The impact of ventilation – perfusion inequality in COVID-19: a computational model

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ABSTRACT

Introduction: Severe COVID-19 infection frequently leads to Acute Respiratory Distress Syndrome (CARDS) in which severe gas exchange derangements are often associated only with mild-moderate infiltrates at the lung Computed Tomography (CT). This implies that mechanisms other than right-to-left shunt play a role in CARDS pathophysiology.

Methods: We designed an algorithm ($Vent_{ri}Q_{lar}$) on the same conceptual grounds described by J.B West in 1969 ($Vent_{ri}Q_{lar}$) that, by using as input a set of measured variables, performs the calculations of 499 ventilation-perfusion (V_A/Q) compartments and selects 10^6 random combinations of blood flow distribution parameters to calculate predicted left atrium compositions. Values close to the actual PaO_2 and $PaCO_2$ are considered valid. As shunt we considered the fraction of non-aerated lung tissue as evaluated by the CT quantitative analysis.

Results: The population consisted of 5 critically-ill patients. The mean PaO_2/FiO_2 ratio was 91.1±18.6 mmHg and $PaCO_2$ 69.0±16.1 mmHg. The fraction of non-aerated tissue was only 0.32±0.07, but the calculated venous admixture was 0.43±0.08. Notably, all patients showed a hyperdynamic circulatory state (cardiac output of 9.58±0.99 l/min).

When we run the algorithm, the recovered VA/Q distributions showed that a remarkably bimodal V_A/Q distribution must be present in CARDS: a large fraction of the blood flow was distributed in low V_A/Q regions (Q_{mean}=0.06±0.02) and a smaller fraction in regions with moderately high V_A/Q. Overall LogSD, Q was 1.74±0.14, sign of a high ventilation-perfusion inequality. The high cardiac output of the subjects, coupled with the extensive intraseptal capillary thrombosis discovered at the autopsy, were likely the pathophysiological causes for this V_A/Q distribution.

Conclusions: Through a theoretical-computational approach we hypothesize that the severe hypoxemia observed in CARDS is not only caused by the shunt associated to the consolidated lung but also to an extreme V_A/Q inequality caused by its peculiar pathophysiology.

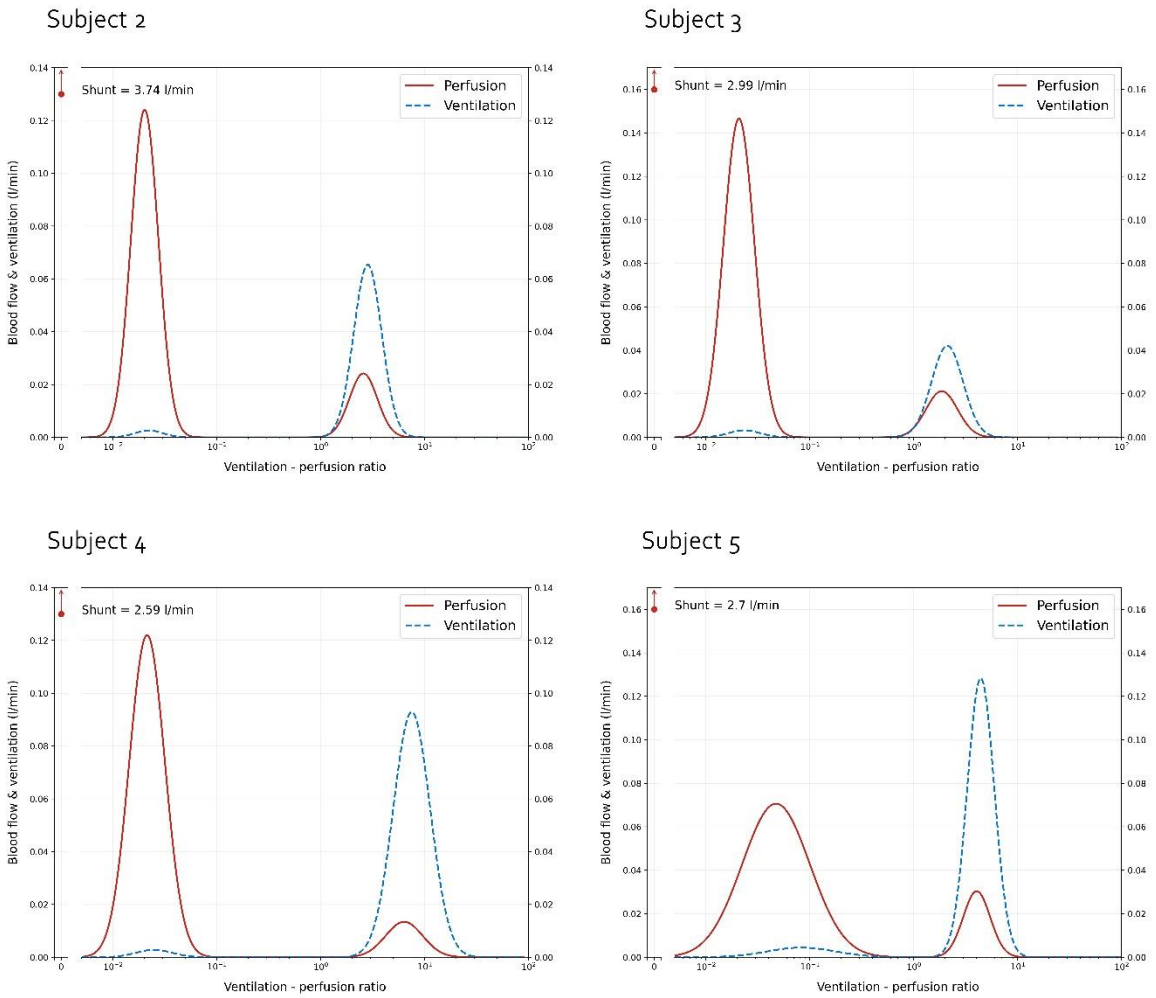

Figure 1: *Graphical representation of the ventilation-perfusion (V_A/Q) distribution of the solution with shortest Euclidean distance from the target for each of the 4 patients for who $Vent_{ri}Q_{lar}$ found a solution. As shown, in all cases, the recovered distribution was remarkably bimodal, with a large fraction of the blood flow was distributed in regions with low or very low V_A/Q, while a smaller fraction in regions with moderately increased V_A/Q. Notably, for subject 1 (the only one with venous admixture < of the fraction of non-aerated lung tissue) we could recover no solution.*