RESPONSE TO LETTER TO THE EDITOR

Response by Yaghi et al to Letter Regarding Article, “SARS-CoV-2 and Stroke in a New York Healthcare System”

Shadi Yaghi, MD; Aaron Lord, MD; Jennifer Frontera, MD

In Response:

First, we would like to thank Albiero et al for the letter they submitted regarding our article.1 In their letter, they highlight the importance of paradoxical embolism as one of the plausible mechanisms in patients with cryptogenic stroke in the setting of coronavirus disease 2019 (COVID-19). This is particularly the case due to the increased prevalence of deep vein thrombosis and pulmonary embolism in hospitalized patients with COVID-19 infection.2,3

We agree with the authors that paradoxical embolism is a potential mechanism, and it may be useful in some patients to look for a cardiac shunt in patients with COVID-19 and ischemic stroke. In our study, only 10% (3/32) had evidence of deep vein thrombosis/pulmonary embolism, which provides indirect evidence that paradoxical embolism may not be the most important mechanism for stroke in these patients. Another yet smaller study, however, reported a higher percentage of deep vein thrombosis/pulmonary embolism in patients with ischemic stroke and COVID-19 infection.4

In our study, we found markedly elevated d-dimer levels (>2000 ng/mL) in 95% (20/21) of patients with cryptogenic stroke subtype suggesting that hypercoagulability is a more compelling mechanism. In addition, it should be noted that nearly 47% (10/21) of patients labeled as cryptogenic stroke in our study had an incomplete diagnostic evaluation and, therefore, it is difficult to consider paradoxical embolism as the mechanism of stroke given the lack of diagnostic tests needed to rule out other high-risk stroke mechanisms.

Unfortunately, in our study and other studies, most patients did not receive a bubble study with the transthoracic echocardiogram. Thus, the true prevalence of patent foramen ovale (PFO) in patients with ischemic stroke and COVID-19 remains unknown, and future studies are needed to compare the prevalence of PFO in patients with cryptogenic stroke with or without COVID-19 to provide evidence whether paradoxical embolism is a compelling mechanism in cryptogenic stroke in the setting of COVID-19.

As the relationship between COVID-19 and ischemic stroke remains uncertain, a complete diagnostic evaluation of ischemic stroke in patients with COVID-19 should be performed if possible to rule out conventional stroke mechanisms.5 It is suggested that COVID-19 can lead to ischemic stroke via inflammation and hypercoagulability leading to thrombosis, cardiac dysfunction leading to cardioembolism, and cervical artery dissection.5 These potential mechanisms, in addition to paradoxical embolism, should be considered, particularly in those patients whose ischemic stroke remained cryptogenic despite a complete diagnostic evaluation.

Although studies have shown a benefit of PFO closure in select patients with PFO and cryptogenic stroke, it remains uncertain whether patients with cryptogenic stroke patients in the setting of COVID-19 would benefit from PFO closure. In fact, PFO closure trials excluded those patients with underlying hypercoagulability. Therefore, detecting a PFO in patients with ischemic stroke and COVID-19 infection may not necessarily lead to a change in clinical management, especially that anticoagulation treatment has been suggested for primary and secondary prevention in patients with COVID-19 and elevated d-dimer levels.

Again, we thank Albiero et al for their letter, and we hope that future studies address the possibility of paradoxical embolism as a potential mechanism in patients with cryptogenic ischemic stroke and COVID-19.

ARTICLE INFORMATION

Affiliation
Department of Neurology, NYU Langone Health, New York.

Disclosures
None.

This manuscript was sent to Marc Fisher, Senior Consulting Editor, for editorial decision and final disposition.

For Disclosures, see page XXX.

© 2020 American Heart Association, Inc.

Stroke is available at www.ahajournals.org/journal/str

Stroke. 2020;51:00–00. DOI: 10.1161/STROKEAHA.120.031676
REFERENCES

1. Yaghi S, Ishida K, Torres J, Mac Grory B, Raz E, Humbert K, Henninger N, Trivedi T, Lillemoe K, Alam S, et al. SARS-CoV-2 and stroke in a New York healthcare system. Stroke. 2020;51:2002–2011. doi: 10.1161/STROKEAHA.120.030335.

2. Demelo-Rodríguez P, Cerrella-Muñoz E, Ordieres-Ortega L, Parra-Virto A, Toledano-Macías M, Toledo-Samaniego N, García-García A, García-Fernández-Bravo I, Ji Z, de-Miguel-Diez J, et al. Incidence of asymptomatic deep vein thrombosis in patients with COVID-19 pneumonia and elevated D-dimer levels. Thromb Res. 2020;192:23–26. doi: 10.1016/j.thromres.2020.05.018.

3. Al-Ani F, Chehade S, Lazo-Langner A. Thrombosis risk associated with COVID-19 infection. A scoping review. Thromb Res. 2020;192:152–160. doi: 10.1016/j.thromres.2020.05.039.

4. Beyrouti R, Adams ME, Benjamin L, Cohen H, Farmer SF, Goh YY, Humphries F, Jäger HR, Losseff NA, Perry RJ, et al. Characteristics of ischaemic stroke associated with COVID-19. J Neurol Neurosurg Psychiatry. 2020;91:889–891. doi: 10.1136/jnnp-2020-333586.

5. Valderrama EV, Humbert K, Lord A, Frontera J, Yaghi S. Severe acute respiratory syndrome coronavirus 2 infection and ischemic stroke. Stroke. 2020;51:e124–e127. doi: 10.1161/STROKEAHA.120.030153.