

ÖZGÜN ARAŞTIRMA

ORIGINAL ARTICLE

ACUTE STROKE MANAGEMENT DURING COVID-19 PANDEMIC

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ABSTRACT

INTRODUCTION: In the coronavirus disease 2019 (COVID-19) pandemic, there may be a decrease in the number of acute stroke intervention and acute treatment, and delays in treatment periods. In this study, it was aimed to compare the clinical features of patients presenting with acute stroke during the COVID-19 pandemic and in the pre-pandemic period.

METHODS: Patients hospitalized with the diagnosis of cerebrovascular disease (CVD) between January 01, 2019 and May 31, 2021 were included in the study. Demographic characteristics and stroke risk factors of the patients were recorded. Stroke type and ischemic disease subtypes were determined, and patients' admission National Institutes of Health Stroke Scale (NIHSS) score, symptom-door time, door-consultation time, door-to-door Needle time and door-groin puncture time, intravenous tissue type plasminogen activator (IV tPA) and endovascular thrombectomy (EVT) applications were recorded. Discharge modified Rankin Scale (mRS) and NIHSS scores and mortality rates were evaluated. Patients hospitalized in two separate periods of 14 months each were compared by dividing them into pre-pandemic and pandemic periods.

RESULTS: Before COVID-19, 316 patients (female 45.25%, age: 66.75±13.68 years) and during the pandemic period 341 (female 41.94%, age: 68.34±13.55 years) patients were included in the study. During the pandemic period, an increase in the number of hemorrhagic CVD and transient ischemic attacks, a decrease in the number of ischemic stroke and cerebral venous thrombosis (CVT) hospitalizations, a decrease in cardioembolic strokes and an increase in lacunar ischemic CVD subtypes were observed ($p<0.01$). The number of large vessel atherosclerosis, IV tPA and EVT were found to be similar before and after the pandemic. In the pandemic period, although it did not reach statistical significance compared to the pre-pandemic period, prolongation was recorded in the symptom-door, door-consultation, door-needle and door-groin puncture times ($p>0.05$). The COVID-19 test was positive after hospitalization in 5 (1.8%) patients with ischemic stroke hospitalized during the pandemic period. During the pandemic period, admission NIHSS, discharge NIHSS and mRS scores and mortality rates were found to be significantly higher between hemorrhagic and ischemic stroke patients ($p<0.01$).

DISCUSSION AND CONCLUSION: The COVID-19 pandemic adversely affects the management of acute stroke. The duration of acute stroke treatment is delayed due to pre-hospital and in-hospital reasons. With the heavy burden of stroke during the pandemic period, poor clinical outcome and high mortality are observed.

Keywords: Cerebrovascular disease, ischemic stroke, COVID-19, pandemic.

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COVID-19 PANDEMİSİ DÖNEMİNDE AKUT İNME YÖNETİMİ

ÖZ

GİRİŞ ve AMAÇ: Koronavirüs hastalığı 2019 (COVID-19) pandemisinde akut inme başvurularında ve akut tedavi sayılarında azalma ve tedavi sürelerinde gecikmeler yaşanabilmektedir. Bu çalışmada COVID-19 pandemisinde ve pandemi öncesi dönemde akut inme ile başvuran hastaların klinik özelliklerinin karşılaştırılması amaçlanmıştır.

YÖNTEM ve GEREÇLER: Çalışmaya 01 Ocak 2019 ve 31 Mayıs 2021 tarihleri arasında beyin damar hastalığı (BDH) tanısıyla yatırılan hastalar alınmıştır. Hastaların demografik özellikleri ve inme risk faktörleri kaydedilmiştir. İnme şekli ve iskemik BDH subtipleri belirlenerek hastaların başvuru National Institutes Of Health Stroke Scale (NIHSS) skoru, semptom-kapı zamanı, kapı-konsültasyon zamanı, intravenöz doku tipi plazminojen aktivatörü (IV tPA) ve endovasküler trombektomi (EVT) uygulanma sayıları, kapı-iğne zamanı ve kapı kasık zamanı kaydedilmiştir. Taburculuk modifiye Rankin Skalası (mRS) ve NIHSS skorları ve mortalite oranları değerlendirilmiştir. 14'er aylık iki ayrı periyotta yatırılan hastalar pandemi öncesi ve pandemi dönemi olarak ikiye ayrılarak karşılaştırılmıştır.

