Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Pathophysiology of COVID-19-associated acute respiratory distress syndrome

We congratulate Giacomo Grasselli and colleagues for their important and informative work on the pathophysiology of COVID-19-associated acute respiratory distress syndrome (ARDS).[1] In particular, we appreciate the clarity with which the data show that respiratory system compliance was significantly higher in COVID-19-associated ARDS compared with classical aetiology ARDS, despite the former having more severe hypoxaemia. Along this line, we note their result that "static compliance decreased as [the ratio of partial pressure of arterial oxygen to fractional concentration of oxygen in inspired air] decreased in patients with classical ARDS and in a pneumonia subset of patients with ARDS, while it remained unchanged in patients with COVID-19 ARDS".[1] The CT data also confirm more normally inflated and hyperinflated tissue in COVID-19 ARDS (measured at clinical positive end-expiratory pressure [PEEP]) compared with ARDS from classical aetiologies. This observation indicates that the clinically set PEEP might have been higher than necessary in COVID-19 ARDS, possibly contributing to increased dead space. Accordingly, the authors recommended—correctly, in our view—the use of lower PEEP in patients with COVID-19 ARDS with higher compliance.

While the authors' conclusions are strongly supported by the data they present, we are confused by their recommendations to manage ventilation for COVID-19 ARDS similarly to ventilation strategies for classical ARDS. The Article clearly shows key differences between COVID-19 ARDS and classical ARDS that might affect effectiveness and safety. Indeed, because of the disparity between lung mechanics and the oxygenating efficiency that defines ARDS severity, the available evidence would seem to question the necessity of maintaining all standard guidelines (such as setting high PEEP based on PEEP–FiO_2 tables and tightly restricting tidal volume to its lowest range, independent of plateau pressure).

We are strong supporters of ventilation strategies that achieve the maximum degree of lung protection by minimising stress and strain; hence, we think that ventilatory settings for COVID-19 ARDS might need to be adapted in individual cases, depending on mechanical characteristics and timing of presentation. The data regarding compliance and overinflation on CT scan support doing so. Finally, patients with COVID-19 ARDS with lower lung compliance and higher levels of immunothrombosis markers (D-dimers) had greatest mortality risk—presumably despite exposure to a similar ventilation strategy. This observation again highlights the novel pathogenesis and outcome determinants of COVID-19. Anticoagulation and immunomodulation might be key modulators in this ARDS variant. We unequivocally agree with Grasselli and colleagues that following lung protective principles is essential; however, unquestioning adherence to pre-existing ARDS ventilation guidelines might not be warranted at all times in the course of what remains an unfamiliar disease.

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1 Grasselli G, Tonetti T, Protti A, et al. Pathophysiology of COVID-19-associated acute respiratory distress syndrome: a multicentre prospective observational study. *Lancet Respir Med* 2020; **8:** 1201–08.