Prevalence of Pulmonary Embolism in Emergency Department Patients With Suspected COVID-19: The Truth Remains Unknown

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To the Editor:

A strong association between pulmonary embolism (PE) and patients hospitalized with COVID-19 (15.3%, overall range = 0%–35%) has been reported,[1] but the prevalence in ED patients remains unknown. The contribution of traditional risk factors is likewise unclear.[2] While Freund et al.[3] attempted to answer to this question, we have methodologic concerns we feel require attention before emergency physicians proceed as if COVID-19 does not increase risk of PE.

First, attempting to establish disease prevalence when only those tested for disease are included can lead to erroneous estimates of prevalence, an epidemiologic pitfall known as the "referral filter."[4] Prevalence may be over- or underestimated, depending on the similarity between the tested and nontested groups. No data about patient volume or characteristics are provided by Freund et al. for the nontested group, and thus readers cannot understand the potential impact of selection bias—a critical limitation preventing application of these data to other populations.[5] The referral filter tends to suppress missed cases of disease,[6] so the rate of PE observed in this retrospective study may simply relate to the type of patients in whom computed tomography pulmonary angiograms (CTPAs) were ordered. The pandemic nature of COVID-19 may have deterred minimally symptomatic patients from visiting the ED, potentially inflating PE prevalence. Alternatively, given the rise in out-of-hospital cardiac arrest in COVID-19 hotspots,[7] patients with PE and COVID-19 may have died before seeking care, thereby decreasing PE prevalence. Furthermore, knowledge of CTPA usage and PE prevalence in nonpandemic time periods would be useful as significant differences from the study period would suggest additional confounding.

Second, the study period encompasses the early pandemic, when little was known about the disease and diagnostic and treatment strategies changed rapidly. The authors adjust for this by including a "week" variable in their regression model. While they report no effect therefrom, data for weekly PE incidence are not presented, the effect size the study would have power to detect in terms of per-week PE incidence is not discussed, and no attempt is made to control for the number of patients "at risk" during the study period (e.g., CTPAs/1,000 visits). Taken together, we believe that these factors preclude the exclusion of study week as a potential confounder and that changes in diagnostic approach likely influenced reported PE prevalence. Despite the authors' statements to the contrary, at least nine papers exploring COVID-19–associated coagulopathy and increased thrombotic burden were published before the study period concluded.[8–16] Therefore, we suspect that increased awareness of COVID-19–associated coagulopathy led to greater use of CTPA and thus a biased estimate of PE prevalence in this study.

Freund et al. have undertaken a task of great import, as determination of the association of PE and COVID-19 in ED patients affects diagnostic and therapeutic interventions. While the study has a litany of strengths, we feel that there are key limitations in recruitment and analysis that cast substantial doubt on the finding of equal PE prevalence between groups. As such, we believe that prudence requires continued consideration of COVID-19 as risk factor for PE until a

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methodologically rigorous epidemiologic study can be performed.

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