

## BRIEF REPORT

# Early Brain Imaging Shows Increased Severity of Acute Ischemic Strokes With Large Vessel Occlusion in COVID-19 Patients

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**BACKGROUND AND PURPOSE:** Reports are emerging regarding the association of acute ischemic strokes with large vessel occlusion and coronavirus disease 2019 (COVID-19). While a higher severity of these patients could be expected from the addition of both respiratory and neurological injury, COVID-19 patients with strokes can present with mild or none respiratory symptoms. We aimed to compare anterior circulation large vessel occlusion strokes severity between patients with and without COVID-19.

**METHODS:** We performed a comparative cohort study between patients with COVID-19 who had anterior circulation large vessel occlusion and early brain imaging within 3 hours from onset, in our institution during the 6 first weeks of the COVID-19 outbreak and a control group admitted during the same calendar period in 2019.

**RESULTS:** Twelve COVID-19 patients with anterior circulation large vessel occlusion and early brain imaging were included during the study period and compared with 34 control patients with anterior circulation large vessel occlusion and early brain imaging in 2019. Patients in the COVID-19 group were younger ( $P=0.032$ ) and had a history of diabetes mellitus more frequently ( $P=0.039$ ). Patients did not significantly differ on initial National Institutes of Health Stroke Scale nor time from onset to imaging ( $P=0.18$  and  $P=0.6$ , respectively). Patients with COVID-19 had more severe strokes than patients without COVID-19, with a significantly lower clot burden score (median: 6.5 versus 8,  $P=0.016$ ), higher rate of multivessel occlusion (50% versus 8.8%,  $P=0.005$ ), lower DWI-ASPECTS (Diffusion-Weighted Imaging–Alberta Stroke Program Early Computed Tomography Scores; median: 5 versus 8,  $P=0.006$ ), and higher infarct core volume (median: 58 versus 6 mL,  $P=0.004$ ). Successful recanalization rate was similar in both groups ( $P=0.767$ ). In-hospital mortality was higher in the COVID-19 patients' group (41.7% versus 11.8%,  $P=0.025$ ).

**CONCLUSIONS:** Early brain imaging showed higher severity large vessel occlusion strokes in patients with COVID-19. Given the massive number of infected patients, concerns should be raised about the coming neurovascular impact of the pandemic worldwide.

**Key Words:** brain ■ coronavirus ■ ischemia ■ prognosis ■ stroke

Reports are emerging regarding the association of large vessel strokes and coronavirus disease 2019 (COVID-19).<sup>1,2</sup> While a higher severity of these patients could be expected from the association of respiratory infection and neurological injury,<sup>3</sup> COVID-19 strokes can present with mild or none respiratory symptoms.<sup>1,2,4,5</sup> We aimed to compare anterior circulation large

vessel occlusion strokes (aLVO) severity between with and without COVID-19.

## METHODS

According to the Transparency and Openness Promotion Guidelines, the authors declare that the data which support

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## Nonstandard Abbreviations and Acronyms

<b>aLVO</b>	anterior circulation large vessel occlusion
<b>COVID-19</b>	coronavirus disease 2019

the findings of this study are available from the corresponding author upon reasonable request. Our local ethics committee approved the use of patient data for this research protocol. In accordance with French legislation, informed consent was not needed from patients because this study analyzed anonymized data collected prospectively as a part of routine clinical care.

## Patients Selection

All consecutive early diagnosed aLVO with real-time polymerase chain reaction confirmed COVID-19 treated in our institution between March 15, 2020 and April 30, 2020 were included. For the purpose of investigating the potentially higher severity of aLVO in patients with COVID-19, patients with late diagnosis (first imaging later than 3 hours from onset), or unknown onset were excluded.

As stroke patients were not systematically screened with real-time polymerase chain reaction during this time period, patients with unknown status regarding COVID-19 were excluded, and the comparative control cohort was constituted with early diagnosed aLVO treated in our institution during the same calendar period in 2019.

