

LETTER TO THE EDITOR

Letter by Albiero and Seresini Regarding Article, “SARS-CoV-2 and Stroke in a New York Healthcare System”

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To the Editor:

We read with great interest the study by Yaghi et al.¹ They identified, of 3556 patients hospitalized with coronavirus disease 2019 (COVID-19) infection during the study period, a total of 32 patients (0.9%) who had radiologically proven ischemic stroke. In these 32 patients, who had severe COVID-19 and required mechanical ventilation in 81.3%, cryptogenic stroke subtype was more common (65.6%) as compared with contemporary controls (30.4%; $P=0.003$) and historical controls (25.0%; $P<0.001$), possibly related to an acquired associated hypercoagulability. However, they did not evaluate the relationship with patent foramen ovale (PFO) that is present in 40% to 50% of patients who experience a cryptogenic stroke.² Foramen ovale is a flap-like opening in the atrial septum that allows right-to-left shunting in the fetus and usually closes within 3 months after birth. An autopsy study of unselected adults revealed a PFO in 27% of individuals.³ Shunting across a PFO is rare in healthy individuals because the left atrial pressure is 5- to 7-mm Hg higher than the right atrial pressure. However, in patients with severe COVID-19 with acute respiratory distress syndrome that requires mechanical ventilation, reversal of the normal interatrial pressure gradient due to an increase in pulmonary artery pressure might result in an increased PFO right-to-left shunt, resulting in an increased risk of paradoxical embolism and ischemic stroke. This hypothesis is supported by the results of a study of patients with acute respiratory distress syndrome and PFO⁴ that demonstrated the presence of a moderate-to-large PFO shunting in 19.2% of patients and was associated with a smaller oxygenation response to positive end-expiratory pressure titration, greater use of adjunctive interventions, and longer periods on assisted ventilation and in the intensive care unit compared with patients without PFO shunting. In addition, a study of

hospitalized patients with confirmed COVID-19 pneumonia⁵ found a high prevalence (46.1%) of deep vein thrombosis associated with a higher proportion of acute respiratory distress syndrome (90.9% versus 58.5%; $P<0.001$) and pulmonary artery hypertension (34.4% versus 12.8%; $P=0.022$) than non-deep vein thrombosis patients. Future studies should test the hypothesis of a relationship between PFO and the prevalence of the cryptogenic stroke subtype in patients with severe COVID-19 and stroke. As a screening test to detect a PFO in severe COVID-19 patients, we suggest the use of contrast-enhanced transcranial Doppler that has a high sensibility in detecting a cardiac right-to-left shunt but does not exclude an extracardiac shunt. Therefore, a contrast-enhanced transthoracic echocardiogram/transesophageal echocardiogram is required to confirm a PFO. Most PFO-related paradoxical emboli are likely to present as ischemic strokes, given the anatomy of the aortic arch. However, systemic embolization to the gut, kidneys, limbs, and myocardium has been described. For example, elevated troponin levels associated with significant ST/T-wave changes on ECG in a young COVID-19 patient with stroke, acute respiratory distress syndrome, deep vein thrombosis, and the absence of risk factors for atherosclerosis should arise the suspicion of paradoxical embolization from a PFO. Studies are also needed to evaluate whether patients with severe COVID-19, once the suspicion of PFO is confirmed, may benefit of a more aggressive anticoagulation therapy for stroke and other thrombotic event prevention.

ARTICLE INFORMATION

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Disclosures

None.

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

For Disclosures, see page XXX.

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