



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.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.

Awake prone positioning for COVID-19 acute respiratory failure: imaging and histological background

We read with great interest the article by Stephan Ehrmann and coworkers¹, which highlights the beneficial effects of awake proning in COVID-19 acute hypoxaemic respiratory failure with reduction of the incidence of treatment failure and the need for intubation within 28 days without any sign of harm. These beneficial effects might be explained by taking into account data provided by histopathology and by CT scan in supine and prone positions. Doglioni and colleagues,² in cryobiopsy samples obtained from patients with mild to moderate COVID-19 interstitial pneumonia, showed that the main findings were patchy type II pneumocytes hyperplasia, perivenular lymphocytic infiltrates, hyperplasia of alveolar capillaries with dilated lumina, and dilatation of the lumen of postcapillary veins. Hyaline membranes and collapsed alveoli were not

detected. Interestingly, endothelial cells expressed indoleamine deoxygenase, an enzyme involved in the control of the vascular tone.

In lungs from patients with COVID-19 pneumonia, an increased amount of new interalveolar vessels was also documented by Ackermann and colleagues³ in an autopsy series. Our group has furthermore documented that the higher density observed in CT scan (ground glass attenuation or even alveolar consolidation) is mainly related to the hyperperfusion and vasoplegia in affected areas.⁴ In fact, a drop of density, the redistribution of the pulmonary infiltrates in the more gravity dependent zones of the lung, and a reduction of the lumen of the effluent veins were observed while passing from the supine to the prone position (figure). In acute respiratory distress syndrome, owing to different causes, the morphological background is diffuse alveolar damage with necrosis of type I pneumocytes, intra-alveolar and interstitial oedema and alveolar septa partly covered by hyaline membranes.⁵

In this context, the alveoli appear collapsed and the beneficial effects of proning in terms of oxygenation

and survival are more consistent in patients who are mechanically ventilated because of the partial recruitment of alveoli inside these atelectatic zones. In mild to moderate COVID-19 pneumonia, the pathophysiological mechanism leading to hypoxaemia is a right to left shunt due to a tangle of dilated interalveolar capillaries surrounding almost normal alveoli. Use of C-PAP or even high flow nasal cannula along with pronation in patients who are awake helps to squeeze and redistribute the blood from the more affected areas to less inflamed and hyperhaemic zones, and could further contribute to reduction of the right to left shunt and amelioration of blood oxygenation.

We declare no competing interests.

*Sara Piciucchi, Claudia Ravaglia, Antonio Vizzuso, Emanuela Giampalma, Venerino Poletti
piciucchi.sara@gmail.com

Department of Radiology, Ospedale GB Morgagni, University of Bologna, Forlì, Italy (SP, AV, EG); Department of Diseases of the Thorax, Ospedale GB Morgagni, University of Bologna, Forlì (CR, VP); Department of Respiratory Diseases and Allergy, Aarhus University, Aarhus, Denmark (VP)

- 1 Ehrmann S, Li J, Ibarra-Estrada M, et al. Awake prone positioning for COVID-19 acute hypoxaemic respiratory failure: a randomised, controlled, multinational, open-label meta-trial. *Lancet Respir Med* 2021; **9**: 1387–95.
- 2 Doglioni C, Ravaglia C, Chilosi M, et al. Covid-19 interstitial pneumonia: histological and immunohistochemical features on cryobiopsies. *Respiration* 2021; **100**: 488–98.
- 3 Ackermann M, Verleden SE, Kuehnel M, et al. Pulmonary vascular endothelialitis, thrombosis, and angiogenesis in Covid-19. *N Engl J Med* 2020; **383**: 120–28.
- 4 Piciucchi S, Ravaglia C, Vizzuso A, Bertocco M, Poletti V. Reversibility of venous dilatation and parenchymal changes density in Sars-Cov-2 pneumonia: toward the definition of a peculiar pattern. *Pulmonology* 2021; **27**: 353–57.
- 5 Katzenstein AL-A. Katzenstein and Askin's surgical pathology of non-neoplastic lung disease, 4th edn. Philadelphia: Saunders Elsevier, 2006: 17–49.

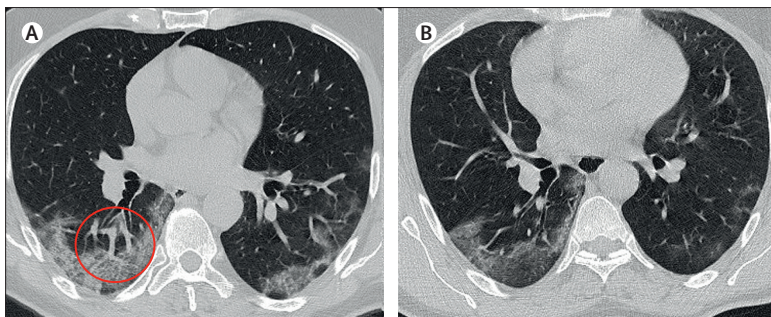


Figure: CT scan in the supine (A) and prone (B) positions in a male aged 53 years, with bilateral COVID-19 pneumonia, 7 days after the onset of the symptoms

First, the patient is lying in the supine position, with evidence of bilateral so-called crazy paving and ground glass attenuation, associated with the increased diameter of the effluent vein (red circle). A few minutes after the prone decubitus has been adopted, the crazy paving areas of attenuation change into mild ground glass attenuation.