**Table. Patient Characteristics**

	Total (n=46)	COVID-19 (n=12)	Non-COVID-19 (n=34)	P Value
<b>Characteristic</b>				
Mean age (SD), y	67.6±15.2	60.1±12.6	70.3±15.3	0.032*
Male sex, n (%)	30 (65.2)	10 (83.3)	20 (58.8)	0.170
Median baseline mRS (IQR)	0 (0–1)	1 (0–1)	0 (0–1)	0.222
<b>Risk factor, n (%)</b>				
Hypertension	29 (63.0)	5 (41.7)	24 (70.6)	0.093
Diabetes mellitus	9 (19.6)	5 (41.7)	4 (11.8)	0.039*
Hypercholesterolemia	11 (23.9)	3 (25.0)	8 (23.5)	1
Smoking (1 missing in non-COVID-19)	3 (6.7)	0 (0)	3 (9.1)	0.554
Atrial fibrillation	14 (38.9)	1 (8.3)	13 (38.2)	0.073
<b>Stroke characteristic</b>				
Median NIHSS (IQR)	18 (13–23)	19 (17.75–24.25)	17.5 (12.25–21.5)	0.180
Median time from onset to imaging (IQR), min	107.5 (75–135)	116 (86–135)	104 (74–133)	0.661
<b>Brain imaging findings</b>				
MRI with angioMR, n (%)	40 (87.0)	10 (83.3)	30 (88.2)	
CT with angioCT, n (%)	6 (13.0)	2 (16.7)	(11.8)	
Occlusion site, n (%)				0.731
Carotid terminus	8 (17.4)	3 (25.0)	5 (14.7)	
Middle cerebral artery-M1	27 (58.7)	7 (58.3)	20 (58.8)	
Middle cerebral artery-M2	11 (23.9)	2 (16.7)	9 (26.5)	
Associated ACA or PCA occlusion, n (%)	9 (19.6)	6 (50)	3 (8.8)	0.005*
Median clot burden (IQR)	8 (6–8)	6.5 (5–7.25)	8 (7.25–8.75)	0.016*
<b>MRI only findings</b>				
All patients (with or without associated ACA or PCA occlusion), n (%)	40 (87.0)	10 (83.3)	30 (88.2)	
Median DWI-lesion volume (IQR), mL	12 (4–38)	58 (33–123)	6 (3–24)	0.004*
Median DWI-ASPECT score (IQR)	7 (6–8)	5 (3–7)	8 (7–9)	0.006*
Among patient without associated ACA or PCA occlusion, n (%)	34 (73.9)	6 (50)	28 (82.3)	
Median DWI-lesion volume (IQR), mL	7 (4–34)	36 (12–67)	6 (3–24)	0.060*
Median DWI-ASPECT score (IQR)	8 (7–8.75)	6 (3.5–7.75)	8 (7–9)	0.058*
<b>Treatment</b>				
IV thrombolysis, n (%)	25 (54.3)	8 (66.7)	17 (50)	0.319
Mechanical thrombectomy, n (%)	40 (90.9)	12 (100)	28 (82.3)	0.311
Successful recanalization, n (%)	43 (93.5)	11 (91.7)	32 (94.1)	0.767
In-hospital mortality, n (%)	9 (19.6)	5 (41.7)	4 (11.8)	0.025*

COVID-19 indicates coronavirus disease 2019; CT, computed tomography; DWI, diffusion-weighted imaging; DWI-ASPECT, Diffusion-Weighted Imaging–Alberta Stroke Program Early Computed Tomography Scores; IQR, interquartile range; IV, intravenous; MRI, magnetic resonance imaging; mRS, modified Rankin Scale; and NIHSS, National Institutes of Health Stroke Scale.

\*Statistically significant.

