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The impact of COVID-19 on stroke rehabilitation

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Abstract

In literature, it has been suggested that SARS-CoV-2's impact on the heart and brain may contribute to immune-mediated thrombosis, the renin-angiotensin system related to the pathogenesis of ischemic stroke. Our study compares the rehabilitation outcomes of stroke patients with and without a history of COVID-19. Our study aims to compare rehabilitation results of COVID-19-associated ischemic stroke patients and non-COVID-19 patients, as thrombotic complications and ischemic stroke have largely been reported since the pandemic's beginning. This study included 83 stroke patients aged 18-80 years who were hospitalized and rehabilitated. Patients' age, gender, lesion location, Brunnstrom stage, ambulation level, comorbidities, Charlson comorbidity index, stroke type, pre-stroke history of COVID-19 and symptoms, previous stroke history, and duration of physical therapy program were recorded. Those with a history of COVID-19 reverse transcriptase polymerase chain reaction test being positive and/or a history of pneumonia compatible with COVID-19 on thoracic computed tomography examination (28 patients) were included in the COVID-19 group while those without those conditions were included in the non-COVID-19 group (55 patients). Factors contributing to rehabilitation results were compared between the groups. The rehabilitation outcomes were similar across the groups, with no differences in ambulation levels or Brunnstrom staging (hand, upper and lower extremities) (p values 0.237, 0.155, 0.380, 0.192, respectively). However, the COVID-19 group had higher rates of ischemic heart disease and hypothyroidism, no prior history of cerebrovascular accident, more periventricular infarctions, and initially more adversely affected ambulation levels (p values 0.047, 0.038, 0.042, 0.037, 0.028, respectively). The study concluded that there was no apparent difference between the two groups' outcome parameters. Although the COVID-19 group's ambulation level was initially more negatively impacted, no detrimental effects on rehabilitation outcomes were found.

Keywords: cerebrovascular accident, COVID-19, ischemic heart disease, rehabilitation, stroke

1. Introduction

Coronavirus disease 2019 (COVID-19) has been reported to potentially increase the risk of acute ischemic stroke in several small case series. The increased risk of ischemic stroke with COVID-19 is likely multifactorial, with activation of coagulation. The international panel of stroke experts from 18 countries was recommended to conduct further studies to understand whether there are differences in risk factors and symptoms (1).

A high prevalence of thrombotic events has been reported even in asymptomatic and mildly symptomatic patients in the early stages of the pandemic, notably in severe COVID-19 patients (2,3).

Despite the increase in research associating ischemic stroke to COVID-19 that has been published, it is still unclear if SARS-CoV-2 causes ischemic stroke. However, several potential inflammatory and prothrombotic mechanisms may contribute to the risk of cardiovascular events and stroke in patients with COVID-19 (4).

Studies have shown that COVID-19 infection triggers a wave of inflammatory cytokines that induce coagulopathy, which induces endothelial cell dysfunction and increases the risk of stroke or thrombosis. Inflammation of the endothelium following infection can also disrupt the atherosclerotic plaque and cause thrombotic paralysis. While not common, there have also been reports of hemorrhagic stroke associated with COVID-19. Possible mechanisms include an increase in blood pressure caused by infection leading to a decrease in angiotensin-converting enzyme-2 (ACE-2) levels; this leads to an imbalance in the renin-angiotensin system, resulting in inflammation and vasoconstriction. Coagulopathy has also been suggested as a contributing factor to hemorrhagic stroke in COVID-19 patients, as demonstrated by the high prothrombin time (5).

Although the relationship between COVID-19 and ischemic stroke has not been clearly established yet, there are many studies and reviews about COVID-19 and stroke. However, we have not come across many studies on the results of stroke rehabilitation. For this reason, we need to investigate the effect of having a COVID-19 infection before a

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cerebrovascular accident (CVA) on the rehabilitation outcomes of stroke patients.

2. Materials and Methods

The records of patients who were admitted to our clinic due to stroke and received inpatient rehabilitation between April 2020 and December 2021, when the COVID-19 pandemic was intense, were scanned retrospectively. The records of a total of 117 patients were scanned, and 83 patients who met the inclusion criteria were included in the study.

