

## Risk of Acute Cerebrovascular Events in Patients with COVID-19 Infection



Neurologic symptoms are reported in patients with coronavirus disease 2019 (COVID-19) with a higher prevalence in more severe cases; these symptoms can include altered mental status, dizziness, headache, and anosmia.<sup>1</sup> Coagulopathy and vascular endothelial injury in COVID-19 infection are also reported and may contribute to multiorgan dysfunction.<sup>2,3</sup> The risk of acute cerebrovascular events (CVE), however, is poorly defined.<sup>1,4</sup> A group from Union Hospital, Tongji Medical College in China detailed in their single-center experience that the risk of acute CVE, including hemorrhagic and ischemic stroke, was approximately 5% (11 of 219 patients).<sup>4</sup> Here, we report a similar risk of acute CVE at a large academic institution in the United States.

During a 2-week period between March 27 and April 10, 2020, four hundred sixty-eight patients hospitalized at our institution tested positive for COVID-19 by real-time polymerase chain reaction: 105 underwent neuroimaging (CT or MR imaging). The most common indication was altered mental status, followed by head trauma and clinical concern of stroke (Table). Six cases were found to have acute CVE on imaging; 4 cases were hemorrhagic in nature (lobar intracranial hemorrhage in 2, subarachnoid hemorrhage in 1, and multifocal microhemorrhages in 1); and 2 were ischemic in nature (internal capsule infarct in 1 and subcortical frontal lobe infarct in 1). The acute CVE risk was 5.7% for all patients with COVID-19 who underwent neuroimaging in our study, similar to the 5% acute CVE risk reported by the Tongji Medical College group from China.<sup>4</sup> If all patients with COVID-19 without neuroimaging were presumed to be negative for CVE, however, the risk would decrease to 1.3%. A challenge with acute CVE estimates in the general COVID-19 population, however, is the possibility of missing clinically silent strokes, especially given the difficulty in clinical detection of stroke in critically ill patients. A high proportion of patients in our cohort with acute CVE were critically ill, with 4 of the 6 patients with acute CVE (67%) admitted to the intensive care unit, 3 of whom required intubation. Furthermore, 2 of the 6 (33%) patients with acute CVE in our study died. Overall, these findings are consistent with the current literature suggesting a potentially dysfunc-

tional inflammatory response, coagulopathy, and endothelial damage in critically ill patients with COVID-19 infection.<sup>2,3,5</sup>

In contrast to previous reports, we found no significant differences in age and comorbidities between patients with COVID-19 with and without acute CVE (Table).<sup>4</sup> This finding suggests that the risk of acute CVE may be increased in general for critically ill patients with COVID-19 infection and attention should not be limited to older patients with cerebrovascular risk factors as previously proposed. This is further supported by a case series reporting large-vessel stroke in 5 patients with COVID-19 younger than 50 years of age.<sup>3</sup> Further research on this topic is needed.

COVID-19 infection appears, therefore, to be associated with a more diffuse pattern of vascular abnormalities with multiorgan involvement. Acute CVE should be considered in critically ill patients with COVID-19 with new neurologic deficits, and despite the logistical challenges posed by this population, there should be a relatively low threshold for obtaining neuroimaging when clinically indicated.

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## Summary of patient characteristics

Characteristics	Patients with COVID-19 with Acute CVE (n = 6)	Patients with COVID-19 without Acute CVE (n = 99)	P value
Mean age (yr)	62 ± 14	66 ± 17	0.41 <sup>a</sup>
< 50 yrs, n (%)	1 (17)	14 (14)	>0.99 <sup>b</sup>
≥ 50 yrs, n (%)	5 (83)	85 (86)	
Sex, n (%)			0.40 <sup>b</sup>
Male	5 (83)	57 (58)	
Female	1 (17)	42 (42)	
Indication for neuroimaging, n (%)			0.08 <sup>c</sup>
Altered mental status	1 (17)	47 (47)	
Trauma	1 (17)	24 (24)	
Stroke symptoms	4 (67)	14 (14)	
Headache	0 (0)	7 (7)	
Seizure	0 (0)	3 (3)	
Syncope	0 (0)	3 (3)	
Dizziness	0 (0)	1 (1)	
Comorbidities, n (%)			
Current smoker	0 (0)	7 (7)	>0.99 <sup>b</sup>
Ex-smoker	1 (17)	8 (8)	0.42 <sup>b</sup>
Hypertension	3 (50)	62 (63)	0.67 <sup>b</sup>
Diabetes	2 (33)	38 (38)	>0.99 <sup>b</sup>
Obesity	3 (50)	20 (20)	0.12 <sup>b</sup>
COPD/asthma/OSA	2 (33)	18 (18)	0.32 <sup>b</sup>
Malignancy	0 (0)	11 (11)	>0.99 <sup>b</sup>
Cardiovascular disease	1 (17)	11 (11)	0.53 <sup>b</sup>
Cerebrovascular disease	0 (0)	7 (7)	>0.99 <sup>b</sup>
Requiring ICU admission, n (%)	4 (67)	47 (47)	0.43 <sup>b</sup>
With intubation	3 (50)	42 (42)	>0.99 <sup>b</sup>
Discharged, n (%)	2 (33)	46 (46)	0.69 <sup>b</sup>
Deceased, n (%)	2 (33)	11 (11)	0.16

**Note:**—COPD indicates chronic obstructive pulmonary disease; OSA, obstructive sleep apnea; ICU, intensive care unit.

<sup>a</sup> Two-tailed t-test.

<sup>b</sup> Fisher's exact test.

<sup>c</sup> Chi-squared test.

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