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Original Article

CT and Angiographic Findings among COVID-19-Positive Patients Presenting with Stroke and Their Outcomes

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Abstract

Background The study aims to assess and compare the computed tomographic and angiographic findings and clinical outcomes among coronavirus disease 2019 (COVID-19)-positive and COVID-19-negative patients.

Methods We conducted a retrospective study of all patients presenting with acute stroke to our facility between March 2020 and October 2021. Demographics, risk factors, COVID-19 status, National Institute of Health Stroke Scale (NIHSS), mode of treatment, length of hospital stay, imaging findings, and angiographic and clinical outcomes were extracted from electronic medical records. Descriptive statistics were used to summarize the data. Pregnant patients, those under the age of 18, and those found to have an alternative diagnosis were excluded. We identified 103 patients with acute stroke who underwent thrombolysis and/or mechanical thrombectomy, 16 of whom were found to be COVID-positive (study group), while 87 of them had negative status (control group).

Result The mean age of both groups (COVID-19 positive and COVID-19 negative) was 56 years, and 85% were male. The most frequently involved vessel was the M1 segment of the middle cerebral artery (37% in COVID-19-positive patients vs. 41% in COVID-19-negative patients). Sixty-one patients underwent thrombectomy, and both groups had comparable successful recanalization. Patients with COVID-19 infection were more likely to have a more extended hospital stay and a higher average NIHSS score at discharge.

Conclusion Our study shows that ischemic stroke in COVID-19 occurs in predominantly male patients, with the middle cerebral artery being the most frequently involved vascular territory. Furthermore, there is a longer hospital stay and worse morbidity regardless of the mode of treatment and imaging findings in COVID-19-positive patients.

Keywords
- COVID-19
- stroke
- imaging
- angiography
- ischemic stroke
- large vessel occlusion
- thrombectomy

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Introduction

Ischemic stroke is one of the major complications in the era of coronavirus disease 2019 (COVID-19) infection and is often treated by administering a thrombolytic agent or endovascular treatment. A study conducted in China reported an incidence of acute cerebrovascular disease up to 5.8%.[1–4] The tendency of developing thromboembolic events in patients with COVID-19 has been attributed to possible virus-related proinflammatory activation of cytokines and coagulation cascade, leading to hypercoagulability status, evident by the coagulation profile derangement including elevated D-dimer, partial thromboplastin time, and prothrombin.[5–8] Therefore, it has been recommended to initiate prophylactic anticoagulation with low-molecular-weight heparin, except when it is contraindicated.[6,7] According to Siegler et al mortality rate among these patients was high, ranging between 6 and39%, with a higher rate in older patients with positive COVID-19 infection and associated comorbidities.[6,9] While acute stroke is not a common complication of COVID-19, it is a significant risk factor contributing to mortality.[10,11]

Imaging plays a vital role in diagnosing and managing COVID-19-positive patients presenting with neurological symptoms typical of stroke, such as motor or sensory loss. Computed tomography (CT) scan of the brain is the best initial imaging modality for diagnosis, which is confirmed with a CT angiogram.[12,13] According to the American Heart Association/American Stroke Association, treatment involves either intravenous thrombolysis and/or endovascular mechanical thrombectomy, depending on eligibility.[14] Techniques of endovascular thrombectomy include stent retriever and aspiration techniques.[13] Concurrent COVID-19 infection with stroke has been noted to delay the endovascular treatment process, leading to poorer clinical outcomes.[8,15–17] Therefore, understanding the association between COVID-19 infection and the development of stroke and its implications will improve early diagnosis, provide effective management, and improve the overall prognosis of these patients.