As inclusion criteria, patients aged 18-80 years who had a stroke and were hospitalized and rehabilitated were included in this study. Exclusion criteria were the presence of vasculitis, trauma, coagulopathy, and tumor that may cause stroke, drug use that may cause stroke, aphasia that prevents communication, severe hearing and vision loss, other causes of dementia, and psychiatric diseases.

Patients' age, gender, lesion location, Brunnstrom stage, ambulation level, comorbidities, Charlson comorbidity index, stroke type (ischemic, hemorrhagic), pre-stroke history of COVID-19 and symptoms, previous stroke history, and duration of physical therapy program were recorded.

The level of motor recovery was measured by Brunnstrom staging. This staging evaluates and interprets movement patterns according to the motor function recovery stage. Scoring is done between 1-6 (6).

The ambulation level was divided into four levels: unsupported, supported, wheelchair, and bed-level.

The Charlson comorbidity index is a scoring system used to classify comorbidities, determine their severity, and predict mortality. Each patient's comorbidity score is between 1-6, and the total score is between 0-37 (7).

A conventional rehabilitation program was applied to all patients. The program included a range of motion, strengthening, stretching, balance and occupational exercise, and daily living exercises according to the tolerance and needs of each patient.

Out of 83 patients, those with a history of COVID-19 reverse transcriptase polymerase chain reaction test (RT-PCR) being positive and/or a history of pneumonia compatible with COVID-19 on thoracic computed tomography (CT) examination (n=28 patients) were included in the COVID-19 group while those without these conditions were included in the non-COVID-19 group (n=55 patients). Demographic and disease characteristics of both groups and pre- and post-treatment results of clinical evaluations were compared.

2.1. Statistical analysis

Data were statistically analyzed using the Statistical Package for the Social Sciences (SPSS) 22.0 software. The conformity of continuous variables to normal distribution was evaluated using the Kolmogorov-Smirnov test. Descriptive statistics were presented as mean ± standard deviation (SD) or median (minimum-maximum) for continuous variables, frequency (n), and percent (%) for nominal and categorical variables. Independent sample T-test (age) and Mann Whitney-U test were used for continuous variables, χ^2, and Fisher's precision test were used for nominal variables to compare the evaluation parameters between the groups. A p-value of <0.05 was considered statistically significant.

3. Results

The demographic and clinical characteristics of all patients included in the study, as well as comparisons of patients with and without COVID-19, are presented in Table 1.

Table 1. Demographic and clinical characteristics of the patients

		Patients total (n=83)	Patients w/ COVID-19 (n=28)	Patient w/o COVID-19 (n=55)	p
Age mean (SD)		64.81±12.78	66.10 (8.74)	64.16 (14.45)	0.516
Gender n(%)					
Female		29 (34.9)	6 (21.4)	23 (41.8)	0.089
Male		54 (65.1)	22 (78.6)	32 (58.2)	
Comorbidity n(%)					
Diabetes Mellitus		34 (41)	14 (50)	20 (36.4)	0.248
Hypertension		48 (57.8)	19 (67.9)	29 (52.7)	0.242
Heart valve disease		4 (4.8)	3 (10.7)	1 (1.8)	0.109
Ischemic heart disease		22 (26.5)	11 (39.3)	11 (20)	0.047
Hyperlipidemia		18 (21.7)	8 (28.6)	10 (18.2)	0.207
Hypothyroidism		3 (3.6)	3 (10.7)	0	0.038
Chronic obstructive pulmonary disease (COPD)		6 (7.2)	0	6 (10.9)	0.072
Previous CVA history n(%)		7 (8.4)	0	7 (12.7)	0.042
Charlson comorbidity index Median (min-max)		5.0 (3.0-9.0)	5.0 (4.0-7.0)	5.0 (3.0-9.0)	0.080
Affected brain area n(%)					
Periventricular infarction n(%)	Right	24 (28.9)	12 (42.9)	12 (21.8)	0.037
	Left	11 (13.3)	3 (10.7)	8 (14.5)	0.454
Pons Infarct	Right	1 (1.2)	0	1 (1.8)	0.663
	Left	4 (4.8)	0	4 (7.3)	0.186
Mesencephalon infarct	Right	3 (3.6)	2 (7.1)	1 (1.8)	0.262
	Left	2 (2.4)	0	2 (3.6)	0.436

