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.

Progressive respiratory failure in COVID-19: a hypothesis

The coronavirus disease 2019 (COVID-19) pandemic is a challenge for intensive care units (ICUs) worldwide because of the large numbers of patients, a scarcity of resources, the poor prognosis of patients they treat, and uncertainty regarding the disease's pathogenesis. The first case of COVID-19 in the Netherlands was confirmed on Feb 27, 2020, and the patient was put on mechanical ventilation in our ICU department at Erasmus Medical Center (Rotterdam, Netherlands). Currently, our department is the largest COVID-19 ICU in the Netherlands. We would like to share our findings regarding a possible mechanism of progressive respiratory failure.

From the date of the first confirmed case up to April 5, a total of 90 patients were admitted to our ICU, most of whom were male (n=68 [76%]), of older age (mean age 62 years [SD 14]), and obese (mean body-mass index 29 kg/m^2 [SD 5]). Treatment consisted of prone positioning, low tidal volumes, positive end-expiratory pressure (PEEP) titration according to the higher PEEP, lower fraction of inspired oxygen table,[1] and restrictive fluid management. These methods resulted in low driving pressures, no pneumothoraxes, low vasopressor doses, and weaning from mechanical ventilation approximately 2 weeks after ICU admission. However, some patients (n=17 [19%]) deteriorated within 2 weeks and no longer responded to prone positioning. All of these patients had major pulmonary embolism established by lung CT or cardiac ultrasound.

Initially, patients with COVID-19 on our ICU developed increased alveolar capillary permeability and subsequent interstitial oedema. The presence of oedema is illustrated by ground-glass opacities of the lung parenchyma on lung CT.[2] If patients require mechanical ventilation, oxygenation improves following prone positioning, higher PEEP, and restrictive fluid management. Subsequently, their condition might deteriorate suddenly, and pulmonary embolism can occur, detected by contrast-enhanced lung CT scan.[3] On our ICU, five further patients had progressive respiratory failure, in whom we did lung CT and found pulmonary embolism, either located centrally or segmentally, in all cases. In addition, we were confronted with these patients developing deep venous thrombosis, and frequent coagulation of renal replacement therapy filters. We hypothesise that the patients with COVID-19 with pulmonary embolism entered a hypercoagulable state with endothelial activation following an increase in proinflammatory cytokines.

An association between increased coagulation status and increased capillary permeability might exist. A plasma D-dimer concentration greater than 4 µg/mL, combined with increasing inflammatory markers such as interleukin-6 (IL-6), and loss of response to prone positioning might be useful parameters to identify patients at risk of pulmonary embolism. Based on our early findings in our first 90 patients with COVID-19, we now include D-dimer and IL-6 in our routine laboratory tests in patients with COVID-19, and increase the prophylactic dose of low-molecular-weight heparin (nadroparin 5700 IU subcutaneously, from once a day to twice a day).[4] In addition, we do a lung CT even at a low level of suspicion of pulmonary embolism, and we encourage others to do the same.

In summary, COVID-19 might be associated with hypercoagulability, and clinicians should consider a pulmonary embolism in cases of progressive respiratory failure.

DG has received speakers fees and travel expenses from Dräger, GE Healthcare (medical advisory board 2009–12), Maquet, and Novalung (medical advisory board 2015–18). All other authors declare no competing interests. HE conceived the work and all authors drafted and revised the Correspondence piece.

*Henrik Endeman, *Philip van der Zee, Michel E van Genderen, Johannes P C van den Akker, Diederik Gommers*

p.vanderzee@erasmusmc.nl

Department of Adult Intensive Care, Erasmus Medical Center, 3015 GD Rotterdam, Netherlands

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Published **Online** April 29, 2020 https://doi.org/10.1016/S1473-3099(20)30366-2

Hypoxaemia related to COVID-19: vascular and perfusion abnormalities on dual-energy CT

Studies have shown that some patients with coronavirus disease 2019 (COVID-19) and acute hypoxaemic respiratory failure have preserved lung compliance, suggesting that processes other than alveolar damage might be involved in hypoxaemia related to COVID-19 pneumonia.[1] The typical imaging features of COVID-19 pneumonia, including peripheral ground-glass opacities with or without consolidation, are also non-specific and can be seen in many other diseases.[2] There has been increasing attention on microvascular thrombi as a possible explanation for the severe hypoxaemia related to COVID-19.[3,4]

Dual-energy CT imaging can be used to characterise lung perfusion and is done as part of the standard protocol for imaging pulmonary embolism at our institution. Three patients with COVID-19, as confirmed by nasopharyngeal RT-PCR at our

Published **Online** April 30, 2020 https://doi.org/10.1016/S1473-3099(20)30367-4