Methods

Study Design

This is a retrospective, observational study of patients admitted with the primary diagnosis of ischemic stroke positive early signs of ischemic stroke on plain CT and or positive CT angiography of vessel occlusion. Data were collected from all consecutive patients more than 18 years of age presenting to our local hospital that has been diagnosed with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) using oropharyngeal polymerase chain reaction (PCR) with clinical and radiological evidence of acute ischemic stroke (AIS) in the period spanning from March 2020 to October 2021 (the period of peak incidence of positive COVID-19 infection cases in UAE; (►**Fig. 1**). As per our hospital protocol, screening for COVID-19 was mandatory for every patient presenting to the emergency department during the pandemic. Treatment was initiated and full protective and safety measures, in accordance with hospital protocol, were followed, regardless of the results, and without any delay. All patients with pending results were managed with treating staff equipped with personal protective equipment during procedures.

Patients under 18 years, pregnant females, patients with coagulation disorders on CT, cases who were out-of-window and did not undergo any treatment, and patients with incomplete medical records or those who were negative for stroke having an alternative diagnosis such as transient ischemic attack, dural venous sinus thrombosis, and migraine were excluded (►**Fig. 1**). The local institutional review board approved the study, and written informed consent was waived.

Data Collection

All eligible patients were recruited from our radiology department's electronic imaging recording system. The study group was identified as the patients presenting with clinical symptoms of stroke and found to be COVID-19 positive either before or at the time of admission from the period March 2020 until the period of October 2021 (the period of the COVID-19 pandemic). The control group was chosen from the electronic medical records section using International Classification of Diseases codes—those

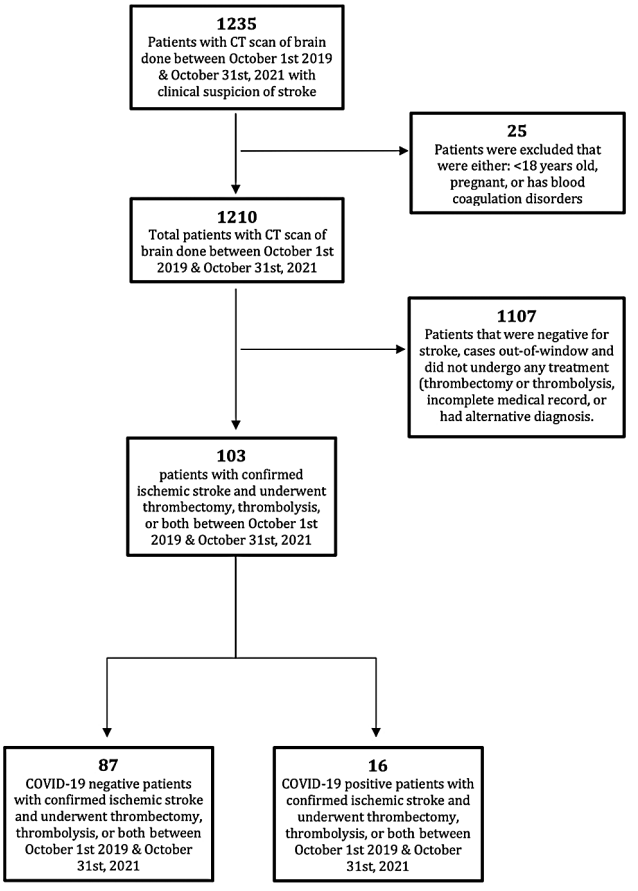

Fig. 1 Study flowchart of patients with clinical and radiological diagnosis of ischemic stroke that are hospitalized and underwent mechanical thrombectomy, thrombolysis, or both between October 1st, 2019 and October 31st, 2021. COVID-19, coronavirus disease 2019; CT, computed tomography.

presenting with stroke who did not have PCR-proven COVID-19 infection were selected from the same period.

Patients' demographics, the clinical presentation including the National Institute of Health Stroke Scale (NIHSS) score, comorbidities (hypertension, diabetes mellitus, etc.), procedural metrics including thrombolysis in cerebral infarction (TICI) scale, hospital care course as well as 90-days follow-up as per the modified Rankin score (MRS) were collected and analyzed through the Epic electronic medical record system. The diagnosis of AIS was confirmed by a brain CT scan.

