LETTER TO THE EDITOR

Ventilation-perfusion inequality in COVID-19 pneumonia

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TO THE EDITOR: COVID-19 pneumonia is unusual in the severity of the hypoxemia relative to the degree of atelectasis or consolidation observed in the lung (1). To explore this further, Busana et al. (2) recently reported findings for five patients with severe COVID-19 in whom the fraction of nonaerated lung tissue had been quantified by computed tomography. They assumed that the shunt flow fraction was proportional to the nonaerated lung fraction, and sought to identify ventilation-perfusion (V/Q) distributions for the aerated element of the lung that would generate the observed arterial PCO2 and PO2 values. They found that a large fraction of the blood flow was probably distributed toward regions with very low V/Q, and that overall the results were suggestive of high V/Q inequality.

Although the authors should be congratulated for making such observations on these patients, there are several aspects of the analysis that give rise to concern. The first is that the authors considered that any randomly generated V/Q distribution that predicted values for arterial PCO2 and PO2 to within 10% of the observed values was a potential solution. Although this is approximate at best, of greater concern is that the predicted arterial PCO2 and PO2 values did not scatter around the true value, but rather they were all grouped away from the true value in the direction of higher arterial PCO2 and PO2 (Fig. 6). This suggests that the authors’ methodology for identifying V/Q distributions to describe the patient data was not particularly successful.

The second problem is physiological. In the modeling of Busana et al. (2), regions of very low V/Q in the lung were required to ensure that the alveolar PO2 was sufficiently low so that it could not fully oxygenate the blood. A corollary is that the alveolar PN2 has to be relatively high. However, the inspired O2 fraction was high for all patients, and thus the inspired PN2 has to be some 100 s of mmHg lower than in the low V/Q regions. In these extremely poorly ventilated regions where alveolar PN2 is much higher, it is inconceivable that N2 will not diffuse significantly both into the blood and retrogradely into the airways. This violates an assumption made implicitly in the model of Busana et al. (2) that all N2 exchange occurs via convection. In particular, an equal convective flow of N2 into and out of all alveolar units is used to generate the relationship between the inspired and expired alveolar ventilation, which, in turn, is required for the derivation of the exact form of the alveolar gas equation (see item 2.2 under Computational Model). Although in many cases this approximation is reasonable, it will break down when both diffusion gradients are very high and convective flows (alveolar ventilation) are very low, as is the case here.

Busana et al. (2) concluded that “shunt alone cannot completely account for the hypoxemia and a significant V/Q abnormality must be present in COVID-19.” In contrast, we consider it likely that their starting assumption that the shunt blood flow fraction is proportional to the nonaerated lung fraction is incorrect. Damage to the pulmonary vascular endothelium by SARS-CoV-2 (3, 4) is likely to impair hypoxic pulmonary vasoconstriction and contribute to a shunt fraction significantly greater than otherwise expected. A higher shunt flow fraction then obviates the need for the extreme V/Q distributions (and improbable alveolar PN2 values) postulated by the modeling of Busana et al. (2).

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