Letters to the Editor

COVID-19 and Pulmonary Thromboembolism

From
Mark M. Hammer, MD,* and Constantine A. Raptis, MD†
Department of Radiology, Brigham and Women's Hospital, Harvard Medical School, 75 Francis St, Boston, MA 02115*
e-mail: *mmhammer@bwh.harvard.edu*
Mallinckrodt Institute of Radiology, Washington University School of Medicine, St Louis, Mo†

Editor:

We read with interest the recent meta-analysis by Dr Suh and colleagues in the February 2021 issue of *Radiology* regarding the incidence of pulmonary embolism (PE) in patients with coronavirus disease 2019 (COVID-19) (1). They reported that, by collating data from 27 studies, the incidence of PE in patients with COVID-19 is 16.5%, notably less than some initial reports of 27%–30% (2,3). However, although we commend Dr Suh and colleagues for attempting to establish an accurate point estimate of PE incidence, it is unfortunate that they were not able to obtain similar data from control patients. Lacking a context, it is difficult to interpret a 16.5% incidence standing alone, particularly because patients with COVID-19 are often critically ill and patients who are critically ill are at high risk of thrombosis (4).

Whereas at least 27 studies have been performed evaluating the incidence of PE in patients with COVID-19, few studies have been performed that compare these rates to those in patients who do not have COVID-19. Poissy et al (5) evaluated patients in the intensive care unit (ICU) with COVID-19 compared with two control groups: all patients in the ICU at the same time in the prior year and patients in the ICU with influenza. They found PE in approximately 21% of patients with COVID-19 compared with 6%–8% in the control groups. Whereas only 15% of the first control group underwent CT pulmonary angiography, 43% of the second control group underwent CT pulmonary angiography, similar to the 32% in the COVID-19 group. A second, multicenter cohort study performed by Helms et al (6) evaluated patients in the ICU with COVID-19 compared with historical control patients with acute respiratory distress syndrome. They found a PE rate of 12% in the COVID-19 group compared with 2% in the control patients; whereas 66% of the COVID-19 group underwent CT pulmonary angiography, the fraction of patients who underwent CT pulmonary angiography was not reported in the control group. Thus, it is possible that PEs were underdiagnosed in the control group because of fewer CT pulmonary angiographic examinations. Finally, a study performed by one of our groups evaluated patients who underwent COVID-19 testing and CT pulmonary angiography, comparing those with tests positive for COVID-19 to the control participants who were negative for COVID-19 (7). We found that 12% of the CT pulmonary angiography examinations were positive for PE in patients with COVID-19 compared with 9% in the control group, a difference that was not statistically significant. Indeed, a multivariable logistic regression analysis showed that D-dimer level, but not COVID-19 status, was predictive of PE diagnosis. We did find that among intubated patients the rate of PE was higher in the COVID-19 group compared with the control group (30% vs 18%, respectively), though this was not statistically significant because of the small number of such cases.

Given the data presented by Dr Suh and colleagues (1) and previous studies, we believe that the conclusion of a substantially increased risk of PE among patients with COVID-19 is not justified, nor is there clarity on the treatment implications and clinical relevance of this observation. In our anecdotal experience, we have seen an increase in ordering of CT pulmonary angiography in patients with COVID-19 likely because of literature that suggests such a risk. However, as borne out by the literature, the vast majority of these are negative for PE. Thus, we commend Dr Suh and colleagues for their work, but we believe it begs for the context of a relevant control group and an estimate of relative risk of thrombosis, both for all comers with COVID-19 and those who are critically ill. More research is needed to answer these questions.

Disclosures of Conflicts of Interest: M.M.H. disclosed no relevant relationships. **C.A.R.** disclosed no relevant relationships.