Statistical Analysis

Mean and standard deviations were used for baseline data for continuous variables. Categorical variables were expressed as counts and percentages. Continuous variables were compared by using independent-sample *t*-tests. Finally, proportions for categorical variables were compared using Fisher's exact test. All statistical analyses were performed with the assistance of a statistician and SPSS statistical software.

Results

Demographics

Of 103 patients presenting with AIS and undergoing treatment during the study period, we identified 16 COVID-19-positive patients. The mean age of both groups was 56 years (54 vs. 58, $p = 0.282$), and 85% were male. No significant differences were noticed between the two groups regarding the pre-existing comorbidities or the clinical outcomes, including intensive care unit (ICU) admission, length of stay in the hospital, or mortality rate. The main comorbidities identified in the COVID-19 negative group included hyperlipidemia (18 vs. 19%, $p = 0.999$), diabetes mellitus (30 vs. 56%, $p = 0.052$), and hypertension (59 vs. 44%, $p = 0.288$) that were comparable to the COVID-19-positive group. In addition, NIHSS score on admission was also similar in both groups as per the table (10.6 vs. 14, $p = 0.071$), and COVID-19-positive patients had significantly higher NIHSS scores on discharge (4.4 vs. 9.6, $p = 0.050$) irrespective of their treatment method or outcomes of imaging. Regarding the ASPECT score, there was no significant change between the two groups (8 vs. 7, $p = 0.253$). The baseline characteristics, including the demographics and clinical outcomes, are presented in ►**Table 1**.

On 90 days follow-up, according to the MRS, there was no significant statistical significance between patients with COVID-19-positive status and patients with COVID-19-negative status (1.9 vs. 2.4, $p = 0.154$)

Treatment

The most frequently involved vessel was the M1 segment of the middle cerebral artery (39.8%). Patients with COVID-19

Table 1 Clinical characteristics of patients with ischemic stroke and differences in clinical features between patients with positive COVID-19 status and negative COVID-19 status

	COVID-19 negative ($n = 87$)	COVID-19 positive ($n = 16$)	*p*-Value[a]
Age	Mean: 54.28	Mean: 58	0.282
Gender			
Female	15 (13%)	0 (0%)	0.999
Male	72 (82%)	16 (100%)	
Comorbidities			
Smoking history	9 (10%)	0 (0%)	0.348
Hyperlipidemia	16 (18%)	3 (19%)	0.999
Diabetes mellitus	26 (30%)	9 (56%)	0.052
Hypertension	51 (59%)	7 (44%)	0.288
Atrial fibrillation	6 (7%)	8 (50%)	0.607
Prior stroke	8 (9%)	2 (13%)	0.652
Clinical and imaging presentation			
NIHSS on admission	10.6 ± 5.9	14 ± 7.3	0.071
ASPECTS	8 ± 2.3	7 ± 2.7	0.253
Clinical outcomes			
Length of hospital stay	14 days $\pm$ 21.7	40 days $\pm$ 44	<0.001
NIHSS on discharge	4.4 ± 4.7	9.6 ± 9.5	0.050
Death	9 (10%)	3 (19%)	0.277
Follow-up (modified Rankin Scale)	1.9 ± 1.2	2.4 ± 1.9	0.152

Abbreviations: COVID-19, coronavirus disease 2019; NIHSS, National Institute of Health Stroke Scale.
Data are presented as mean or total numbers, with percentage or standard deviation in parentheses.
[a]*p*-Values indicate differences between patients with positive COVID-19 and negative COVID-19. $p < 0.05$ was considered statistically significant.