## Imaging Analysis

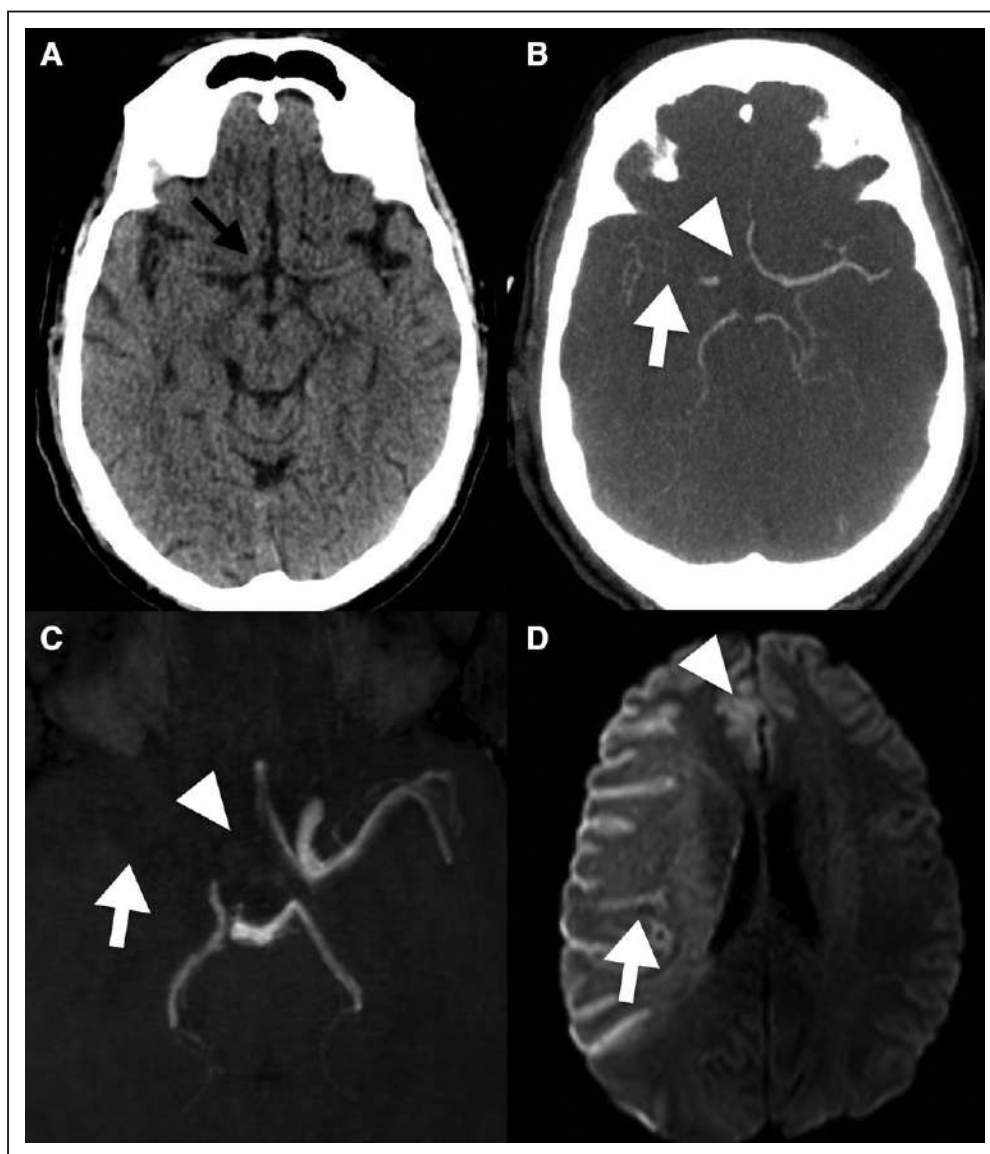
All imaging data were prospectively gathered, at the exception of infarct core volumes. Multivessel occlusion was defined as a simultaneous occlusion of the middle cerebral artery and either the anterior or the posterior cerebral artery. Two authors (Drs Chalumeau and C. Escalard) blinded to the COVID-19 status (and time of acquisition) of the cases were asked to independently measure the infarct core volume<sup>6</sup> for all patients, on a b1000 diffusion-weighted imaging sequence, using Food and Drug Administration– and Conformité Européenne–cleared software Osirix MD (Pixmeo, Geneva, Switzerland). In cases of discordance, a simultaneous reading to reach consensus was achieved.

## Statistical Analysis

Comparisons between the 2 study groups were made using the Student *t* test for gaussian continuous variables, the Mann-Whitney *U* test for nongaussian continuous variables, and the  $\chi^2$  (or Fisher exact test when the expected cell frequency was <5) for categorical variables, as appropriate. All analyses were done with R software V.3.3.2 and a significance level of 5%.

## RESULTS

During the study period, 15 patients with large vessel occlusion and confirmed COVID-19 were treated in our



**Figure.** Early brain imaging findings in coronavirus disease 2019 (COVID-19) patients with large vessel occlusion strokes.