Thalamus infarct	Right	2 82.4)	0	2 (3.6)	0.436
	Left	3 (3.6)	0	3 (5.5)	0.286
Cerebellar infarct	Right	4 (4.8)	3 (10.7)	1 (1.8)	0.109
	Left	2 82.4)	0	2 (3.6)	0.436
Pons hematoma	Right	1 (1.2)	0	1 (1.8)	0.663
	Left	1 (1.2)	0	1 (1.8)	0.663
Mesencephalon hematoma	Right	1 (1.2)	0	1 (1.8)	0.663
	Left	1 (1.2)	0	1 (1.8)	0.663
Parietal infarct	Right	15 (18.1)	6 (21.4)	9 (16.4)	0.388
	Left	18 (21.7)	6 (21.4)	12 (21.8)	0.601
Capsular interna infarct	Right	1 (1.2)	0	0	1.000
	Left	1 (1.2)	0	1 (1.8)	0.663
Parietooccipital infarct	Right	5 (6.0)	0	5 (9.1)	0.120
	Left	0	0	0	1.000
Parietooccipital hematoma	Right	0	0	0	1.000
	Left	4 (4.8)	3 (10.7)	1 (1.8)	0.109
Temporal infarction	Right	16 (19.3)	6 (21.4)	10 (18.2)	0.468
	Left	12 (14.5)	6 (21.4)	6 (10.9)	0.168
Temporooccipital infarct	Right	11 (13.3)	6 (21.4)	5 (9.1)	0.112
	Left	3 (3.6)	0	3 (5.5)	0.286
Thalamic hematoma	Right	2 (2.4)	0	2 (3.6)	0.436
	Left	4 (4.8)	2 (7.1)	2 (3.6)	0.415
Periventricular hematoma	Right	0	0	0	1.000
	Left	1 (1.2)	0	1 (1.8)	0.663
Basal ganglia hematoma	Right	2 (2.4)	0	2 (3.6)	0.436
	Left	0	0	0	1.000
Basal ganglia infarction	Right	13 (15.7)	3 (10.7)	10 (18.2)	0.293
	Left	7 (8.4)	3 (10.7)	4 (7.3)	0.439
Bilateral centrum semiovale infarction		1 (1.2)	0	1 (1.8)	0.663
Parietotemporal hematoma	Right	0	0	0	1.000
	Left	1 (1.2)	0	1 (1.8)	0.663
Frontoparietal infarction	Right	5 (6)	0	5 (9.1)	0.120
	Left	3 (3.6)	0	3 (5.5)	0.286
CVA type n(%)					
Hemorrhagic		14 (16.9)	5 (17.9)	9 (16.4)	0.546
Ischemic		69 (83.1)	23 (82.1)	46 (83.6)	
Time from CVA median (min-max)		24.5 (5-52)	24.5 (8.0-52.0)	25.0 (5.0-46.0)	0.547

CVA: cerebrovascular accident

Disease characteristics and outcomes of COVID-19 before CVA are shown in Table 2. Patients who required intensive care during COVID-19 infection had a history of steroid use.

Table 2. Characteristics of patients with COVID-19 before CVA

	n=28
Time from CVA to COVID-19, days median (min-max)	30.0(8.0-150.0)
COVID-19 symptoms n(%)	
Fever	11 (39.3)
Myalgia	9 (32.1)
Headache	3 (10.7)
Cough	4 (14.3)
Weakness	5 (17.9)
Patient using favipiravir n(%)	8 (28.6)
Hospitalization requirement n(%)	9 (32.1)
Need for hospitalization in ICU n(%)	9 (32.1)
Family history of COVID-19 n(%)	20 (71.4)
Hospitalization in the family n(%)	6 (21.4)
ICU admission in the family n(%)	6 (21.4)
Death in the family from COVID-19 n(%)	4 (14.3)

CVA: cerebrovascular accident, **ICU:** intensive care unit

The COVID-19 group had higher rates of ischemic heart disease and hypothyroidism, no prior history of cerebrovascular accident, more periventricular infarctions, and initially more adversely affected ambulation levels (p values 0.047, 0.038, 0.042, 0.037, 0.028, respectively).