BULGULAR: COVID-19 öncesi 316 (kadın %45,25, yaş: 66,75±13,68 yıl), pandemi döneminde ise 341 (kadın %41,94, yaş: 68,34±13,55 yıl) hasta çalışmaya dahil edilmiştir. Pandemi döneminde hemorajik BDH ve geçici iskemik atak sayılarında artma, iskemik inme ve serebral venöz tromboz (SVT) yatış sayılarında azalma, iskemik BDH subtiplerinde ise kardiyembolik inmelerde azalma, lakünlere artma gözlenmiştir (p<0,01). Büyük damar aterosklerozu, IV tPA ve EVT sayıları pandemi öncesi ve sonrasında benzer bulunmuştur. Pandemi döneminde, pandemi öncesi döneme göre istatistiksel anlamlılığa ulaşmasa da semptom-kapı, kapı-konsültasyon, kapı-iğne ve kapı-kasık sürelerinde uzama kayıtlanmıştır (p>0,05). Pandemi döneminde yatan 5 iskemik inme hastasında (%1,8) yatıştan sonra COVID-19 testi pozitif çıkmıştır. Pandemi döneminde hemorajik ve iskemik inme hastaları arasında başvuru NIHSS, taburculuk NIHSS ve mRS skorları ve mortalite oranları anlamlı olarak daha yüksek bulunmuştur (p<0,01).

TARTIŞMA ve SONUÇ: COVID-19 pandemisi akut inme yönetimini olumsuz olarak etkilemektedir. Akut inme tedavi süresi hastane öncesi ve hastane içi sebeplerle gecikmektedir. Pandemi döneminde inme yükünün ağır olmasıyla birlikte kötü klinik sonuçlar ve yüksek mortalite görülmektedir.

Anahtar Sözcükler: Beyin damar hastalığı, iskemik inme, COVID-19, pandemi.

INTRODUCTION

A new type of coronavirus (acute respiratory syndrome coronavirus 2-Severe Acute Respiratory Syndrome-Coronavirus 2; SARS-CoV-2) with high pathogenic properties and multiple organ involvement was identified in December 2019. It spread globally in a short time with high contagiousness and the World Health Organization (WHO) declared coronavirus disease 2019 (COVID-19) caused by SARS-CoV2 as a pandemic on March 11, 2020. On the same day, the first case occurred in Turkey and the first death occurred on March 15, 2020. According to the WHO data, the total number of cases in the world was 420 million and the number of deaths was 5.9 million, while the total number of cases in Turkey reached 13.5 million and the number of deaths reached 92,000 as of February 2022.

Different neurological diseases and symptoms, including cerebrovascular disease (CeVD), have been identified during COVID-19 infection. No specific stroke subtype associated with COVID-19 has yet been identified. The presence of a prothrombotic inflammatory reaction due to infection, endothelial dysfunction and predisposition to thrombosis are thought to

be the causes of stroke (1,2). During the pandemic, a decrease has been reported globally in admission and hospitalization with acute stroke in stroke centers, and a decrease and delay have been reported in the number of acute stroke treatments (intravenous tissue-type plasminogen activator-IV tPA, endovascular thrombectomy-EVT) (3-10). These negativities in diagnosis and treatment can cause more damage to patients with stroke compared to the viral infection itself (8,11). This study aimed to compare the clinical characteristics of patients who presented with acute stroke during and before the COVID-19 pandemic.

METHODS

The study included patients who were admitted to Ondokuz Mayıs University Faculty of Medicine Hospital between January 1, 2019, and May 31, 2021, and hospitalized in the Neurology Clinic, Stroke Unit, and Neurology Intensive Care Unit with the diagnosis of CeVD. Patients hospitalized in March 2020, when the pandemic started, were excluded from the study, and the patients were classified into two groups. Patients hospitalized before February 29, 2020, were grouped as pre-pandemic period and patients

hospitalized after April 1, 2020, were grouped as the pandemic period. A retrospective review was performed on 472 pre-pandemic and 467 pandemic patient files containing the diagnostic codes of CeVD (I60-69, G45-46) according to the "The International Statistical Classification of Diseases and Related Health Problems (ICD-10)" classification (12). Demographic characteristics of the patients such as age, gender, and stroke risk factors (Hypertension-HT, diabetes mellitus-DM, coronary artery disease-CAD, hyperlipidemia-HL, and atrial fibrillation-AF) were recorded. The type of stroke was classified as hemorrhagic CeVD, ischemic CeVD, transient ischemic attack (TIA), and cerebral venous thrombosis (CVT). Patients with primary parenchymal bleeding were included in the hemorrhagic CeVD group. According to the 'Causative Classification System for Ischemic Stroke' (CCS) classification, the subtypes of ischemic CeVD were determined as large vessel disease, cardioembolism, small vessel disease (lacuna), other rare causes of stroke, and strokes with unidentified causes (13). The "National Institutes of Health Stroke Scale" (NIHSS) scores, symptom-to-door times, door-to-consultation times, the number IV tPA and EVT administrations as the acute treatments of ischemic CeVD, door-to-needle times, and door-to-groin times at the time of admission were recorded. The length of hospital stay and the unit of hospitalization (ward and intensive care unit) were determined. Discharge was classified into two groups according to the modified Rankin Scale (mRS) scores as 0-2 and 3-6, and discharge NIHSS score and mortality rates were evaluated. Patients with incorrect codes and incomplete data in the patient files reviewed were excluded from the study and a total of 657 patients (316 pre-pandemic, 341 pandemics) were evaluated. Patients hospitalized during two separate periods of 14 months were classified into two groups, which were pre-pandemic and pandemic, and comparisons were made.

