

CORRESPONDENCE



Anatomical, physiological and clinical similarities and differences in ARDS physiological subtypes

Ajay Kumar Jha*

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This letter is in response to an article by Chiumello et al. recently published in *Intensive Care Medicine* [1]. This paper compared respiratory mechanics in acute respiratory distress syndrome (ARDS) phenotypes and observed several interesting clinico-physiologic contradictions. However, their physiological justification needs some more introspection. ARDS due to coronavirus disease 2019 (COVID-19) had a lower P/F ($\text{PaO}_2/\text{FiO}_2$) ratio than compliance-matched-ARDS despite having a lower non-aerated lung volume. Furthermore, venous admixture was also noted in COVID-19-ARDS patients with low non-aerated lung fraction. Ventilation perfusion mismatch due to low-ventilation/perfusion (V/Q) ratio leads to venous admixture. In COVID-19-ARDS, we expect a higher V/Q ratio due to pulmonary microthrombosis and the higher aerated lung fraction [2]. Even then, segments of the lung may develop low V/Q areas due to diversion of blood from thrombotic vessels to normal vessels. However, this diversion may further increase segments with high V/Q ratio and subsequent increase in alveolar dead space and that was surprisingly not different in COVID-19-ARDS compared to compliance-matched ARDS. Lung with a higher fraction of high V/Q ratio rarely leads to hypoxemia and low P/F ratio because it may get compensated by high minute ventilation during spontaneous or intermittent mandatory ventilation. However, in this study, the authors used matched cohorts of ARDS patients with controlled ventilation. It is likely that controlled ventilation in COVID-19-ARDS with compliant lung and a high V/Q ratio could have produced hypoxemia and low P/F. Notably, COVID-19-ARDS is known

to induce ventilatory drive more than the ARDS due to other causes and minute ventilation is generally much higher when patients are allowed to breathe spontaneously during mechanical ventilation. Additionally, ventilatory ratio could have been significantly higher in COVID-19-ARDS than compliance-matched-ARDS in non-paralyzed patients.

PaCO_2 is also expected to rise if minute ventilation compensated higher V/Q segments is undone by controlled minute ventilation [3]. Therefore, mechanical, physiological and clinical correlation between different ARDS physiological subtypes should have been done in non-paralyzed patients or at least should have been performed before and after use of neuromuscular blocking agents (NMBA). Similarly, despite substantial differences in the aerated lung volume compared to P/F-matched-ARDS, alveolar dead space and ventilatory ratio were almost similar in COVID-19-ARDS. A higher ventilatory ratio (1.76 vs. 1.72) and a lower alveolar dead space (0.23 vs. 0.29) in COVID-19-ARDS compared to P/F-matched ARDS were also noticeable.

Additionally, incremental positive end expiratory pressure (PEEP) in non-paralyzed mechanically ventilated ARDS patient leads to reduction in minute ventilation and it generally produces an exaggerated effect in poorly compliant lung. Therefore, the effect of higher PEEP on compliance and minute ventilation in intermittent ventilatory mode and controlled ventilatory mode may have divergent effects in patients with high and low compliance. Dissociation in compliance and P/F ratio without an appreciable increase in alveolar dead space after PEEP test in COVID-19-ARDS was equally surprising. Interestingly, compliance predicted mortality better than P/F ratio, alveolar dead space and ventilatory ratio in all three

*Correspondence: drajaykja@rediffmail.com

Department of Anaesthesiology and Critical Care, Jawaharlal Institute of Postgraduate Medical Education and Research, Pondicherry, India

ARDS cohorts. Nevertheless, similar to compliance, an increase in ventilatory ratio and dead space ventilation has also been associated with an increase in mortality [4]. Study of anatomical, physiological and clinical properties of ARDS physiological subtypes in different stages of ARDS during controlled ventilation under the effect of NMBAs may not be considered a pragmatic approach. Additionally, NMBAs are rarely used in mild to moderate ARDS and are only preferred in severe ARDS patients with refractory hypoxemia and patient-ventilator asynchrony. Moreover, use of NMBA has not been associated with improvement in clinical outcomes or prognosis in ARDS [5].

A further interpretation of respiratory mechanics and clinical parameters based on venous admixture, alveolar dead space and ventilatory ratio matched ARDS cohorts in COVID-19 and non-COVID-19 patients would have been interesting.

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Compliance with ethical standards

Conflicts of interest

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