References

1. Suh YJ, Hong H, Ohana M, et al. Pulmonary Embolism and Deep Vein Thrombosis in COVID-19: A Systematic Review and Meta-Analysis. Radiology 2021;298(2):E70–E80.
2. Leonard-Lorant I, Delabranche X, Severac F, et al. Acute Pulmonary Embolism in COVID-19 Patients on CT Angiography and Relationship to D-Dimer Levels. Radiology 2020;296(3):E189–E191.
3. Poyiadji N, Cormier P, Patel PY, et al. Acute Pulmonary Embolism and COVID-19. Radiology 2020;297(3):E335–E338.
4. Kaplan D, Casper TC, Elliott CG, et al. VTE Incidence and Risk Factors in Patients With Severe Sepsis and Septic Shock. Chest 2015;148(5):1224–1230.
5. Poissy J, Goutay J, Caplan M, et al. Pulmonary Embolism in Patients With COVID-19: Awareness of an Increased Prevalence. Circulation 2020;142(2):184–186.
6. Helms J, Tacquard C, Severac F, et al. High risk of thrombosis in patients with severe SARS-CoV-2 infection: a multicenter prospective cohort study. Intensive Care Med 2020;46(6):1089–1098.
7. Hammer MM, Hunsaker AR, Gooptu M, Hatabu H. Frequency of Pulmonary Embolism in Patients With COVID-19. JACC Cardiovasc Imaging 2020;13(11):2478–2479.

Response

From
Young Joo Suh, MD, PhD,* and Soon Ho Yoon, MD, PhD†
Department of Radiology, Research Institute of Radiological Science, Severance Hospital, Yonsei University College of Medicine, Seoul, Korea*
Department of Radiology, UMass Memorial Medical Center, 55 Lake Avenue North, Worcester, MA 01655, US; and Department of Radiology, Seoul National University Hospital, Seoul National University College of Medicine, Seoul, Korea†
e-mail: *yshoka@gmail.com*

We appreciate your interest on our recent work (1) and agree that a lack of control patients could limit the interpretation of our analysis. Indeed, only a few included studies reporting the incidence of PE in patients with COVID-19 had data from control patients without COVID-19, and the proportion of patients who underwent CT pulmonary angiography and the disease severity of the study population also varied among the included studies. Nevertheless, it is well recognized that prothrombotic abnormalities are frequently observed (2) and associated with adverse outcomes in COVID-19 (3,4). Furthermore, direct invasion of the pulmonary vascular endothelium by severe acute respiratory syndrome coronavirus 2 is a distinctive finding from influenza virus, and pulmonary microthrombi were found to be more prevalent in patients with COVID-19 than in those with influenza virus at histopathologic examinations (5). The potential mechanisms of prevalent pulmonary thrombosis in COVID-19 are intense endothelial inflammation, altered pulmonary blood flow due to pneumonia, and classic migration of deep vein thrombosis into pulmonary arteries. Several guidelines recommend a prophylactic dose of low-molecular-weight heparin for patients hospitalized with COVID-19 (2).

Jointly considering the aforementioned findings and those of our systematic review and meta-analysis, PE needs to be considered as a complication of COVID-19, particularly in patients at risk for thrombotic events.

Disclosures of Conflicts of Interest: Y.J.S. disclosed no relevant relationships. **S.H.Y.** Activities related to the present article: disclosed no relevant relationships. Activities not related to the present article: disclosed employment from Medicalip. Other relationships: disclosed no relevant relationships.

References

1. Suh YJ, Hong H, Ohana M, et al. Pulmonary Embolism and Deep Vein Thrombosis in COVID-19: A Systematic Review and Meta-Analysis. Radiology 2021;298(2):E70–E80https://doi.org/10.1148/radiol.2020203557.
2. Piazza G, Morrow DA. Diagnosis, Management, and Pathophysiology of Arterial and Venous Thrombosis in COVID-19. JAMA 2020;324(24):2548–2549https://doi.org/10.1001/jama.2020.23422.
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):1054–1062https://doi.org/10.1016/S0140-6736(20)30566-3.</jrn>
4. Wu C, Chen X, Cai Y, et al. Risk Factors Associated With Acute Respiratory Distress Syndrome and Death in Patients With Coronavirus Disease 2019 Pneumonia in Wuhan, China. JAMA Intern Med 2020;180(7):934–943https://doi.org/10.1001/jamainternmed.2020.0994.
5. Ackermann M, Verleden SE, Kuehnel M, et al. Pulmonary Vascular Endothelialitis, Thrombosis, and Angiogenesis in Covid-19. N Engl J Med 2020;383(2):120–128https://doi.org/10.1056/NEJMoa2015432.<