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Early View

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IL-6 and intrapulmonary shunt

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To the Editor:

We read with interest the article by Kotwica and colleagues [1] showing the utility of clinical pulse oximetry measurements to quantify shunt and ventilation-perfusion (V/Q) mismatch and their predictive value in severe COVID-19. The authors found that shunt correlated with markers of activated inflammatory response (i.e. C-reactive protein) but not those of activated coagulation (such as D-dimer). Their results reinforce the growing evidence for the role of impaired hypoxic pulmonary vasoconstriction (HPV) as a primary cause for SARS-CoV-2-induced hypoxemia [2].

We would like to draw the attention of the readers to a possible pathophysiological role of IL-6 in intrapulmonary shunt associated to SARS-CoV-2-induced ARDS that has been overlooked. IL-6 is a fundamental player in the inflammation associated to COVID-19 and the level of this cytokine serves as a biomarker of poor prognosis [3]. Moreover, although controversy remains regarding the population of patients that may benefit from anti-IL-6 therapies in COVID-19, two large randomized clinical trials have shown reduced mortality in patients treated with tocilizumab [4, 5], and seven RCTs have shown reduced risk of mechanical ventilation [6].

The initial evidence for the involvement of IL-6 in impaired HPV comes from studies in mice and rats. Thus, human recombinant IL-6 inhibited HPV in mice [7]. We also observed that IL-6 inhibited HPV and an antibody against IL-6 prevented the impairment of HPV induced by bacterial endotoxin in isolated rat pulmonary arteries [8]. In addition, several studies have demonstrated a positive impact of tocilizumab on arterial oxygenation in patients with severe COVID-19 [9, 10].

In conclusion, we speculate that IL-6 is involved in the impaired HPV associated to COVID-19. The relationship of intrapulmonary shunt with IL-6 levels and with anti-IL-6 therapies deserves further investigation.

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