Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Time to move away from an oxygen-centric model of pulmonary infarction?

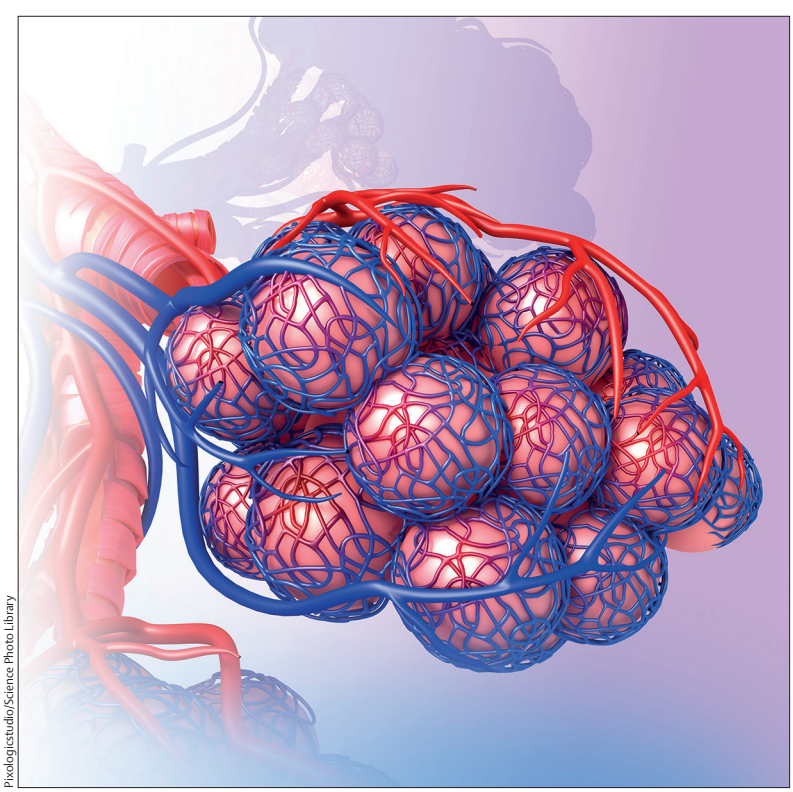
Authors' reply

We would like to thank Robin Cherian and Bharatendu Chandra for commenting on our tricompartmental model for severe COVID-19. To briefly summarise, in our Series paper in *The Lancet Respiratory Medicine*, we placed an emphasis on the extensive immunothrombosis of the vascular compartment closely juxtaposed to the alveolus that is the target of SARS-CoV-2 alveolitis.[1] Specifically, this extensive virally-mediated alveolar-centric pathology with perialveolar inflammation triggers immunothrombosis in the involved capillary networks, but also in the small adjacent arteriolar and perialveolar venular circulation. Because the terminal bronchiolar circulation anastomoses with the alveolar network, then this portal circulation in its terminal branches can also be affected by the disease process, although further pathological studies are needed to clarify this mechanism. Ultimately, this immunothrombosis is a homoeostatic mechanism aimed at constraining the SARS-CoV-2 virus, and it might fail in severe COVID-19 with the development of RNAaemia and severe systemic consequences.

Cherian and Chandra point out that the low levels of extraction of oxygen from the alveolus following pulmonary embolism indicates that hypoxia is not a mechanism of injury. However, the initial event in severe COVID-19 pneumonia appears to be an active viral alveolitis, and like any pneumonic process, it certainly causes hypoxia. Therefore, an oxygen-centric model for pulmonary infarction is logical in severe COVID-19 compared with isolated pulmonary embolism.

Cherian and Chandra raise the issue that right-to-left shunting of deoxygenated blood can contribute to hypoxaemia, which we propose is primarily caused by alveolitis and immunothrombosis, but we agree that extensive immunothrombosis in the juxta-alveolar vessels might be an additional factor contributing to shunting of deoxygenated blood.

Cherian and Chandra suggest that alveolar haemorrhage resulting from increased flow into the alveolus from the higher-pressure bronchial artery (systemic pressure) is a contributory factor in pulmonary infarction, which historically has been a proposed mechanism. However, interesting insights come from patients who have had a lung transplant and in whom the bronchial artery is absent.[2] The increased severity of COVID-19 in these patients coupled with the high incidence of pulmonary infarction in patients who have had a pulmonary transplant and who have pulmonary embolism highlights the unique and rarely-discussed role of the bronchial artery in preventing pulmonary infarction, and supports our tricompartmental model, whereby we attribute infarction in COVID-19 to combined alveolitis and bronchial artery occlusion.[3]



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We declare no competing interests.

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1 McGonagle D, Bridgewood C, Meaney JFM. A tricompartmental model of lung oxygenation disruption to explain pulmonary and systemic pathology in severe COVID-19. *Lancet Respir Med* 2021; **9:** 665–72.

2 Krivokuca I, van de Graaf EA, van Kessel DA, van den Bosch JMM, Grutters JC, Kwakkel-van Erp JM. Pulmonary embolism and pulmonary infarction after lung transplantation. *Clin Appl Thromb Hemost* 2011; **17:** 421–24.

3 Verleden GM, Godinas L, Lorent N, et al. COVID-19 in lung transplant patients: a case series. *Am J Transplant* 2020; **20:** 3234–38.

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