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R. Jain

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## **Evolving Neuroimaging Findings during COVID-19**

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The coronavirus 2019 (COVID-19) pandemic first appeared in the United States in late February, and New York City (NYC) had its first case on March 1, 2020, with the outbreak reaching its peak in NYC around April 7. NYC hospitals started to see a surge of patients with COVID-19 during the early pandemic epoch, which quickly saturated the health care resources. During the early pandemic epoch, most patients were treated for pulmonary symptoms with respiratory supportive measures. A small percentage of patients presented with neurologic symptoms, including acute stroke or encephalopathy, through the emergency departments (EDs).

Neuroimaging volume for ED/inpatients saw a pronounced drop, similar to the trends for other imaging subspecialties except chest imaging. In the initial phase of the pandemic (March 1 to April 13), ED/inpatient CT and MR imaging brain examinations decreased by 40% and 27%, respectively (NYU Tisch Hospital, R. Jain's unpublished data, accessed on May 20, 2020), compared with the prepandemic epoch (February 1–27, 2020). Neuroimaging use in the early phase centered mostly on acute stroke assessment, and there was concern for an increased incidence of acute large-vessel stroke in younger patients during the early phase of the pandemic. This was reflected in clinical practice as neuroradiologists in hot spots saw a larger percentage of cases in the reading rooms being centered around acute ischemic strokes. This discrepancy became more pronounced due to a significant reduction in the nonstroke routine outpatient and ED/inpatient neuroimaging volumes.

Publications during this early phase had a similar trend because they were mostly case reports of acute stroke.<sup>2</sup> However, recent publications in large cohorts have demonstrated that the incidence of acute stroke in hospitalized patients with COVID-19 is not >1%-2%.<sup>1,3</sup> Although acute stroke is a major neurologic complication of COVID-19 and a poor prognostic marker, its incidence during the pandemic is not more than the percentage share of ED hospital admissions for stroke during the prepandemic epoch.<sup>1</sup> A recent publication has shown a 39% decrease in stroke imaging use in the prepandemic epoch versus the early pandemic epoch in the entire United States,<sup>4</sup> indirectly supporting the possibility that acute stroke incidence in COVID-19 may not be as high as initially predicted.<sup>1,3</sup>

The published COVID-19 literature toward the peak of the pandemic in early April started to support previous evidence that

From the Departments of Radiology and Neurosurgery, NYU Langone Health, New York, New York.

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these patients are at a very high thrombotic risk.<sup>5</sup> At this point, the use of therapeutic or prophylactic anticoagulation started to increase for hospitalized patients. For clinical neuroradiologists, more brain imaging demonstrated hemorrhagic strokes, whether hemorrhagic conversion of ischemic stroke or parenchymal hemorrhages, of which many were in patients receiving therapeutic or prophylactic anticoagulation.<sup>6</sup> Hemorrhagic stroke constituted about 25% of positive neuroimaging findings during this early and midphase of the pandemic.<sup>1,6</sup>

Neuroradiologists have seen their share of various zoonotic viral outbreaks affecting the central nervous system in the past few decades.<sup>7</sup> Neurologic injury in COVID-19 is hypothesized to be due to 2 mechanisms: 1) direct virus injury; and 2) indirect injury-related cytokine storm and increased coagulation. There is weak evidence that direct CNS injury in COVID-19 could cause meningoencephalitis or encephalopathy.8 However, the probability could be difficult to conclusively establish without a detailed CSF analysis or brain biopsy, which could be a challenge to obtain in most of these very sick patients. Another major issue with an accurate estimate of encephalitis has been a restrictive use of neuroimaging and particularly MR imaging during the pandemic. Most hospitalized patients were under strict contact precautions and isolation and on various kinds of respiratory support, making their transportation to MR imaging suites a challenge, especially during the early phase when health care resources were stretched thin.

Now, during the delayed phase of the pandemic in NYC, there is an uptick in the use of neuroimaging for hospitalized patients. More critically ill patients with COVID-19 are undergoing MR imaging brain studies, especially to evaluate their continued and prolonged poor mental status. Hence, the spectrum of brain imaging findings has shifted to more subacute and early chronic processes such as leukoencephalopathy and microhemorrhages. These imaging findings seem to be associated with prolonged respiratory failure and periods of hypoxemia and are usually seen in patients treated with prolonged ventilator support, who also have consumption coagulopathy characterized by elevated D-dimer levels and fibrinogen-degradation products (R. Jain's unpublished data, accessed on May 20, 2020).

Apart from the common neurologic manifestations and imaging findings, there is also a growing interest and knowledge base about COVID-19-related inflammatory disease processes like Guillain-Barré syndrome and Kawasaki-like disease (especially in pediatric populations). Head and neck radiologists are also exploring possible associations of cranial neuropathies and other soft-tissue neck abnormalities with COVID-19. Moving forward, the focus of neuroimaging findings and research will shift to more delayed and long-term complications in critically ill patients. It would be a great opportunity for neuroradiologists to correlate COVID-19-related imaging findings with the long-term morbidity and mortality of these patients, with the focus on chronic brain injury, atrophy, and dementia.

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