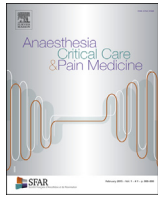




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## Letter to the editor

### Treating hypoxemic patients with SARS-CoV-2 pneumonia: Back to applied physiology



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As medical doctors, we are facing terrible and unprecedented challenges in the provision of medical care to patients infected with SARS-CoV-2 pneumonia (severe acute respiratory syndrome coronavirus 2). Intensive Care Units around the world are straining as demand for intubation and mechanical ventilation (MV) continues its ever-upward curve. In this regard, as intensivists, we would like to share some thoughts on how applied physiology might relate to SARS-CoV-2 pneumonia (pneumonitis).

We will describe our experience in dealing with patients who were intubated and ventilated with positive pressure MV. Up to this day, we have admitted 89 patients into our critical care unit of which 92% needed invasive MV (up to this day 26 patients have been discharged). During the first two days of mechanical ventilation, the majority surprisingly exhibited good lung compliance with preserved lung mechanics and diffuse and bilateral ground glass areas on Computed Tomography and coalescent B2 lines on bedside lung ultrasound [1]. It appears that at the initial stage, SARS-CoV-2 pneumonia induces high permeability-type pulmonary oedema with a large capillary leak syndrome and a significant venous admixture (poorly aerated-perfused lung regions) concomitant with a loss of hypoxic vasoconstriction (Euler-Liljestrand mechanism) [2]. Thus, the observed benefit after intubation and positive pressure MV, at the early stage of SARS-CoV-2 pneumonia, does not seem to be related to the usual recruitment of lung volume but mainly to a decrease in venous return, right ventricular output, transpulmonary blood flow and finally intrapulmonary shunt [3,4]. The positive impact of reverse Trendelenburg positioning on  $\text{SaO}_2$  values, in selected patients, can be spectacular.

However, some patients with a history of lung disease, and/or late bacterial superinfection, or following 48 hours of MV thereby inducing heterogeneous mechanical stress, will present a typical

inflammatory ARDS phenotype with large consolidations predominating in dependent lower lobes [5]. The present condition generates large areas of true pulmonary shunt (non-aerated/perfused lung regions), that further worsen oxygenation, decrease respiratory compliance and may require a higher PEEP, a lower tidal volume, prone positioning, neuromuscular blocking agents and, for the worst cases, VV-ECMO. Obviously, this second phenotype, more typical of classical ARDS, will need a longer MV period. Interestingly, the initial, high permeability-type pulmonary oedema phenotype that characterises SARS-CoV-2 pneumonia with apparently preserved lung mechanics, while undergoing positive pressure MV, may shift to the typical ARDS phenotype in absence of timely weaning MV.

A closer look at the pathophysiology of this hypoxemic alveolar state reveals that a decrease in venous admixture induced by decreasing in transpulmonary blood flow may be obtained mechanically (PPV), chemically (nitroglycerin in cardiogenic pulmonary oedema), by body posture (reverse Trendelenburg positioning) or a combination of these. However, when capillary hydrostatic pressure is low or normal as observed in high permeability-type pulmonary oedema, a medication like almitrine bismesylate, that promotes hypoxic pulmonary vasoconstriction [6], may improve hypoxemia resulting from SARS-CoV-2 pneumonia. Indeed, there are several studies indicating that upon intravenous administration, almitrine is effective in human ARDS by increasing arterial  $\text{PO}_2$  if the rise in pulmonary artery pressure is adequately supported by the right ventricle and cardiac output does not fall [7]. Unfortunately, almitrine is not available in Switzerland.

It is notable that patients with severe SARS-Cov-2 pneumonia tend to be elderly and/or have limited organs functional reserve. In this regard, we may think that it is unfortunate to be forced to treat selected clinically stable patients with temporary hypoxemia (silent hypoxemia) using invasive MV to decrease their initial venous admixture, when instead we could potentially treat them by decreasing transpulmonary blood flow (almitrine, continuous positive airway pressure [CPAP], reverse Trendelenburg positioning, fluid depletion. . .). Indeed, in-hospital mortality reported from Wuhan was very high among patients requiring invasive mechanical ventilation, of whom between 62% and 97% of patients died [8].

The present message highlights that the mortality is very high among patients with severe SRAS-CoV-2 pneumonia who are under or requiring MV [8]. Thus, any therapy and procedures that could prevent intubation and MV, or enhance MV weaning, without further deterioration of the patient's parlous state would be welcome. The present approach seems rational in a situation where we are facing terrible challenges in the provision of ICU beds and ventilators [9]. All procedures seem justified as long as they do not obscure clinical detection of the need for MV and does not increase the transmission dynamics of COVID-19 by aerosol-generating

procedures (in absence of protective equipment for healthcare professionals).

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#### Disclosure of interest

The author declares that he has no competing interest.

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