Reviewer's report

Title: The effect of changing ventilator settings on indices of ventilation inhomogeneity in small ventilated lungs

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Reviewer: Ola Hjalmarson

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General
The object of this work was to evaluate the effect of changing positive inspiratory pressure (PIP) at mechanical ventilation on some common indices of distribution of ventilation or ventilation inhomogeneity in theory and in animal studies.

The authors are a well-known and experienced group in neonatal pulmonary research. They are familiar with the methods they have used in this study. The methods are well suited and they have been described previously. The results are well presented and easy to follow.

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

Discretionary Revisions (which the author can choose to ignore)

There are two ways to see the problem of the VD/VT and VT/FRC dependency of the indices. The authors have adopted one of them: the dependency of the indices on the ratios mentioned is a disadvantage and a source of error when trying to interpret the indices as markers of ventilation inhomogeneity in the periphery of the lungs. This is true and the authors have demonstrated it both in theory by citing algorithms, and in computer simulations, and animal experiments.

Another way to look at the problem is to regard the indices to express the efficiency of the vital respiratory function to mix fresh inspired gas with the lung gas which constitutes the FRC. Several physical and physiological mechanisms are involved and can influence this function, e.g. uneven ventilation, alveolar size, flow rate and size of anatomical dead space in relation to tidal volume and tidal volume in relation to FRC. Although indices can be constructed to stress some components more than others it must be understood that gas mixing is a complex function and the measures we use cannot focus on one mechanism only. As an optimal gas mixing is a prerequisite for optimal gas exchange, any impairment of this function may be harmful, regardless if its cause is an increased dead space, low tidal volume, high breathing frequency, deformation of the airways or some other factor. The importance of measuring gas mixing efficiency by wash-out methods is that this function can be quantified, not that a certain cause can be identified.

The manuscript highlights the importance of PIP for the efficiency of gas mixing in the lungs, or, in other words, that gas mixing efficiency may change when ventilator settings are changed. In my view, the value of the paper would increase if the authors reasoned from a gas mixing perspective instead of from that of ventilation homogeneity. It would also lead to an interesting discussion about how to optimise ventilatory settings from a gas mixing perspective and, most likely, to further research in this interesting and important area.

What next?: Accept after discretionary revisions

Level of interest: An article whose findings are important to those with closely related research interests
Quality of written English: Acceptable

Statistical review: No

Declaration of competing interests:
I declare that I have no competing interests