Critical Care

LETTER

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The knowns and unknowns of perfusion disturbances in COVID-19 pneumonia

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Editor,

Ball et al. [1] recently proposed a thoughtful quantitative analysis of gas and blood distribution in the lungs of patients with severe COVID-19 pneumonia. The paper offers some interesting cues that we consider worth discussing.

First, the images of dual-energy CT scan (DECT) were used as surrogates of the ventilation and perfusion distribution in the lung. However, other imaging techniques, like scintigraphy and SPECT, might be more suitable for this task. Indeed, while perfusion is likely accurately depicted by DECT, *ventilation* is not. Indeed, for at least two reasons, the gas content measured by this technique (notably during tidal breathing and not at constant airway pressure) may not represent a good surrogate of the distribution of ventilation:

1. Airway closure may dissociate the instantaneous gas volume from the actual ventilation, and the phenomenon may be more common than currently thought [2];
2. The opening pressures cannot be investigated by a single CT scan [3]. It follows that undetected recruitability (possibly nonlinear along the pressure–volume curve) may contribute to the uncoupling between measured gas volume and alveolar ventilation.

This leads, in our opinion, to some inconsistencies. Most importantly, in Fig. 4, the authors show a plot reasonably inspired by the V_A/Q_T distributions obtained with the multiple inert gas elimination technique. Unfortunately, such distribution is likely far from what we may expect from COVID-19 pneumonia. Indeed, the displayed distributions are essentially centered on a gas–blood volume ratio ~ 1. However, as we have shown in our theoretical model [4], such distribution (coupled with the relatively low shunt fraction reported in Table 2) is not compatible with the severe hypoxemia observed in these patients.

As a side note, considering that the analysis performed by Ball et al. excluded large vessels, one may wonder how the presence of abnormal vasodilation and vascular anastomoses [5] would affect their results. Indeed, *non-functional* vessels in a "gas-rich" region may escape the definition of shunt used by the authors.

Conclusions

The impact of perfusion alterations on gas exchange in COVID-19 is far from being understood. Despite the aforementioned limitations, Ball et al. must be congratulated for their effort in reporting compelling data that represent a smart step forward in the understanding and, most importantly, in the quantification of the problem.

This comment refers to the article available online at https://doi.org/10.1186/s13054-021-03610-9.

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Reply to:The knowns and unknowns of perfusiondisturbances in COVID-19 pneumonia

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We would like to thank Dr. Busana and Dr. Giosa for their interest in our study [1] and for giving us the opportunity to expand the discussion regarding disturbances of lung perfusion in COVID-19 patients. They highlighted the differences between ventilation and static aeration as assessed by CT; questioned the interpretation of our gas:blood ratio distribution plots and the definition of shunt, comparing our in vivo results with those of their computational theoretical model [4]. As per local practice during the COVID-19 pandemic, CT scans were acquired during breath-hold and we used lung aeration to define shunt, dead space, and non-aerated/non-perfused areas. Lung aeration may be considered as a potential surrogate of ventilation, especially when protective tidal volume and limited inspiratory plateau pressure are used, as in the case of COVID-19 mechanically ventilated patients [6]. In this context, it seems reasonable to assume that non-aerated areas are also non-ventilated and that aerated regions receive a certain amount of ventilation, especially given the small extent of hyperaeration and poor recruitment with application of PEEP observed in these patients [7]. The pulmonary gas:blood volume ratio was defined as:

$$\text{Gas: Blood volume ratio} = \frac{f_A \cdot \overline{PBV}}{PBV \cdot \overline{f_A}}$$

namely as the ratio of mean-normalized gas fraction to mean-normalized pulmonary blood volume: based on this definition, the values of the ratio are centered around 1 in each patient and cannot be directly translated into V'_A/Q'_T without knowing the cardiac output and alveolar minute ventilation. Such a ratio allows within-patient comparisons of the relative distribution of aeration and perfusion. We excluded only large lung vessels from the analysis: the vasodilation of peripheral vessels affects V'_A/Q'_T at an anatomical scale well below the size of one CT voxel [8]: voxels comprising dilated vessels and patent alveoli would have an intermediate CT attenuation value and a high pulmonary blood volume, corresponding to our "*gas:blood ratio < 1*" compartment.

Despite several technical limitations of the technique we proposed, our overall interpretation of the data is that in the early stages of the disease, hypoxia is explained by low V'_A/Q'_T responsive to higher inspiratory oxygen fractions and non-invasive respiratory assistance, while also by increased true shunt in the late stages requiring invasive mechanical ventilation.

In conclusion, we believe that our data should not be interpreted as in contrast with your theoretical model, but rather could represent its confirmation and an attempt of explaining in vivo gas-exchange changes in critically ill patients with severe COVID-19 pneumonia.

Abbreviations
DECT: Dual-energy CT scan; SPECT: Single photon emission computed tomography; V_A/Q_T: Ventilation–perfusion distribution.

Acknowledgements
None.

Authors' contributions
Both authors participated in the writing of the present letter.

Funding
NA.

Availability of data and materials
NA.

Declarations

Ethics approval and consent to participate
NA.

Consent for publication
All authors approved the manuscript in the current form.

Competing interests
The authors have no conflicts of interest to disclose.

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Received: 22 July 2021 Accepted: 23 July 2021
Published online: 28 September 2021

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