A 56-year-old man with left hemiplegia (**A** and **B**), the computed tomography (CT) was performed 0.5 h after onset. The noncontrast-CT (**A**) showed no early ischemic changes (black arrow shows the anterior cerebral artery). The CT-angiography (**B**) shows a proximal middle cerebral artery (MCA) occlusion (arrow) associated with a proximal anterior cerebral artery occlusion (arrow head), the clot burden was 5. A 45-year-old female with left hemiplegia (**C** and **D**), the magnetic resonance imaging (MRI) was performed 2.25 h after onset. The 3-dimensional time-of-flight (**C**) shows a carotid terminus occlusion with proximal MCA occlusion (arrow) associated with an anterior cerebral artery occlusion (arrow head), the clot burden was 5. The DWI sequence (**D**) shows ischemic lesions in both MCA and anterior cerebral artery territories (arrow and arrow head, respectively), DWI-ASPECTS (Diffusion-Weighted Imaging–Alberta Stroke Program Early Computed Tomography Scores) was 0, infarct core volume was 186.5 mL.

institution. Twelve had anterior circulation occlusion with early diagnosis imaging (within 3 hours from onset), 2 had late diagnosis, and one had basilar occlusion and were, therefore, excluded from the study. All data regarding patients' characteristics and imaging findings are reported in the Table. Patients in the COVID-19 group were younger with a mean age of  $60.1 \pm 12.6$  years old ( $P=0.032$ ) and had a history of diabetes mellitus more frequently ( $P=0.039$ ). The median National Institutes of Health Stroke Scale at admission was 19 ( $P=0.18$ ). The median time from stroke onset to imaging was 116 minutes (interquartile range, 86–135). Ten patients (83.3%) had a brain magnetic resonance imaging and 2 patients had a computed tomography with computed tomography angiography for early diagnosis of stroke. Patients with COVID-19 had more severe strokes than patients without COVID-19, with a significantly lower clot burden score (median: 6.5 versus 8,  $P=0.016$ ), higher rate of multivessel occlusion (50% versus 8.8%,  $P=0.005$ ), lower DWI-ASPECT (Diffusion-Weighted Imaging–Alberta Stroke Program Early Computed Tomography Scores; median: 5 versus 8,  $P=0.006$ ), and higher infarct core volume (median: 58 versus 6 mL,  $P=0.004$ ). Subgroup analysis of patients without multivessel occlusion showed a trend towards lower DWI-ASPECT and higher infarct core volume in patients with COVID-19, but the difference did not reach significance ( $P=0.058$  and  $P=0.06$ , respectively). Successful recanalization (defined by a modified Thrombolysis in Cerebral Infarction score  $\geq 2B$ ) rate after mechanical thrombectomy was similar in both groups ( $P=0.767$ ). In-hospital mortality was higher in the COVID-19 patients' group (41.7% versus 11.8%,  $P=0.025$ ). Two illustrative cases are presented in the Figure.

## DISCUSSION

Our study provides evidence that patients with COVID-19 experience more severe aLVO than patients without COVID-19, as assessed by early brain imaging. Despite a small number of patients, we found that COVID-19 patients with aLVO had lower clot burden scores, associated with lower rate of recanalization after thrombolysis,<sup>7</sup> higher rates of multivessel occlusions, associated with lower rate of recanalization after thrombectomy,<sup>8</sup> lower DWI-ASPECTS and higher infarct core volume, which are well-established predictors of poor outcome in ischemic stroke.<sup>9</sup> As a result, in-hospital mortality was much higher in patients with COVID-19. We think that systemic inflammation, coagulation disorders, and endothelial dysfunction<sup>10,11</sup> associated with COVID-19 could be involved in the trend observed towards higher infarct volumes and lower DWI-ASPECTS in COVID-19 patients without multivessel occlusion. This hypothesis is supported by recent reports regarding the presence of microvascular immunothrombosis in patients with COVID-19.<sup>12,13</sup> These findings are in line with the current literature which has started to emphasize the devastating

extrapulmonary thrombotic complications associated with the COVID-19.<sup>14,15</sup>

In addition to being predicting factors of poor outcome, these factors may negatively influence the decision to propose recanalization treatments such as thrombolysis or thrombectomy,<sup>16</sup> despite early stroke diagnosis (within 3 hours from onset in our series), and therefore severely impact the prognosis of acute ischemic strokes in patients with COVID-19.

A recent large cohort study raised concerns about the potential decrease in the amount of care provided to stroke patients across the United States,<sup>17</sup> stressing at the same time the increased use of advanced-imaging in the decision-making for stroke treatment.<sup>18</sup> Concerns should be raised about the coming neurovascular consequences of the pandemic.

## CONCLUSIONS

Early brain imaging showed higher severity of anterior circulation large vessel occlusion strokes in patients with COVID-19. Given the massive number of infected patients, concerns should be raised about the coming neurovascular impact of the pandemic worldwide.

## ARTICLE INFORMATION

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