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

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Abbreviations: AHRF, COVID-19, ICU, PaO₂/FiO₂, CRP

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Dear Editor,

The severity of acute hypoxemic respiratory failure (AHRF) in 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 & St Thomas’ NHS Trust – London-UK (Ethics reference: 10796).

We used the recorded values at the time of worst PaO\textsubscript{2}/FiO\textsubscript{2} 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 PaO\textsubscript{2}/FiO\textsubscript{2} 128 [121-135] mmHg. When subdivided in four groups based on cut-off PaO\textsubscript{2}/FiO\textsubscript{2} of 150 mmHg and compliance of 40 mL/cmH\textsubscript{2}O; 72% (n=154) had PaO\textsubscript{2}/FiO\textsubscript{2} <150mmHg, of these 112 (73%, or 53% of the overall cohort) had compliance <40 mL/cmH\textsubscript{2}O (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 (Figure 1). Compared with patients with PaO\textsubscript{2}/FiO\textsubscript{2} >150mmHg, patients with PaO\textsubscript{2}/FiO\textsubscript{2} <150mmHg had higher estimated physiological dead space fraction (0.55 [0.52-0.57] vs 0.50 [0.47-0.53]; p=0.036) (Figure 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) (Figure 1B), and ventilatory ratio[5] (1.43 [1.37-1.50] vs 1.29 [1.20-1.38]; p=0.001)
Physiological dead space ventilation, disease severity and outcome in ventilated patients with hypoxaemic respiratory failure due to Coronavirus Disease 2019 (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 to 2,555] ug/L), CRP (219.5 [147.25, 324] mg/L), and troponin (23 [12-62]ng/L) were seen in patients with PaO$_2$/FiO$_2$ <150mmHg, but relatively preserved compliance (>40 mL/cmH$_2$O). 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 AHRF, with no relation with compliance of the respiratory system. Given that both PaO$_2$/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 are mediated through hypoxaemia.
References


Figure 1: Distributions of dead space indices in the groups of compliance and PaO$_2$/FiO$_2$. A: Physiological dead space Fraction; B: Ventilatory Ratio; C: Corrected minute ventilation.

eTable 1: Distribution of patients based on categories of compliance and PaO$_2$/FiO$_2$

<table>
<thead>
<tr>
<th>PaO$_2$/FiO$_2$ ≤ 150mmHg</th>
<th>PaO$_2$/FiO$_2$ &gt; 150mmHg</th>
</tr>
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<tbody>
<tr>
<td>n (%)</td>
<td>154 (72.3)</td>
</tr>
<tr>
<td>PaO$_2$/FiO$_2$, mmHg</td>
<td>103 (98 – 107)</td>
</tr>
<tr>
<td>mean(95% CI)</td>
<td></td>
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<tr>
<td>Compliance ml/cmH$_2$O</td>
<td>33.3 (31.0 – 35.6)</td>
</tr>
<tr>
<td>mean(95% CI)</td>
<td></td>
</tr>
<tr>
<td>n (%)[cohort %]</td>
<td>112 (72.7)[52.6]</td>
</tr>
<tr>
<td>PaO$_2$/FiO$_2$, mmHg</td>
<td>102 (97 - 107)</td>
</tr>
<tr>
<td>mean(95% CI)</td>
<td>(97 - 114)</td>
</tr>
<tr>
<td>Compliance ml/cmH$_2$O</td>
<td>26.2 (24.9 - 27.4)</td>
</tr>
<tr>
<td>mean(95% CI)</td>
<td>(25.5 – 30.0)</td>
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