Table 3. Comparison of evaluation parameters of patients with and without COVID-19 before and after rehabilitation

	Patients w/ COVID-19 (n=28)	Patient w/o COVID-19 (n=55)	p
Brunnstrom phase - at the hospitalization median(min-max)			
Hand	3.5 (1.0-6.0)	3.0 (1.0-6.0)	0.069
Upper extremity	3.5 (1.0-6.0)	3.0 (1.0-6.0)	0.141
Lower extremity	3.5 (1.0-6.0)	4.0 (1.0-6.0)	0.591
Brunnstrom phase - at the discharge median (min-max)			
Hand	4.0 (3.0-6.0)	4.0 (1.0-6.0)	0.237
Upper extremity	4.0 (3.0-6.0)	4.0 (1.0-6.0)	0.155
Lower extremity	4.0 (3.0-5.0)	5.0 (1.0-6.0)	0.380
Ambulation level - at the hospitalization n(%)			
Unsupported	0	9 (16.3)	0.028
Supported	16 (57.1)	15 (27.3)	
Wheelchair	7 (25)	19 (34.5)	
Bed level	5 (17.9)	12 (21.8)	
Ambulation level - at the discharge n(%)			
Unsupported	5 (17.9)	15 (27.3)	0.192
Supported	18 (64.3)	27 (49.1)	
Wheelchair	4 (14.3)	9 (16.3)	
Bed level	1 (3.6)	4 (7.3)	

The comparison between the evaluation parameters of patients with and without a history of COVID-19 before and after rehabilitation is presented in Table 3. The ambulation level was observed to be affected more negatively in patients who had COVID-19 (p=0.028), but the results after rehabilitation were similar between the groups (p=0.192). When we compared the change after rehabilitation between groups, Brunnstrom staging (upper p=0.212, hand p=0.916, lower p=0.347) and ambulation level (p=0.224) did not differ. Physical therapy duration was not different in groups (22.5 in 1st group (10.0-75.0), 20.5 in 2nd group (5.0-70.0) days, p=0.153).

4. Discussion

This study investigated the history of COVID-19, the relationship of this situation with demographic and clinical characteristics, and the effect on rehabilitation outcomes of patients hospitalized for stroke rehabilitation in the rehabilitation clinic during the COVID-19 pandemic. As a result of the study, it was determined that ischemic heart disease and hypothyroidism were more common in the COVID-19 group; there was no previous history of CVA, more periventricular infarction, and ambulation level was more adversely affected initially. No negative impact on rehabilitation results was detected.

Clinical presentations of COVID-19 range from an asymptomatic condition to acute respiratory distress syndrome and multi-organ dysfunction. One of the few reported complications is stroke (3,8,9). Previous studies have shown that recent bacterial and/or viral infections can trigger acute ischemic stroke and be associated with the prothrombotic effects of inflammatory reactions (10). The increase in cryptogenic stroke rate has also complicated stroke due to COVID-19 (11). Although there is no uniform case definition for stroke associated with COVID-19, ischemic stroke predominance has been reported, similar to typical stroke epidemiology, in multiple comparisons of stroke patients with and without COVID-19 (12,13). In our study, periventricular infarction was found more than the control group. There was no significant difference in terms of other areas of the brain affected between the two groups.

A review evaluating the brain images of acute/subacute COVID-19 patients referred for neuroimaging reported that periventricular infarction is among the dominant neuroimaging features in COVID-19 patients (14). This involvement is especially seen in the elderly and causes cognitive and cognitive dysfunction along with white matter changes and a significant decrease in motor functions. This may be the reason why the ambulation level was worse before rehabilitation in our COVID-19 patient group. However, in studies conducted on stroke patients, comorbidities including advanced age, female gender, large vessel occlusion (LVO) on neuroimaging, high C-reactive protein (CRP), ferritin, D-dimer levels, COVID-19 RT-PCR positivity, presence of hypertension and cardiac problems such as atrial fibrillation were associated with negative outcome (15). In another study, COVID-19 compared with patients who have not had a stroke, COVID-19 patients who have had a stroke are reported to be younger, male, and have more severe neurological deficits compared to past controls (16).

