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LETTER



Physiological dead space ventilation, disease severity and outcome in ventilated patients with hypoxaemic respiratory failure due to coronavirus disease 2019

Francesco Vasques¹, Barnaby Sanderson¹, Federico Formenti^{2,4}, Manu Shankar-Hari^{1,3} and Luigi Camporota^{1,2*}

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Dear Editor,

The severity of acute hypoxemic respiratory failure (AHRF) in Coronavirus Disease 2019 (COVID-19) correlates poorly with lung weight and lung mechanics, leading to the proposal of phenotypes that may be associated with similar degree of hypoxaemia but different lung volume, weight, and compliance [1]. The alteration of the pulmonary vascular tone and immune thrombosis of the alveolar capillaries [2] may account for these pathophysiological characteristics and for the high physiological dead space observed in these patients.

To describe estimated indices of physiological dead space—and their association with respiratory mechanics, severity of hypoxaemia, biomarkers, and outcomes—we performed a retrospective analysis of adult patients with COVID-19 respiratory failure requiring mechanical ventilation in four medical Intensive Care Units (ICU) within Guy's and St Thomas' NHS Trust—London, UK (Ethics reference: 10,796).

We used the recorded values at the time of worst PaO₂/FiO₂ observed on the day of critical care admission. Continuous variables were compared using Mann–Whitney

U test. This cohort included 213 patients (73% males), mean (95%CI) age 56 (54–57) years, and PaO₂/FiO₂ 128 (121–135) mmHg. When subdivided in four groups based on cut-off PaO₂/FiO₂ of 150 mmHg and compliance of 40 mL/cmH₂O; 72% (*n*=154) had PaO₂/FiO₂<150 mmHg, of these, 112 (73%, or 53% of the overall cohort) had compliance<40 mL/cmH₂O (eTable 1). The mean (95%CI) estimated physiological dead space fraction [3] was high in the entire cohort at 0.53 (0.51–0.56).

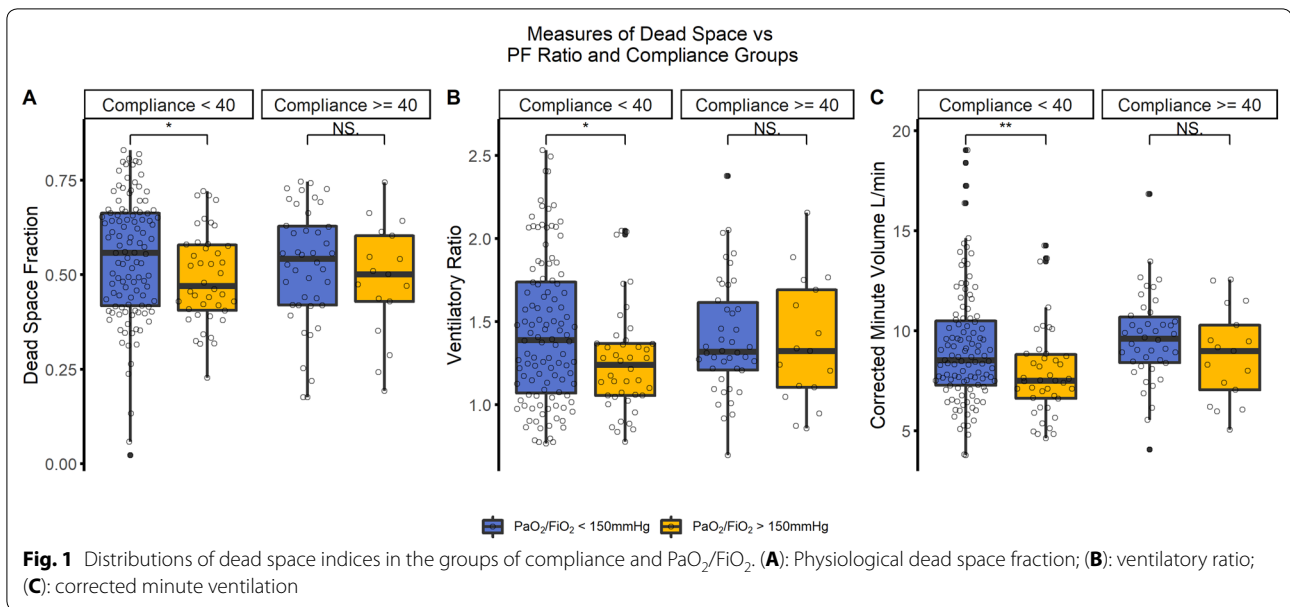
ICU outcome was available for 193 patients, where estimated physiological dead space fraction was higher in non-survivors [median (IQR), 0.57 (0.46–0.65) vs. 0.5 (0.4–0.64); *p*=0.03]. All estimates of physiological dead space increased with the degree of hypoxaemia, but not with the reduction in lung compliance (Fig. 1). Compared with patients with PaO₂/FiO₂>150 mmHg, patients with PaO₂/FiO₂<150 mmHg had higher estimated physiological dead space fraction [0.55 (0.52–0.57) vs. 0.5 (0.47–0.53); *p*=0.036] (Fig. 1A), mean (95%CI) corrected minute volume [4] [9.3(8.8–9.7) vs. 8.2 (7.6–8.8) L/min; *p*=0.004] (Fig. 1B), and ventilatory ratio [5] [1.43 (1.37–1.5) vs. 1.29 (1.2–1.38); *p*=0.001] (Fig. 1C). Although patients with compliance<40 mL/cmH₂O had a higher corrected minute volume [4] [9.4 (8.8–10) vs. 8.8 (8.4–9.3) L/min; *p*=0.023] (Fig. 1C), there was no difference in the two compliance groups in estimated physiological dead space fraction [0.55 (0.48–0.56) vs. 0.54 (0.52–0.56); *p*=0.72] (Fig. 1A) and ventilatory ratio [5] 1.4 (1.3–1.5) vs. 1.4 (1.33–1.46); *p*=0.76] (Fig. 1B).