Table 2 Differences in treatment methods and outcomes between patients with positive COVID-19 status and negative COVID-19 status

	COVID-19 negative ($n = 87$)	COVID-19 positive ($n = 16$)	p-Value[a]
Treatment method			
Thrombolysis only	31 (36%)	6 (37%)	0.187
Thrombectomy only	18 (21%)	7 (44%)	0.999
Combined treatment (thrombectomy and thrombolysis)	38 (43%)	3 (19%)	0.134
Angiographic findings			
Internal carotid artery	13 (15%)	5 (31%)	0.149
Proximal MCA (M1 segment)	36 (41%)	6 (37%)	0.582
Distal MCA (M2-4 segment)	24 (28%)	5 (31%)	0.550
Basilar artery/PCA	8 (9%)	5 (31%)	0.029
Thrombectomy outcomes			
TICI 0	5 (10%)	1 (10%)	>0.05
TICI 1	0 (0%)	0 (0%)	
TICI 2a	1 (2%)	1 (10%)	
TICI 2b	7 (13.7%)	1 (10%)	
TICI 2c	1 (2%)	1 (10%)	
TICI 3	37 (73%)	6 (60%)	
Number of passes	1.6	1.3	0.194

Abbreviations: COVID-19, coronavirus disease 2019; MCA, middle cerebral artery; PCA, posterior cerebral artery; TICI, thrombolysis in cerebral infarction.
Data are presented as mean or total numbers, with percentage or standard deviation in parentheses.
[a]p-Values indicate differences between patients with positive COVID-19 and negative COVID-19. $p < 0.05$ was considered statistically significant.

infection were more likely to have a longer hospital stay and worse outcomes at discharge, with a higher average NIHSS score (9.4). Sixty-one patients underwent thrombectomy, and both groups had comparable successful recanalization.

In both groups (COVID-19 positive and COVID-19 negative), most patients received general anesthesia. There were 28 patients in the positive group who received general anesthesia and 9 in the negative group. In contrast, there were 18 in the positive group and only 1 in the negative group who received local anesthesia.

Furthermore, in both groups (COVID-19 positive and COVID-19 negative), thrombolysis was the first line of therapy for most patients. A total number of 10 mechanical thrombectomy procedures were performed on the COVID-19-positive group, with a comparable 56 procedures in the negative group. Patients from our facility who tested positive for COVID-19 were treated the same as patients who tested negative for COVID-19 (►**Table 2**). Treatment was initiated and full protective and safety measures, in accordance with hospital protocol, were followed, regardless of the results, and without any delay.

The key finding from our hospital's experience with mechanical thrombectomy was successful recanalization with a TICI score of 3 in most patients in both groups, the COVID-19-positive and COVID-19-negative patients with certain clinical and biochemical similarities between the two groups of patients (►**Table 2**).

Discussion

While SARS-CoV-2 is known to cause acute respiratory distress syndrome and interstitial pneumonia, there is mounting evidence of many neurological manifestations as well, one of which is AIS (can also be hemorrhagic); stroke affects around 5% of hospitalized COVID-19 patients, with ischemic stroke accounting for more than 80% of cases. The reported death rate in patients with stroke and COVID-19 infection is 39%, which is significantly greater than the mortality rate recorded in patients with stroke who do not have COVID-19 infection.[12,13,15]

Approximately 1 to 3% of hospitalized patients and up to 6% of those in the ICU experience a stroke, which has been shown to be a rare but potentially fatal consequence of COVID-19. Most patients experiencing a stroke during COVID-19 were found to be males (62%), with a median age of 63 years, and the majority of these patients were more likely to exhibit SARS-CoV-2 symptoms, therefore, necessitating ICU hospitalization. Poor outcomes were also seen in patients with cardiovascular complications in patients with COVID-19 infection.[13,14]

According to Mosconi and Paciaroni, a recent meta-analysis showed that patients with significant COVID-19 had a fivefold increase in the risk of stroke. There was a reasonably substantial frequency of thrombotic events during the early stages of COVID-19, mostly among patients with severe

