Clinical and Applied Thrombosis/Hemostasis
Volume 26: 1-2

DOI: 10.1177/1076029620933953
journals.sagepub.com/home/cat
SAGE

Pulmonary Embolism, Pulmonary Microvascular Thrombosis, or Both in COVID-19?

José A. Páramo[1,2]

Date received: 7 May 2020; revised: 20 May 2020; accepted: 21 May 2020.

An increased incidence of thrombotic complications has been described in COVID-19 patients, particularly in those with severe disease and/or admitted to the intensive care unit. The coagulation system is activated in the majority of patients, and D-dimer, a biomarker of fibrin formation and degradation, also reflects true thrombotic disease.[1-3] In addition, there is a strong association between D-dimer and chest computed tomography (CT) features suggesting pulmonary thrombosis.[4]

While the exact prevalence or incidence of venous thromboembolism (VTE; eg, deep vein thrombosis and/or pulmonary embolism) is unknown, different reports indicate rates of VTE ranging from 15% and 30%. These reports often emphasize that pulmonary embolism was the most frequent thrombotic complication, generally effecting segmental or subsegmental vessels.[1-4]

According to the "classic" definition, pulmonary embolism is, in most cases, caused by blood clots that travel to the lungs from deep veins of the legs or, rarely, from veins in other parts of the body. Although data on pathologic changes of COVID-19 are scarce, postmortem examinations showed diffuse alveolar damage with focal fibrin clusters mixed with mononuclear inflammatory cells as the primary mechanism of respiratory distress associated with COVID-19 and, therefore, disseminated fibrin deposits occur in the pulmonary microcirculation as a consequence of the ongoing inflammatory stimuli leading to acute lung injury and respiratory damage.[5,6] Indeed, it has been suggested the acronym MicroCLOTS (*microvascular COVID-19 lung vessels obstructive thromboinflammatory syndrome*) as the pathophysiological mechanism for the acute respiratory distress syndrome caused by this coronavirus.[7] In line with this pathophysiological approach, a recent study indicates direct viral infection of endothelial cells and diffuse endothelial inflammation in lungs in patients who developed progressive respiratory failure.[8] The fact that no systematic objective screening for VTE (CT pulmonary angiogram and/or ultrasonography) has been applied in many circumstances and the low number of deep vein thrombosis associated with pulmonary embolism in COVID-19 patients suggest that they have intrapulmonary acute microvascular thrombosis rather than embolism.[1,2,9]

We, therefore, propose to include the term primary pulmonary thrombi which develop directly in the lungs without traveling from DVT to refer to the most common thrombotic manifestations in patients with COVID-19 infection, which may have therapeutic implications.

Authors' Note

José A. Páramo designed and wrote the manuscript. Our institution does not require ethical approval for reporting individual cases or case series.

ORCID iD

José A. Páramo https://orcid.org/0000-0003-1497-6242

References

1. Klok FA, Kruip MJHA, van der Meer NJM, et al. Incidence of thrombotic complications in critically ill ICU patients with COVID-19. *Thromb Res*. 2020;191:145-147. doi:10.1016/j.thromres.2020.04.013
2. Llitjos JF, Leclerc M, Chochois C, et al. High incidence of venous thromboembolic events in anticoagulated severe COVID-19 patients. *J Thromb Haemost*. 2020. doi:10.1111/jth.14869
3. Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *Lancet*. 2020;395(10229):1054-1062.
4. Leonard-Lorant I, Delabranche X, Severac F, et al. Acute pulmonary embolism in COVID-19 patients on CT angiography and

[1] Clínica Universidad de Navarra, Pamplona, Spain
[2] CIBERCV, IdiSNa, Pamplona, Spain

Corresponding Author:
José A. Páramo, Clínica Universidad de Navarra, Pamplona, Spain; CIBERCV, IdiSNa, Pamplona, Spain.
Email: japaramo@unav.es

relationship to D-Dimer levels. *Radiology*. 2020. doi:10.1148/radiol.2020201561

5. Xu Z, Shi L, Wang Y, et al. Pathological findings of COVID-19 associated with acute respiratory distress syndrome. *Lancet Respir Med*. 2020;8(4):420-422.
6. Tian S, Xiao SY. Pathology of 2019 novel coronavirus pneumonia: a dynamic disease process. *J Thorac Oncol*. 2020;15(5):e67-e68.
7. Ciceri F, Beretta L, Scandroglio AM, et al. Microvascular COVID-19 lung vessels obstructive thromboinflammatory syndrome (MicroCLOTS): an atypical acute respiratory distress syndrome working hypothesis [published online ahead of print]. *Crit Care Resusc*. 2020.
8. Varga Z, Flammer AJ, Steiger P, et al. Endothelial cell infection and endotheliitis in COVID-19. *Lancet*. 2020;395(10234):1417-1418.
9. Poissy J, Goutay J, Caplan M, et al. Pulmonary embolism in COVID-19 patients: awareness of an increased prevalence. *Circulation*. 2020. doi:10.1161/CIRCULATIONAHA.120.047430