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Reply:


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We thank Marquez et al for their interest in our study. Their points are worthy of a discussion. Our article demonstrates a highly sensitive and specific biomarker, namely apical ground-glass opacification (GGO) seen on carotid CTA, in a cohort of patients with suspected stroke during the pandemic (sensitivity, 75% [95% CI, 56–87]; specificity, 81% [95% CI, 71–88]; OR = 11.65 [95% CI, 4.14–32.78]; $P = .001$). The sample was accrued continuously from March through April 2020 from a population scanned for the indication of suspected acute stroke, not for suspected coronavirus disease 2019 (COVID-19). This study simply highlights the importance of vigilance in assessment of the lung apices when reporting carotid CTAs in the population with suspected acute stroke. Most patients in our study were without typical symptoms of COVID-19. We used other information readily available at the time of the carotid CTA acquisition but were unable to find any other additional biomarkers. This included demographics, clinical history, symptoms and signs, as well as chest radiographs$^2$ (which are typically obtained shortly after the admission of patients with acute stroke). In summary, we recommend routinely analyzing lung apices in patients with stroke undergoing carotid CTA, because this rapid and easy assessment of apices is valuable, opportunistic, and “free” information in a routine and unmodified scan. The apical analysis simply identifies patients likely to have COVID-19 with early downstream benefits such as limiting disease transmission.

We reiterate that reverse transcriptase polymerase chain reaction (RT-PCR) should not be omitted or replaced. Such patients still require formal RT-PCR testing according to hospital policy. In some hospitals, RT-PCR testing may be required for all emergency admissions; in others, it may be just for those patients who have clinical features suggestive of COVID-19. Regardless of RT-PCR indication, we again point out that RT-PCR takes hours to process. In the interim, the opportunistic and free information we describe in analyzing the lung apices is of benefit. In our hospitals, apical analysis is now articulated in reports to good effect. In other words, having developed the biomarker, we should now benefit from further rigorous temporal and spatial validation. In our study (hypertension, diabetes mellitus, atrial fibrillation, hyperlipidemia, history of stroke/TIA, and smoking status) and were incorporated as covariates in the bivariate and multivariate analyses.

Our primary objective was to determine candidate diagnostic biomarkers for COVID-19, but we agree there were some interesting additional findings from our study regarding the association between SARS-CoV-2 infection and stroke. For example, a contributory mechanism to COVID-19-related excess mortality might be thromboembolic because increased carotid occlusion was associated with GGO (16.0% versus 3.4%, $P = .004$; OR = 6.82 [95% CI, 1.97–23.53]; $P = .002$), and our multivariate analysis suggested carotid occlusion was likely to be an independent predictor of death.

While this study was based in London, United Kingdom, and included 3 hospitals with a nonwhite population ranging from 10% to 40%, with patients from a variety of socioeconomic status in the catchment area, we believe the biomarker would benefit from further rigorous temporal and spatial validation. In other words, having developed the biomarker, we should now test it on a cohort of patients from hospitals throughout an entire nation with prospective data collection at a subsequent time point in the pandemic. Such a study to obtain highly representative samples of the populations with acute stroke during the COVID-19 pandemic is currently underway.$^5$

### References


4. The Royal College of Radiologists. The role of CT in patients suspected with COVID-19 infection. https://www.rcr.ac.uk/college/


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