

## Letter: Outcomes and Spectrum of Major Neurovascular Events Among COVID-19 Patients: A 3-Center Experience

To the Editor:

We read with great interest the article published by Taylor et al<sup>1</sup> entitled “Outcomes and Spectrum of Major Neurovascular Events Among COVID-19 Patients: A 3-Center Experience,” where the authors describe the clinical course and results of a series of cases of patients with COVID-19, who developed cerebrovascular events. We thank the authors<sup>1</sup> for providing this type of evidence, which is considered valuable; however, we would like to make some observations. Patients affected by COVID-19 may have multiple neurological manifestations in addition to cerebrovascular involvement. In a systematic review, the following neurological disorders were found in descending order of prevalence: headache (16.8%), dizziness (13.9%), altered state of consciousness (11.2%), vomiting (6.3%), epileptic seizures (1.7%), neuralgia (1.2%), and ataxia (0.7%), being the stroke, the presumptive diagnosis in the third place of consideration, below the acute viral meningoencephalitis and the hypoxic encephalopathy, evidencing then that the suspicion of stroke becomes difficult.<sup>2</sup> Additionally, Chen et al<sup>3</sup> reported that anosmia and dysgeusia (nonspecific symptoms) are the most common neurological symptoms in patients with COVID-19, so the approach for these individuals based on their risk factors to decrease the likelihood of developing complications such as stroke is complex.<sup>3</sup> They also found that acute cerebrovascular episodes occurred mainly in patients with advanced age, severe progression of COVID-19 disease, cardiovascular risk factors (hypertension, diabetes), and history of cardiovascular disease.<sup>3</sup> Advanced age remains one of the main risk factors for the development of severe cerebrovascular events in this type of patients. Goldberg et al<sup>4</sup> reported a case of COVID-19 with acute cerebral infarction, due to the instability of a proximal stenosis of the internal carotid artery at the bifurcation level, and decreased distal flow in the right medial cerebral artery and in both anterior cerebral arteries.<sup>4</sup> Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has been described as a neurotropic virus, from which numerous mechanisms of injury to nervous tissue have been postulated, such as, through the infection of the olfactory epithelium, infection of peripheral nerve endings with structural spread, vascular diffusion, and lesion secondary to immune response, among others, which could ultimately cause serious complications of the disease such as infectious toxic encephalopathy, acute viral meningoencephalitis, and severe cerebrovascular disease.<sup>5</sup> Finally, endothelial damage is an extremely important element in the pathogenesis of stroke in patients with COVID-19, because, at the local level, SARS-CoV-2 infects cells by binding the virus’s Spike protein to the

angiotensin-converting enzyme receptor 2 (ACE2) expressed in the capillary endothelium. Expression of this receptor was recently found in other superspecialized tissues such as glial cells,<sup>6</sup> cerebral cortex, black substance, brain stem, posterior area of the hypothalamus, and striated body.<sup>7</sup> In this order of ideas, not only patients who express the phenotype of COVID-19 may have a risk of thrombogenesis and cerebral ischemia due to the instability of previous pathological conditions, but the state of biochemical hypercoagulability that generates direct vascular injury is sufficient to compromise a person’s life or functional capacity.

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