The study was carried out in accordance with the ethical rules specified in the Helsinki Declaration. Permission was obtained from the Ministry of Health for retrospective data analysis, and the study was approved by Ondokuz Mayıs University Clinical Research Ethics Committee (Date: 09.07.2021, Number: 2021/345).

Statistical Analysis: The data were analyzed using IBM SPSS version 22. A Kolmogorov-Smirnov test was performed to determine

whether the values were normally distributed according to the groups. Mann-Whitney U test was used to compare values with non-normal distributions by groups and the Chi-square test was used to compare categorical variables. The results of the analysis were presented as mean \pm SD deviation for quantitative data. The level of significance was taken as $p < 0.05$.

RESULTS

A total of 316 patients were hospitalized in the fourteen-month period before COVID-19, and 341 patients were hospitalized in the 14-month period of the pandemic. The mean age of the patients hospitalized in the pre-pandemic period was 66.75 ± 13.68 years, 45.25% of the patients were female, and 54.75% were male. The mean age of the patients with stroke who were hospitalized during the pandemic was 68.34 ± 13.55 years, 41.94% were female, and 58.06% were male. There was no statistically significant difference between the patients with cerebrovascular diseases before and after the COVID-19 pandemic in terms of current risk factors such as age, gender, HT, DM, CAD, HL, and stroke history ($p > 0.05$). The frequency of AF was lower with a statistical significance in stroke patients hospitalized during the COVID-19 pandemic ($p < 0.05$) (Table).

Looking at the types of stroke, when the patients hospitalized in the pandemic period were compared with the patients hospitalized in the pre-pandemic period, an increase was observed in hemorrhagic CeVD (39% vs 9%, $p < 0.01$) and TIA counts (5.34% vs 1.65%, $p < 0.01$), while fewer patients with ischemic stroke (81.83% vs 90.22%, $p < 0.01$) and CVT (1.52% vs 5.42%, $p < 0.01$) were hospitalized (Table).

When the subtypes of ischemic CeVD were compared, it was observed that there were fewer cardioembolic cases hospitalized during the pandemic period (38.94% versus 31.18%), and there was an increase in the number of patients with lacunas who were hospitalized during the pandemic (4.21% versus 18.63%) ($p < 0.05$). The rate of major vascular atherosclerosis among the patients that were hospitalized was similar before and after the pandemic (Table).

During the pandemic period, the NIHSS values of patients with ischemic stroke at the time of admission were significantly higher (6.34 vs.

Table. Characteristic clinical features and results of patients with acute stroke.