*Correspondence: luigi.camporota@gstt.nhs.uk

¹ Department of Adult Critical Care, Guy's and St Thomas' NHS Foundation Trust, King's Health Partners, St Thomas' Hospital, 1st Floor East Wing, Westminster Bridge Road, London SE1 7EH, UK

Full author information is available at the end of the article

Luigi Camporota and Manu Shankar-Hari are to be considered joint last (senior) authors.



Physiological dead space correlated with hypoxaemia, but it was dissociated from alterations in lung mechanics in COVID-19 ventilated patients. Immuno-thrombosis is a mechanism that may explain both the increase in physiological dead space and hypoxaemia. Interestingly, we found that the highest median (IQR) levels of D-Dimers [2.1 (1–7) mg/L]; ferritin [1,627 (914–2555) ug/L], CRP [219.5 (147.25–324) mg/L], and troponin [23 (12–62) ng/L] were seen in patients with $\text{PaO}_2/\text{FiO}_2 < 150$ mmHg, but relatively preserved compliance (> 40 mL/cmH₂O). However, these values were statistically similar to the ones recorded in the other groups.

In conclusion, these data suggest that increased physiological dead space is a characteristic of patients with COVID-19 AHRE, with no relation with compliance of the respiratory system. Given that both $\text{PaO}_2/\text{FiO}_2$ and physiological dead space are worse in non-survivors, it is unclear if dead space is independently associated with mortality or if its effect on outcome is mediated through hypoxaemia.

Electronic supplementary material

The online version of this article (<https://doi.org/10.1007/s00134-020-06197-x>) contains supplementary material, which is available to authorized users.

Author details

¹ Department of Adult Critical Care, Guy's and St Thomas' NHS Foundation Trust, King's Health Partners, St Thomas' Hospital, 1st Floor East Wing, Westminster Bridge Road, London SE1 7EH, UK. ² Centre of Human Applied Physiological Sciences, King's College London, London, UK. ³ School of Immunology and Microbial Sciences, King's College London, London SE1 9RT, UK. ⁴ Nuffield Department of Clinical Neurosciences, Nuffield Division of Anaesthetics, University of Oxford, Oxford, UK.

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Compliance with ethical standards

Conflicts of interest

The authors declare no conflict of interest.

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