COVID-19 but also among moderately symptomatic or asymptomatic individuals. SARS-CoV-2 infection increases the incidence of ischemic stroke, myocardial infarction, and thrombotic events; however, the exact mechanisms remain unknown, and despite the high number of cases linking ischemic stroke to COVID-19, a clear association with SARS-CoV-2 infection remains unknown.[17] Almost all patients had numerous risk factors, such as advanced age, hypertension, diabetes, atrial fibrillation, and hyperlipidemia. Many of these disorders are thought to be related to greater severity and mortality in COVID-19.[17]

Another study in Germany showed a total number of 213 individuals with a primary diagnosis of AIS and a secondary diagnostic of COVID-19 where the mean age of COVID-19-infected AIS patients was not substantially higher than that of noninfected AIS patients (76.1 vs. 74.0 years $p = 0.107$), and there was no difference in gender distribution (F/M: 46.7%/53.3% vs. 47.2%/52.8%; $p = 0.833$).[8] In patients with AIS with concomitant COVID-19 infection, the in-hospital death rate was considerably more significant (22.5 vs. 7.8%, $p = 0.001$). Patients treated in an ICU had the highest in-hospital death rate (42.9%) compared to stroke patients.

Mechanical thrombectomy in patients with COVID-19 infection can be challenging due to the increased risk of complications related to the infection. For example, COVID-19 can cause respiratory distress, and patients undergoing mechanical thrombectomy may need to be intubated and placed on a ventilator. Additionally, the risk of bleeding complications may be higher in COVID-19 patients due to the hypercoagulable state caused by the infection.

It has been suggested that the underlying mechanism is that the viral infection causes activation of multiple inflammatory responses that lead to an increase in proinflammatory cytokine production and endothelial microvascular damage.[18]

Mechanical thrombectomy can effectively treat ischemic stroke in COVID-19 patients despite these challenges. The decision to perform a mechanical thrombectomy should be made on a case-by-case basis in consultation with a team of healthcare providers, including neurologists, interventional radiologists, and infectious disease specialists. In addition to mechanical thrombectomy, COVID-19 patients with ischemic stroke may benefit from other treatments such as anticoagulation therapy, supportive care, and rehabilitation. The specific treatment approach will depend on the individual patient's needs and the severity of their condition.

In our study, the M2-4 segment of the middle cerebral artery was found to be the most commonly involved vessel in COVID-19-positive patients with stroke, accounting for 37% of cases. Large vessel occlusion (LVO) strokes were far more widely seen than small vessel strokes. This likely results from a complex mechanism of neurovascular pathological changes caused by COVID-19 infection, which includes hypercoagulable states, simultaneous endothelial damage, activation of inflammatory mediators, and the emergence of atypical, multiple occlusions and dissection.[19]

The study by Kihira et al first indicated a link between COVID-19 and big vessel strokes. Their study showed that 62% of LVO strokes were caused by blockage of the M1-M2 segments of the middle cerebral artery.[20,21]

One of the main factors thought to play a role in patient outcome with a higher NIHSS score at discharge is patients presenting late due to many reasons including concerns of attending hospitals during the pandemic in fear of contracting the COVID-19 infection, curfew hours, and mobility issues.

There are a few limitations to this study. First, because this was a single-center observational retrospective study, we were constrained by the available data. We had no control over the data-gathering method, and the results may not be generalized. Furthermore, the sample size was small, which may have compromised the study's statistical power. However, despite these limitations, our findings are supported by the fact that the demographics of the control and sick groups were comparable. This implies that any observed variations between the two groups are more likely to result from the COVID-19 disease's existence or absence rather than confounding variables.

Conclusion

Since its discovery in late 2019, COVID-19 has been linked to a number of complications and neurological manifestations one of which is AIS; our study discerns patients presenting with AIS symptoms confirmed through imaging and were also found to be of COVID-19-positive status tend to have a more extended hospital stay and a worse outcome at discharge irrespective of their known risk factors, imaging findings, and treatment received (thrombolysis vs. mechanical thrombectomy or both combined). A multicentric study with more study subjects is recommended to validate our findings further.

Conflict of Interest
None declared.

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