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Commentary

Mechanical ventilation in early COVID-19 ARDS

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ARTICLE INFO

Article History: Received 30 September 2020 Revised 13 October 2020 Accepted 14 October 2020 Available online xxx

"It is not enough to do your best, you must know what to do, and then do your best." — W. Edwards Deming

A hallmark of acute respiratory distress syndrome (ARDS) is severe impairment of gas exchange. Mechanical ventilation to ensure oxygenation and carbon dioxide clearance is a cornerstone of the treatment of severe respiratory failure. Over the past five decades, significant progress has been made in defining principles and practices of invasive mechanical ventilation (IMV) in ARDS.

Respiratory failure due to Coronavirus disease 2019 (COVID-19) sparked a debate on when and how to apply IMV in these patients, as it has been proposed that severe COVID-19 causes "atypical" ARDS [1]. As published in *EClinicalMedicine*, Mittermaier and colleagues [2] investigated the effects of IMV, positive end-expiratory pressure (PEEP) and prone positioning (PP) on oxygenation and lung recruitability in patients with COVID-19-related ARDS (CARDS). All three interventions led to markedly improved oxygenation in CARDS. Initiation of IMV also led to a significant reduction in opacity indices assessed by chest X-ray indicating lung recruitability. This recruitment could not be further increased by PP. Despite low numbers in the groups, it becomes clear that PEEP and PP are able to improve oxygenation in CARDS.

PEEP has been used in the first description of ARDS and led to an increase in P_aO_2 or oxygen saturation in five of the twelve initial patients treated this way [3]. PEEP to increase functional residual capacity (FRC) and thus keep small airways and alveoli open (leading to a reduction of lung inhomogeneity) is now a universal accepted principle of ARDS treatment. The practice to set PEEP right in patients with ARDS is in contrast somewhat vague. It has been suggested that lungs in CARDS patients with high compliance are mainly open, thus PEEP could be set at lower levels and PP might not bring the desired benefits [1,4]. The present study indicates that also CARDS requires

PEEP levels we are accustomed to from usual ARDS. Importantly, from the present study [2] we again learn that PEEP should be applied in an individualized manner. The amount of recruitable lung, an important determinant of harm and benefit from PEEP, varies considerably across patients with ARDS and more PEEP does not necessarily translate into improved gas exchange [5]. In the present study, pulmonary compliance was relatively preserved but increasing FRC by high PEEP levels led to significantly improved oxygenation. PEEP above a certain level might be harmful by increasing dead space, reducing venous return and hence cardiac output leading to reduced net oxygen delivery [6]. This might also be true in patients with ventilation-perfusion (V/Q) mismatch as seen in pulmonary embolism or altered hypoxic pulmonary vasoconstriction. In this sense it is difficult to predict PEEP effects in individual patients as the clinical presentations of these patients are manifold. Interestingly, after careful titration, optimal PEEP in study patients was always lower than the initially applied PEEP [2]. The data suggest that in some patients, even lower levels of PEEP would have been acceptable with regard to oxygenation possibly giving more protection to the right ventricle. Nevertheless, PEEP is a titrated therapy that should be integrated into a CARDS ventilation strategy [7]. Such a strategy must also include PP. PP is associated with improved outcomes in patients with moderate to severe ARDS [8] without the need to change the ventilator to more invasive settings. Just by changing the body position, collapsed alveoli in dependent lung zones are recruited, V/Q mismatching is decreased and lower concentrations of oxygen may be used [9]. In their study, Mittermaier and colleagues [2] presented the effects of PP over a period of a least 12 h. However, PP probably did not change opacity indices in chest x-rays, as COVID-19 may cause a very dissiminated infestation of the lungs.

The present study does not answer the question of whether PEEP applied by non-invasive ventilation (NIV) can improve oxygenation in a similar way as IMV. Thus, the current data leave it open when to start IMV, directly or after NIV. But it adds to the reports indicating that the pathophysiological changes in human lungs due to CARDS can be treated similarly as ARDS induced by other infectious agents. Stage adjusted, this treatment should include titrated PEEP, PP and extracorporeal membrane oxygenation (ECMO) [10]. There is definitely a lot to learn about CARDS, and it seems that the treatment principles are the same as in usual ARDS. The practices will be informed be a plethora of studies, and the study by Mittermaier et al. [2] is one of those helping to guide the way.

Refers to: ECLINM 100579, S2589-5370(20)30323-0(10.1016/j.eclinm.2020.100579, FLA)

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Declaration of Interests

The authors have nothing to declare.

References

- [1] Gattinoni L, Coppola S, Cressoni M, Busana M, Rossi S, Chiumello D. COVID-19 does not lead to a "Typical" acute respiratory distress syndrome. Am J Respir Crit Care Med 2020;201:1299–300.
- [2] Mittermaier M, Pickerodt P, Kurth F, et al. Evaluation of PEEP and prone positioning in early COVID-19 ARDS. EClinicalMedicine 2020. doi: 10.1016/j. eclinm.2020.100579.
- [3] Ashbaugh DG, Bigelow DB, Petty TL, Levine BE. Acute respiratory distress in adults. Lancet 1967;2:319–23.
- [4] Gattinoni L, Chiumello D, Caironi P, et al. COVID-19 pneumonia: different respiratory treatments for different phenotypes? Intensive Care Med 2020;46:1099– 102.

- [5] Goligher EC, Kavanagh BP, Rubenfeld GD, et al. Oxygenation response to positive end-expiratory pressure predicts mortality in acute respiratory distress syndrome. A secondary analysis of the LOVS and ExPress trials. Am J Respir Crit Care Med 2014;190:70–6.
- [6] Suter PM, Fairley B, Isenberg MD. Optimum end-expiratory airway pressure in patients with acute pulmonary failure. N Engl J Med 1975;292:284–9.
- [7] Briel M, Meade M, Mercat A, et al. Higher vs. lower positive end-expiratory pressure in patients with acute lung injury and acute respiratory distress syndrome: systematic review and meta-analysis. JAMA 2010;303:865–73.
- [8] Guerin C, Reignier J, Richard JC, et al. Prone positioning in severe acute respiratory distress syndrome. N Engl J Med 2013;368:2159–68.
- [9] Vieillard-Baron A, Rabiller A, Chergui K, et al. Prone position improves mechanics and alveolar ventilation in acute respiratory distress syndrome. Intensive Care Med 2005;31:220–6.
- [10] Ferrando C, Suarez-Sipmann F, Mellado-Artigas R, et al. Clinical features, ventilatory management, and outcome of ARDS caused by COVID-19 are similar to other causes of ARDS. Intensive Care Med 2020.