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.

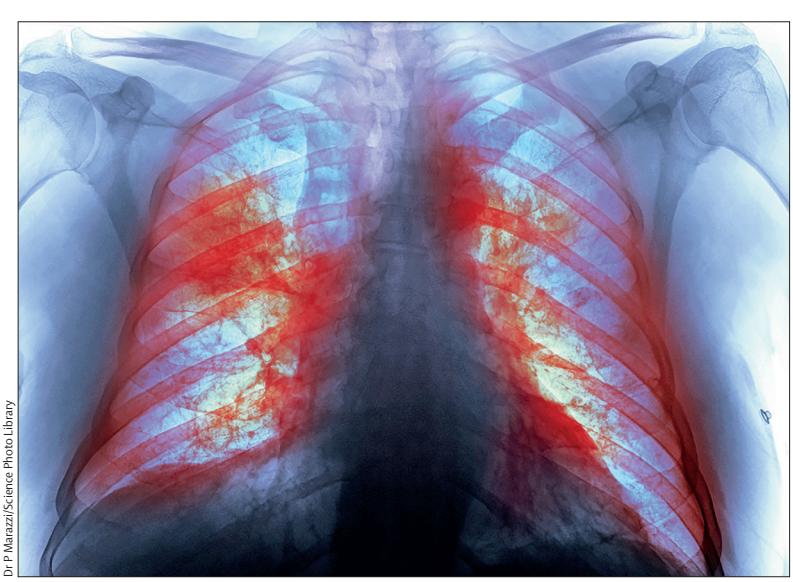
Pathophysiology of COVID-19-associated acute respiratory distress syndrome

We read with great interest Giacomo Grasselli and colleagues' study concerning the pathophysiology of COVID-19-associated acute respiratory distress syndrome (ARDS).[1] The authors conclude that COVID-19 ARDS presents lung mechanics that largely match those of classical ARDS.[1] However, we feel this conclusion is not supported by their findings.

As clearly stated, median static respiratory system compliance was significantly higher in patients with COVID-19 ARDS compared with those with classical ARDS, but the observed 28% difference would have been more pronounced had the groups been better matched (the classical ARDS group had a significantly lower percentage of patients with severe ARDS compared with the COVID-19 ARDS group).[1] Based on Grasselli and colleagues' findings on static compliance according to ARDS severity, we see that as hypoxaemia worsens, static compliance worsens as well in classical ARDS, in an almost linear way; however, in COVID-19 ARDS, static compliance remains unchanged, despite oxygenation worsening (appendix).[1] Therefore, additional factors might contribute to the degree of hypoxaemia that are unrelated to alveolar flooding or collapse, which mark the main pathophysiology in classical ARDS. Lung compliance is a marker of the amount of well aerated lung.[2] A decrease in oxygenation with preserved lung mechanics implies that the alveoli are fairly intact, meaning diffusion must primarily be affected.

It would be very informative if data on lung mechanics (eg, plateau pressure, driving pressure) and particularly positive end-expiratory pressure (PEEP) levels for each COVID-19 ARDS severity category could be provided, as the authors have helpfully done for each D-dimer or static compliance quartile. PEEP seems to have been applied regardless of static compliance,[1] probably based on values of the ratio of partial pressure of arterial oxygen to fractional concentration of oxygen in inspired air (>14 cm H_2O in severe ARDS, according to the ARDSNet protocol). Lower PEEP, when compliance is well preserved, might have decreased dead space, further improving static compliance (appendix). We have found nearly normal static compliance in severe COVID-19 ARDS, while a 25% PEEP reduction improved compliance, decreasing dead space.[3] Unnecessary PEEP increases transpulmonary pressures impeding venous return, ultimately forcing lung zone 3 transition to zone 2 or even 1, inducing dead space. The condition can worsen when the pulmonary capillary bed is injured, as in COVID-19, from extensive microthrombosis, as has been reported by Grasselli and colleagues,[1] among others.[4,5] Increased PEEP could have contributed to hyperinflation and hypoperfusion affecting mainly the upper-anterior lung zones, as shown in the Article.[1]

In our opinion, this is a study of great scientific importance, clearly showing that COVID-19 ARDS is an alveolar-capillary disease that differs sufficiently from classical ARDS to probably warrant a different ventilatory approach concerning PEEP. Lower PEEP than classically used in severe ARDS, with low tidal volumes, might become the lung-protective ventilation of choice for patients with COVID-19, to ensure that alveolar overdistention is avoided.



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See Online for appendix

We declare no competing interests.

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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.

2 Gattinoni L, Meissner K, Marini JJ. The baby lung and the COVID-19 era. *Intensive Care Med* 2020; **46:** 1438–40.

3 Tsolaki V, Siempos I, Magira E, Kokkoris S, Zakynthinos GE, Zakynthinos S. PEEP levels in COVID-19 pneumonia. *Crit Care* 2020; **24:** 303.

4 Ackermann M, Verleden SE, Kuehnel M, et al. Pulmonary vascular endothelialitis, thrombosis, and angiogenesis in Covid-19. *N Engl J Med* 2020; published online May 21. https://doi.org/10.1056/NEJMoa2015432.

5 Bilaloglu S, Aphinyanaphongs Y, Jones S, Iturrate E, Hochman J, Berger JS. Thrombosis in hospitalized patients with COVID-19 in a New York City Health System. *JAMA* 2020; **324:** 799–801.