Hypoxaemia related to COVID-19: vascular and perfusion abnormalities on dual-energy CT

Studies have shown that some patients with coronavirus disease 2019 (COVID-19) and acute hypoxaemic respiratory failure have preserved lung compliance, suggesting that processes other than alveolar damage might be involved in hypoxaemia related to COVID-19 pneumonia.[1] The typical imaging features of COVID-19 pneumonia, including peripheral ground-glass opacities with or without consolidation, are also non-specific and can be seen in many other diseases.[2] There has been increasing attention on microvascular thrombi as a possible explanation for the severe hypoxaemia related to COVID-19.[3,4]

Dual-energy CT imaging can be used to characterise lung perfusion and is done as part of the standard protocol for imaging pulmonary embolism at our institution. Three patients with COVID-19, as confirmed by nasopharyngeal RT-PCR at our hospital, who did not have a history of smoking, asthma, chronic obstructive pulmonary disease, or other pulmonary conditions, underwent dual-energy CT imaging for elevated concentrations of D-dimer (>1000 ng/mL) and clinical suspicion of pulmonary emboli. Although no pulmonary emboli were observed in these individuals, we noted striking perfusion abnormalities that have not been previously described; in retrospect, at least nine other COVID-19 cases also shared these findings. In addition to the typical CT features of COVID-19 pneumonia,[2] we observed considerable proximal and distal pulmonary vessel dilatation and tortuosity, predominately within, or surrounding, areas of lung opacities. Here, we present the first published images from dual-energy CT imaging of COVID-19 pneumonia that show profound vascular and perfusion abnormalities (figure; appendix).

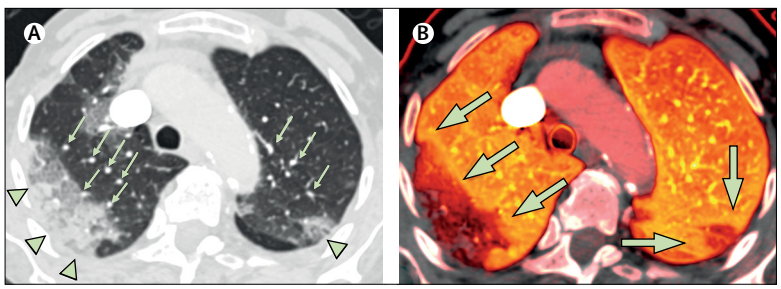

***Figure*: Dual-energy CT in a patient with COVID-19 pneumonia without evidence of pulmonary emboli**
Patient 1, an 87-year-old woman with a history of fever and cough for 5 days, was found on the floor of her nursing home. On admission to hospital, the patient required a non-rebreather mask with a flow rate of 15 L/min to maintain an oxygen saturation of 85%; intubation was not pursued as the patient's status was comfort measures only. (A) There is a large area of peripheral ground-glass opacity and consolidation within the right upper lobe and smaller ground-glass opacity in the posterior left upper lobe (green arrowheads), which are accompanied by dilated subsegmental vessels proximal to, and within, the opacities (green arrows). (B) The accompanying image of pulmonary blood volume shows corresponding wedge-shaped areas of decreased perfusion within the upper lobes, with a peripheral halo of higher perfusion (green arrows). COVID-19=coronavirus disease 2019.

Three major findings from dual-energy CT were observed on the images of pulmonary blood volume perfusion: preferentially increased perfusion of the lungs proximal to areas of lung opacity, decreased areas of peripheral perfusion corresponding to peripheral lung opacities, and a halo of increased perfusion surrounding peripheral areas of consolidation. The observed pulmonary vascular dilation might be due to relative failure of normal, physiological hypoxic pulmonary vasoconstriction in the setting of overactivation of a regional vasodilatation cascade as part of a dysfunctional and diffuse inflammatory process. Additionally, the mosaic perfusion pattern did not correspond to findings of bronchial wall thickening or secretions, making airway disease as the main underlying cause of hypoxaemia unlikely. Therefore, these perfusion abnormalities, combined with the pulmonary vascular dilation we observed, are suggestive of intrapulmonary shunting toward areas where gas exchange is impaired, resulting in a worsening ventilation–perfusion mismatch and clinical hypoxia. Although peripheral opacities with hypoperfusion can be seen in pulmonary infarction, no pulmonary emboli were observed in any of the studies, and segmental increased perfusion to areas of infarction would be very atypical. Furthermore, a peripheral halo of increased perfusion has not been described in pulmonary infarction, but has been described once previously in a case of bacterial pneumonia.[5] However, blood and sputum cultures were negative in the three patients with COVID-19 at our hospital and did not suggest bacterial coinfection. It might be possible that the inflammatory response to COVID-19 resembles more of a bacterial infection than a viral infection. Overall, the combination of these imaging findings is novel for COVID-19 pneumonia.

