More on clinical and computed tomography characteristics of COVID-19 associated acute pulmonary embolism

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Letter to the Editors-in-Chief

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To the editor:

We thank Dr. Tsolaki and colleagues for their interest in our study [1]. They asked for clarification of some of our findings, which we provide below.

First, our data are in line with previous studies that observed a high incidence of thromboembolic complications in critically ill COVID-19 patients [2–4]. Since randomized controlled trials comparing different intensities of pharmacological thromboprophylaxis in COVID-19 patients are still ongoing, the optimal strategy to prevent venous thromboembolism in these patients remains unknown.

Second, the authors suggest that mechanical ventilation, especially with high levels of positive end-expiratory pressure (PEEP), may have contributed to the increased right ventricle to left ventricle ratio (RV/LV ratio) observed in patients with COVID-19 associated pulmonary embolism (PE). Of note, Dr. Tsolaki and colleagues stated that the mean RV/LV ratio of 0.97 in our study would indicate severe right ventricle (RV) dilatation in the COVID-19 patients. However, in current guidelines RV dilatation is defined as a RV/LV ratio > 1.0 and thus the mean RV/LV ratio of 0.97 would be below the threshold for RV dilatation [5]. In our study, the majority (19/23) of COVID-19 patients were mechanically ventilated, with a mean PEEP level of 10 cm H_2O (standard deviation (SD) 1.8 cm H_2O) at the time of the PE diagnosis. However, when comparing the mean RV/LV ratio in patients who were not mechanically ventilated to that in patients with mechanical ventilation, we did not find relevant differences (mean difference of 0.09, 95%CI −0.08 to 0.26; Table 1). Due to the small sample size, the underlying correlation between PEEP levels and RV/LV ratio is difficult to assess, but these observations do not support the hypothesis of Dr. Tsolaki and colleagues. This is also true for other factors, including lung injury and possibly right heart failure in patients with COVID-19 infection. Although we were not able to find an association between the extent of affected lung by COVID-19 infection and RV dilation (mean difference of affected lung by ground-glass opacities and consolidations 13.6% higher in patients without RV dilation, 95%CI −7.5% to 34%), the mechanism of RV dilatation in COVID-19 associated PE is likely to be multifactorial: thrombotic obstruction of the pulmonary artery tree, hypoxemic vasoconstriction, cytokine effect, direct viral damage and possibly a mechanical ventilation effect [5,6].

Third, we were asked to provide details on thrombus load and location as well as mechanical ventilation settings (PEEP levels) in the subgroups of patients with different reasons for suspecting PE. In patients with sudden respiratory deterioration (n = 7), the mean total thrombus load was 26 (SD 26) and the most proximal PE was located in the main pulmonary artery in 1, in segmental artery in 4 and in subsegmental artery in 2 patients. The mean PEEP level was 10 cm H_2O (SD 0.89 cm H_2O; Table 2). In the two patients with hemodynamic collapse, the mean total thrombus load was 34 (SD 23), the most proximal PE was located in the main pulmonary artery and segmental artery, and the mean PEEP level again was 10 cm H_2O (SD 0.00 cm H_2O; Table 2). As the mean PEEP level in the hemodynamic unstable patients was comparable to the mean PEEP level in all patients who were mechanically ventilated, it remains unknown whether the hemodynamic deterioration in these patients could (partially) be attributed to the mechanical ventilation effect.

Fourth, as the pathophysiology of COVID-19 associated PE is still not fully understood, it would be valuable to evaluate follow-up computed tomography pulmonary angiography (CTPA) scans to determine the course of the disease after the initiation of therapeutic anticoagulant treatment. In our cohort, 6 patients (26%) were subjected to a follow-up CTPA scan within 12–28 days after the PE diagnosis was confirmed, because of progressive hemodynamic or respiratory wor-

Table 1
CTPA parameters in patients without versus with mechanical ventilation.

	Patients without mechanical ventilation (n = 4)	Patients mechanically ventilated (n = 19)	Mean difference (95%CI)
RV/LV ratio – mean (SD)	1.1 (0.26)	0.96 (0.13)	0.09 (−0.08 to 0.26)
Total obstruction score – mean (SD)	27 (34)	22 (15)	5.2 (−16 to 26)

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Table 2
CTPA and mechanical ventilation details per group of patients with different reasons for PE suspicion.

	Respiratory deterioration (n = 7)	Hemodynamic deterioration (n = 2)	Ventilation stagnation (n = 7)	Elevation D-dimer (n = 6)	Persistent fever of unknown origin (n = 1)
Total obstruction score – mean (SD)	26 (26)	34 (23)	24 (16)	16 (6.5)	7.5
PEEP levels – mean (SD)	10 (0.89)	10 (0.00)	10 (2.6)	9.3 (1.9)	10

sening. Notably, in all these patients, the thrombus load had considerably decreased. This interesting observation demonstrates the effectiveness of the chosen treatment (low-molecular weight heparin or unfractionated heparin), and supports the hypothesis that (intensified doses of) thromboprophylaxis in critically ill COVID-19 patients may prevent PE.

References

[1] L.F. van Dam, L.J.M. Kroft, L.I. van der Wal, S.C. Cannegieter, J. Eikenboom, E. de Jonge, et al., Clinical and computed tomography characteristics of COVID-19 associated acute pulmonary embolism: a different phenotype of thrombotic disease? Thromb. Res. 193 (2020) 86–89.

[2] F.A. Klok, M. Kruip, N.J.M. van der Meer, M.S. Arbous, D. Gommers, K.M. Kant, et al., Incidence of thrombotic complications in critically ill ICU patients with COVID-19, Thromb. Res. 191 (2020) 145–147.

[3] F.A. Klok, M. Kruip, N.J.M. van der Meer, M.S. Arbous, D. Gommers, K.M. Kant, et al., Confirmation of the high cumulative incidence of thrombotic complications in critically ill ICU patients with COVID-19: an updated analysis, Thromb. Res. 191 (2020) 148–150.

[4] C. Lodigiani, G. Iapichino, L. Carenzo, M. Cecconi, P. Ferrazzi, T. Sebastian, et al., Venous and arterial thromboembolic complications in COVID-19 patients admitted to an academic hospital in Milan, Italy, Thromb. Res. 191 (2020) 9–14.

[5] M.V. Huisman, S. Barco, S.C. Cannegieter, G. Le Gal, S.V. Konstantinides, P.H. Reitsma, et al., Pulmonary embolism, Nat Rev Dis Primers. 4 (2018) 18028.

[6] E. Argulian, K. Sud, B. Vogel, C. Bohra, V.P. Garg, S. Talebi, et al., Right ventricular dilation in hospitalized patients with COVID-19 infection, JACC Cardiovasc. Imaging (2020), https://doi.org/10.1016/j.jcmg.2020.05.010 [Epub ahead of print].

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