In our study, it was noted that ischemic heart disease and hypothyroidism were more common in the COVID-19 group. This result makes us think that the poor ambulation status of our pre-rehabilitation patients, regardless of age and gender, may be related to the pathophysiology of COVID-19. The following is our result: We believe that the literature reveals the contradiction of the importance attributed to age and gender in COVID-19 studies so far.

In studies revealing the relationship between ischemic heart disease and COVID-19, it has been reported that it increases ischemic heart disease by causing acute coronary syndrome with both thrombotic increase and myocardial ischemia and that it continues its cardiac effect with persistent tissue damage and inflammation after its acute effects in long COVID-19 syndrome (17). In the literature, comorbidities such as ischemic heart disease, hypertension, and diabetes mellitus were found to be similarly high in the COVID-19 group (18-20). In addition, the high incidence of hypothyroidism was revealed in a retrospective study conducted last year, and it was reported that both the thyroid has features similar to the lung tissue and symptomatic and subclinical hypothyroidism due to its primary damage (21).

Tissue ischemia is seen as periventricular infarction in the brain in more than half of the patients in this study. Ischemic heart disease and hypothyroidism due to ischemia in myocardial and thyroid tissue indicate that COVID-19 is a systemic disease. In addition, the average duration of COVID-19 infection being 30 days suggests that there may be ongoing effects. Studies have reported that typically, patients develop symptoms of COVID-19 infection, including respiratory symptoms and fever, that occur on average ten days before the onset of stroke (delayed presentation) (19,22,23).

Long COVID syndrome describes lingering complications that extend ≥4 weeks beyond the initial symptoms of COVID-19. Despite publications on the COVID-19 pandemic, there is insufficient evidence to assess the relationship between the extended COVID-19 syndrome and stroke onset. It has also been reported that COVID-19-related stroke may occur up to 92 days after infection (24). Currently, COVID-19 is a disease full of unknowns, but our knowledge and experience on this subject are increasing day by day.

One of the limitations of this study is the difficulty in standardizing the patients, and another is that a retrospective analysis was performed as a file scan. However, the lack of similar studies in the literature created the need for such a study.

As a result of the study, no significant difference was found in the outcome parameters of the two groups. Although the ambulation level was more adversely affected initially, no negative impact on rehabilitation results was detected in the COVID-19 patient group.

Conflict of interest

The authors declared no conflict of interest.

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Authors' contributions

Concept: E.K.U., E.U.A., E.G., Design: E.K.U., E.U.A., E.G., Data Collection or Processing: E.K.U., O.Z.K., M.K.S., A.T., Analysis or Interpretation: E.K.U., O.Z.K., M.K.S., A.T., Literature Search: Y.T., E.K.U., M.K.S., O.Z.K., E.U.A., A.T., E.G., Writing: Y.T., E.K.U., M.K.S., O.Z.K., E.U.A., A.T., E.G.,

Ethical Statement

Approval was obtained from Health Sciences University Dışkapı Yıldırım Beyazıt Education and Research Hospital Clinical Research Ethics Committee, the study started. The ethics committee decision date is 23/08/2021 and the number of ethical committee decisions is 118/04.