Treatment for acute respiratory failure in patients with COVID-19 is challenging in part because of little understanding of the underlying pathophysiology. Our findings are atypical for acute respiratory distress syndrome or thrombotic vascular disease and point to a possible central role for previously underappreciated pulmonary vascular shunting. More detailed assessments of vascular and perfusion changes in patients with COVID-19 are urgently needed.

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Ventilation-Perfusion Mismatches Common With COVID-19-Related Hypoxemia

By Will Boggs MD

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NEW YORK (Reuters Health) - Ventilation-perfusion mismatches in the lungs contribute to hypoxemia in patients with COVID-19, researchers report.

"Our findings suggest that one cause of hypoxemia in patients with COVID-19, even in cases where lung compliance is relatively preserved, might be a dysfunction of pulmonary vessel vasoregulation, leading to ventilation-perfusion (V/Q) mismatches," Dr. Brent P. Little from Massachusetts General Hospital in Boston told Reuters Health by email.

Dr. Little and colleagues used dual-energy CT imaging to characterize lung perfusion in three patients with COVID-19 who presented with elevated concentrations of D-dimer and clinical suspicion of pulmonary emboli.

No pulmonary emboli were observed but there were striking perfusion abnormalities that have not been described previously. The major findings included preferentially increased perfusion of the lungs proximal to areas of lung opacity, decreased areas of peripheral perfusion corresponding to peripheral lung opacities, and a halo of increased perfusion surrounding peripheral areas of consolidation.

"In other types of pneumonia and many other lung diseases, 'hypoxic vasoconstriction' occurs - vessels supplying areas of abnormal lung temporarily constrict, decreasing flow to areas where oxygenation is low and increasing flow to less affected parts of the lungs," Dr. Little explained. "In our CT scans of patients with COVID-19, the reverse often seems to be true: vessels both within and adjacent to areas of abnormal lung are dilated and vessels within less involved lung are smaller in diameter."

"We also found areas of very decreased flow within the outer portions of the lungs, which might represent lung that is too involved by pneumonia to be perfused, or where the vessels are damaged or contain small thrombi," he said. "Interestingly, a rim of increased flow and dilated vessels around these areas is frequently present, suggesting that in spite of the peripheral lung perfusion defects, blood flow is still being shunted toward these abnormal regions. We also found abnormally dilated vessels at the lung periphery, suggesting that distal small vessel shunting might be occurring."

The authors identified, in retrospect, at least nine other COVID-19 cases that shared these findings, according to the online report in The Lancet Infectious Diseases.

These perfusion abnormalities, combined with considerable proximal and distal pulmonary vessel dilatation, are suggestive of intrapulmonary shunting toward areas where gas exchange is impaired, resulting in a worsening ventilation-perfusion mismatch and clinical hypoxia.

"Vascular dysfunction may play a central role in the pathophysiology of COVID-19," Dr. Little said. "While recent reports have focused on the thrombogenic effects of the infection, including frequent pulmonary embolism, the effects on the pulmonary vasculature may extend well beyond thrombosis, which might not even be the most important feature of the disease."

"Although a V/Q mismatch can be seen in other lung disease, including ARDS (acute respiratory distress syndrome), COVID-19 pneumonia may show earlier, more severe, or more frequent mismatching than occurs in other diseases," he said. "Microvascular damage and perhaps thrombosis, as has been suggested by some recent pathology reports, may also be occurring."

"Although our findings cannot adjudicate the precise mechanisms, we believe that the topic of pulmonary vascular dysfunction in COVID-19 deserves much more study, and we hope to prompt more investigation with our report," Dr. Little said.

SOURCE: https://bit.ly/2ygqGb7 The Lancet Infectious Diseases, online April 30, 2020.

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