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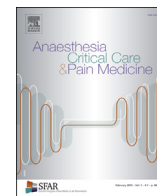
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Letter to the Editor

The meaning of the Low Optimum End-Expiratory Airway Pressure value found in some COVID-19 patients



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COVID-19 viral pneumonia (pneumonitis) is an acute respiratory illness associated with a new droplet-borne coronavirus (SARS-CoV-2). To this day, the pandemic has resulted in over 57 million infections worldwide and has caused over 1,365,000 deaths. Even if many of those who have been infected have had an uneventful recovery, the disease is associated with a profound disruption of the world's health systems and economy.

Surprisingly, the majority of infected patients exhibit good thoraco-pulmonary compliance with preserved lung mechanics following intubation and mechanical ventilation (MV) [1,2]. In an editorial published in the *Journal of the American Medical Association*, Marini and Gattinoni argue that deep sedation and MV should be implemented early on in order to prevent COVID-19 patients from generating spontaneous inspiratory efforts [2]. The authors, appropriately, state that in the early phase of lung infection, the high transpulmonary pressures associated with spontaneous vigorous inspiratory efforts may provoke self-induced lung injuries (P-SILI) [2].

If we look to Geneva experience when dealing with hypoxaemic patients who were intubated and ventilated with positive pressure mechanical ventilation during the first and the second wave (86% of 233 patients needed invasive MV), we may confirm that during the first days following intubation, patients with SARS-CoV-2 pneumonia present normal thoraco-pulmonary compliance and low pulmonary recruitability [1]. The exhibited good lung compliance with preserved lung mechanics implies that alveolar overdistension may be avoided if positive end-expiratory pressure (PEEP) value is set on the basis of the maximum respiratory system compliance (Crs) and not on the basis of oxygenation (pairing of PEEP and FiO₂ into a PEEP/FiO₂ table), even if the latter is a common tool to titrate PEEP in ARDS critically ill patients.

Indeed, PEEP/FiO₂ tables provide a reasonable treatment strategy, in patients with non-focal rather than focal ARDS [3]. The patients with focal ARDS respond poorly to high PEEP and recruitment manoeuvres and benefit more from lower PEEP [3]. When used for patients with focal ARDS, misclassified patients ventilated with high PEEP had bad prognosis [3]. Patients with COVID-19 viral pneumonia, before the secondary endothelial alveolar injury, have the same

response to PEEP that focal-ARDS. A high PEEP value, may provoke deleterious effects, so that the harm derived on the lung exceed the benefit [4]. Setting PEEP according to PaO₂/FiO₂ is questionable when the disease is related to a viral pneumonia associated with a diffuse endotheliopathy and thrombosis, two phenomena that may explain deep hypoxaemia with sub-normal lung mechanics. In this regard, it is not uncommon to measure an optimum PEEP value (best compliance produced by PEEP) [5] in these COVID-19 patients around 6 cm H₂O. Then what about this finding of a so low "Best PEEP" assessed from simultaneous recordings of expired tidal volume and airway pressure [5]?

PEEP titration to identify the PEEP at which lung compliance is maximal [static total lung and chest wall compliance (Crs)], presumably represents the best balance between recruitment and overdistention. Regarding the BERLIN ARDS definition, COVID-19 pneumonitis should not be classified as an ARDS, due to onset of the disease (most of time the history begins around 10 days before acutisation). Moreover, the sub-normal compliance is inline with a weak lung oedema. Nevertheless, applying a low "best" PEEP value to a COVID-19 patient and adjusting a safe transpulmonary pressure may be a good strategy in view of the regional variability (non-uniformity) of COVID-19 lung injuries. The present strategy assumes that the dysfunctional alveolar regions will not be immediately recruited and need more time to heal. It also assumes the potential benefits to avoid additional damage with end-inspiratory alveolar over-distention of healthy functional parts of the lungs. Setting the ventilator with a low best PEEP value also permits to avoid both an increase in dead space and the impairment of haemodynamic.

ARDS is a heterogeneous syndrome involving different lung morphology and phenotypes with distinct clinical and outcome characteristics. The stubborn posture of setting PEEP value on the basis of oxygenation is a short term strategy which long-term threat healthy lung areas. Therefore, allowing part of the lung to stay closed with permissive atelectasis may be more patient-protective than aggressive efforts to keep the lung open. Indeed, we have to keep in mind that arterial oxygenation reflects a complex interplay of shunt and oxygen transport, which goes beyond the problem of ventilator mechanics. In the same line of thought, we hope to help prevent the use of high PEEP when there is no benefit.

Current evidence points highlight that, in COVID-19 patients, high PEEP value should be targeted to those who will really benefit as in absence of recruitable lung, PEEP had little effect and should be minimised. Maybe the Best we can do while ventilating these patients is to apply the historical optimum PEEP associated to an acceptable transpulmonary pressure.

Declaration of interest

The authors declare that they have no competing interest.

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