References

1. Qureshi AI, Baskett WI, Huang W, Shyu D, Myers D, Raju M, et al. Acute Ischemic Stroke and COVID-19: An Analysis of 27 676 Patients. Stroke. 2021;52(3):905-912.
2. Klok FA, Kruip MJHA, van der Meer NJM, Arbous MS, Gommers DAMPJ, Kant KM, et al. Incidence of thrombotic complications in critically ill ICU patients with COVID-19. Thromb Res. 2020;191:145-147.
3. Oxley TJ, Mocco J, Majidi S, Kellner CP, Shoirah H, Singh IP, et al. Large-vessel stroke is a presenting feature of COVID-19 in the young. N Engl J Med. 2020;382:e60.
4. Sagris D, Papanikolaou A, Kvernland A, Korompoki E, Frontera JA, Troxel AB, et al. COVID-19 and ischemic stroke. Eur J Neurol. 2021;28(11):3826-3836.
5. Ahmad SJ, Feigen CM, Vazquez JP, Kobets AJ, Altschul DJ. Neurological Sequelae of COVID-19. J Integr Neurosci. 2022;21(3):77.
6. Wade DT. Measurement in neurological rehabilitation. Curr Opin Neurol Neurosurg. 1992;5(5):682–6.
7. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: Development and validation. J Chronic Dis. 1987;40(5):373–83.
8. Ashrafi F, Zali A, Ommi D, Salari M, Fatemi A, Arab-Ahmadi M, et al. COVID-19-related strokes in adults below 55 years of age: a case series. Neurol Sci. 2020;41(8):1985-1989.
9. Avula A, Nalleballe K, Narula N, Sapozhnikov S, Dandu V, Toom S, et al. COVID-19 presenting as stroke. Brain Behav Immun. 2020;87:115-119.
10. Grau AJ, Buggle F, Becher H, Zimmermann E, Spiel M, Fent T, et al. Recent bacterial and viral infection is a risk factor for cerebrovascular ischemia: clinical and biochemical studies. Neurology. 1998;50(1):196–203.
11. Luo W, Liu X, Bao K, Huang C. Ischemic stroke associated with COVID-19: a systematic review and meta-analysis. J Neurol. 2022;269(4):1731-1740.
12. Kolominsky-Rabas PL, Weber M, Gefeller O, Neundoerfer B, Heuschmann PU. Epidemiology of ischemic stroke subtypes according to TOAST criteria: incidence, recurrence, and long-term survival in ischemic stroke subtypes: a population-based study. Stroke 2001;32(12):2735-40.
13. Adams HP. Classification of subtype of acute ischemic stroke. Definitions for use in a multicenter clinical trial. TOAST. Trial of Org 10172 in Acute Stroke Treatment. Stroke. 1993;24:35–41.
14. Egbert AR, Cankurtaran S, Karpiak S. Brain abnormalities in COVID-19 acute/subacute phase: A rapid systematic review. Brain Behav Immun. 2020;89:543-554.
15. Altiparmak T, Can C, Hazal SC. COVID-19 hastalarında iskemik inme: Tek merkezin bir yıllık tecrübesi. Turk Beyin Damar Hastaliklari Dergisi 2022; 28(1): 23-30.
16. Mao L, Jin H, Wang M, Hu Y, Chen S, He Q, et al. Neurologic manifestations of hospitalized patients with coronavirus disease 2019 in Wuhan, China. JAMA Neurology. 2020; 77: 683- 690.
17. Zhang R, Hao Y, Wang Y, Yang H. Significant association between ischemic heart disease and elevated risk for COVID-19 mortality: A meta-analysis. Am J Emerg Med. 2022;55:95-97.
18. Zhang S, Zhang J, Wang C, Chen X, Zhao X, Jing H, et al. COVID-19 and ischemic stroke: Mechanisms of hypercoagulability (Review). Int J Mol Med 2021; 47(3): 21.
19. Li Y, Li M, Wang M, Zhou Y, Chang J, Xian Y, et al. Acute cerebrovascular disease following COVID-19: a single center, retrospective, observational study. Stroke Vasc Neurol 2020; 5(3): 279- 284.
20. Zhao J, Li H, Kung D, Fisher M, Shen Y, Liu R. Impact of the COVID-19 Epidemic on Stroke Care and Potential Solutions. Stroke 2020; 51(7): 1996-2001.
21. Burekovic A, Halilovic D, Sahbaz A. Hypothyroidism and Subclinical Hypothyroidism as a Consequence of COVID-19 Infection. Med Arch. 2022;76(1):12-16.
22. Ellul MA, Benjamin L, Singh B, Lant S, Michael BD, Easton A et al. Neurological associations of COVID-19. Lancet Neurol. 2020;19(9):767-783.
23. Tan YK, Goh C, Leow AST, Tambyah PA, Ang A, Yap ES, et al. COVID-19 and ischemic stroke: a systematic review and meta-summary of the literature. J Thromb Thrombolysis. 2020;50(3):587-595.
24. Fleming C, Chakraborty A, Jaiswal T, Patel P, Nair S. Onset of stroke in patients with post-COVID-19 syndrome following hospitalization for severe COVID-19 infection: a systematic literature review. Value Health. 2022;25(1):S121