusion corresponding to peripheral lung opacities, and only one-third demonstrated a halo of increased perfusion surrounding peripheral opacities. If HPV loss occurs in consolidated regions, PBV should have increased, producing hyperemia rather than oligemia. We instead propose an angiotensin II–mediated, nonimmune, noninflammatory mechanism to explain the mosaic perfusion pattern.

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection of alveolar epithelium results in downregulation of angiotensin-converting enzyme 2 (ACE-2) and ACE-angiotensin II-angiotensin II type 1 receptor pathway overactivity, producing heterogeneous small vessel vasoconstriction (2) and recruitment of segment/subsegmental vessels with relatively less vasoconstriction, causing regional overperfusion, reduced diffusion capacity, increased shunt and hypoxia, even in the absence of radiologically evident lesions. Where precapillary constriction is intense (due to high local concentration of angiotensin II), PBV would decrease, reducing perfusion even in normal lung or may produce wedge-shaped areas of pulmonary deficit on DECT (3). In areas of ineffective constriction due to lower concentrations of angiotensin II, capillary filtration pressure would increase, resulting in capillary stress failure and hydrostatic interstitial edema with patchy ground-glass opacities (GGOs) on CT. Disruption of the alveolocapillary membrane develops, with SARS-CoV-2 directly infecting endothelial cells. Endothelitis with intracapillary fibrin-microthrombi blocks alveolar capillaries and further decreases perfusion within the areas of GGOs and consolidation but, with dilatation of proximal subsegmental arterioles, along with a halo of increased perfusion surrounding regions of consolidation. Thus, in COVID-19 pneumonia as the GGOs worsens to consolidation, oligemia or hyperemia in the area of consolidation is largely determined by the balance between the endothelialitis-mediated capillary obstruction (in consolidation regions) versus angiotensin II-mediated regional vasoconstriction (in healthy lung regions) (3,4).

Our theory is supported by high incidence of raised PVR and right ventricular dysfunction in early COVID-19 disease (5) and reports of lung perfusion deficits that do not overlap with GGOs or consolidation and are not associated with major vessel occlusion (3). We believe determining the predominant pathophysiology—heterogeneous pulmonary vasoconstriction versus pulmonary vasoplegia—has treatment implications: pulmonary vasiconstrictors versus vasodilators.

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Response
From
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We read the letter “Mosaic Perfusion Pattern” on Dual-Energy CT in COVID-19 Pneumonia: Pulmonary Vasoplegia or Vasoconstriction?” with great interest. The angiotensin II–mediated, nonimmune, noninflammatory mechanism proposed by the authors is well aligned with our imaging observations. First, the authors suggested that the recruitment of segmental/subsegmental vessels via angiotensin II-angiotensin II type 1 receptor pathway may lead to regional overperfusion. We noted increased regional perfusion toward areas of diseased lung on DECT imaging, described as a “hyperemic halo” in 36% of cases (1). Furthermore, we described unusual dilatation of vessels proximal to and within pulmonary opacities, and dilated vessels along the pleura and fissures. Consistent with the
authors’ proposed mechanisms, our radiologic observations are suggestive of abnormal vessel recruitment and abnormal shunting of blood toward areas of poor gas exchange, possibly explaining the pronounced hypoxemia seen in a subset of patients with COVID-19 pneumonia.

Second, the authors suggest endothelialitis with intracapillary fibrin-microthrombi as well as capillary stress failure as a possible explanation for the GGO and consolidation seen in COVID-19 pneumonia. This again is compatible with our vascular findings suggesting that a pronounced underlying vascular process may be at play. GGO may in part be a result of capillary leakage from endothelial injury and increased hydrostatic pressure from abnormal hyperperfusion, concordant with the authors’ proposal and our prior published correspondence (2,3). GGOs may subsequently develop into consolidation as the result of ongoing accumulation of fluid, inflammatory cells, and cellular debris. The “hyperemic halo” around the areas of consolidation may therefore represent evolving regions of diseased lung and may reflect earlier stages of infection characterized by hyperperfusion. Importantly, decreased iodine distribution within areas of consolidation is a nonspecific finding that can be seen in other pneumonias, pulmonary infarcts, and noninfectious inflammatory conditions. The imaging and clinical findings of COVID-19 pneumonia likely result from a combination of several pathologic/pathophysiologic mechanisms.

Finally, the authors broach an interesting point regarding the high incidence of elevated PVR and right ventricular dysfunction in patients with COVID-19. The vascular abnormalities reported in our article, including dilated vessels and mosaic attenuation and perfusion, were not limited to areas of diseased lung. This suggests that shunting and alterations in pulmonary perfusion is diffuse and that the cumulative effect may lead to elevated PVR and right ventricular dysfunction as the authors reported.

We appreciate the authors’ letter and think their proposed underlying mechanisms are congruent with our findings and may help explain development of severe hypoxemia in a subset of patients with COVID-19 pneumonia. Finally, these thrombogenic and direct vascular/endothelial abnormalities may also contribute to multiorgan involvement in COVID-19 cases.

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