	Before COVID (n=316)	After COVID (n=341)	OR (95% CI)	p
Age (mean ± SD)	66.75±13.68	68.34±13.55	1.009 (0.997-1.020)	>0.05
Male (n,%)	173 (54.75%)	198 (58.06%)	0.874 (0.642-1.190)	>0.05
Female (n,%)	143 (45.25%)	143 (41.94%)	1.145 (0.840-1.559)	>0.05
Hypertension (n,%)	258 (81.62%)	287 (84.24%)	1.079 (0.702-1.658)	>0.05
Diabetes (n,%)	121 (39.93%)	144 (42.23%)	0.910 (0.664-1.246)	>0.05
Coronary artery disease (n,%)	117 (38.65%)	134 (39.34%)	0.972 (0.707-1.335)	>0.05
Hyperlipidemia (n, %)	206 (68%)	220 (64.52%)	1.168 (0.842-1.621)	>0.05
Atrial fibrillation (n, %)	86 (28.42%)	72 (21.13%)	1.481 (1.032-2.123)	<0.05
History of stroke (n, %)	98 (31.01%)	94 (27.62%)	1.181 (0.844-1.654)	>0.05
Type of stroke				<0.01
Hemorrhagic CeVD (n, %)	9 (2.82%)	39 (11.41%)		
Ischemic CeVD (n, %)	285 (90.22%)	279 (81.83%)		
Temporary ischemic attack (n, %)	5 (1.65%)	18 (5.34%)		
Cerebral vein thrombosis (n, %)	17 (5.42%)	5 (1.52%)		
Subtype of Ischemic CeVD				<0.01
Large artery disease (n, %)	89 (31.22%)	85 (30.46%)		
Cardioembolism (n,%)	111 (38.94%)	87 (31.18%)		
Lacuna (n,%)	12 (4.21%)	52 (18.63%)		
Other	25 (8.77%)	22 (7.88%)		
Cryptogenic (n,%)	48 (16.84%)	33 (11.82%)		
NIHSS at the time of admission (mean ± SD)	6.34±6.02	7.66±5.97	1.049 (1.021-1.077)	<0.01
Symptom-to-door time (min) (mean ± SD)	907.37±1874.84	980.24±1862.44	1.000(1.000-1.000)	>0.05
Door-to-consultation time (min) (mean ± SD)	52.83±71.877	74.31±134.33	1.002 (1.000-1.005)	>0.05
IV tPA (n,%)	19 (6%)	19 (5.6%)	1.084 (0.563-2.088)	>0.05
IV tPA door-to-needle time (min) (mean ± SD)	55±43.61	60±38.38	1.006 (0.990-1.022)	>0.05
Endovascular thrombectomy (n, %)	11 (3.5%)	16 (4.7%)	0.733 (0.335-1.604)	>0.05
Door-to-groin time (min) (mean ± SD)	85±56.13	100 (±29.66)	0.992 (0.973-1.011)	>0.05
Unit of hospitalization				<0.01
Neurology clinic (n, %)	266 (84.18%)	223 (65.40%)		
Neurology Intensive Care/Stroke Unit (n, %)	50 (15.82%)	118 (34.60%)		
Length of stay (day) (mean ± SD)	12.93±13.14	8.37±6.37	0.972 (0.958-0.986)	<0.01
mRS 0-2 at discharge (n,%)	232 (73.42%)	197 (57.77%)	0.495 (0.356-0.689)	<0.01
mRS 3-6 at discharge (n,%)	84 (26.58%)	144 (42.23%)	2.019 (1.452-2.806)	<0.01
NIHSS score at the time of admission (mean ± SD)	2.72±3.65	3.10±3.08	1.034 (0.983-1.087)	<0.01
Mortality (n,%)	45 (14.2%)	80 (23.5%)	0.542 (0.362-0.810)	<0.01

Abbreviations: OR: odds ratio, CI: confidence interval, SD: standard deviation, CeVD: cerebrovascular disease, IV tPA: intravenous tissue type plasminogen activator, NIHSS: National Institutes of Health Stroke Scale.

7.66. $p < 0.01$). There was no difference between the rates of systemic intravenous thrombolytic treatment or mechanical thrombectomy in the pre-pandemic and post-pandemic periods. There was an increase in symptom-to-door, door-to-consultation, door-to-needle, and door-to-groin times during the pandemic compared to the pre-pandemic period; however, it was not statistically significant (Table).

It was found that the mean length of hospital stay was significantly shorter during the pandemic period (12.93±13.14 vs. 8.37±6.37, $p < 0.01$). The hospitalization rates of the patients with stroke in the intensive care unit during the pandemic were higher (34.6% vs. 15.82% $p < 0.01$). The COVID-19 test was positive after hospitalization in 5 patients with ischemic stroke (1.8%) hospitalized during the pandemic. The mRS and NIHSS scores at discharge were significantly higher among the

patients with hemorrhagic and ischemic stroke during the pandemic ($p < 0.01$). While the mortality rate was 14.2% in the pre-pandemic period, it increased to 23.5% in the pandemic period ($p < 0.01$).

DISCUSSION AND CONCLUSION

In this study, the differences between acute stroke patients hospitalized in the Neurology clinic before and during the COVID-19 pandemic were investigated, and it was aimed to show the effects of COVID-19 on the management of stroke.

In a study conducted during the pandemic period, acute stroke hospitalizations were grouped according to age groups and it was observed that hospitalizations over 65 years of age decreased. Lockdowns, difficulty in accessing the hospital, and infection transmission anxiety have been emphasized as the causes (14).

In our study, it was observed that there was no difference in the age and gender of patients with stroke hospitalized during the pandemic compared to the period before the pandemic.

At the beginning of the pandemic, there were global decreases in the hospitalization of patients with acute stroke (8,10). Disruptions in the ambulance system and pandemic orders of the hospitals have been demonstrated as the causes (15). On the other hand, in a study reporting that excessive sodium, fast food consumption, and exposure to polluted air decreased during the pandemic, it was argued that this situation contributed to the decrease in the number of admissions due to CeVD similar to cardiovascular cases (16). In our study, there was no decrease in the total number of hospitalizations of patients with acute stroke; however, it was observed that the rate of ischemic stroke and CVT decreased and the rates of hospitalizations due to hemorrhagic CeVD and TIA increased among patients hospitalized during the pandemic. A significant decrease of 6 to 51 was demonstrated in a study comparing the admissions due to ischemic stroke during the first month of the pandemic with the average monthly admissions concerning the previous five years (17). In another study comparing weekly admissions of acute stroke, the number temporarily decreased at the beginning of the pandemic; however, it continued to increase (18). Our observations suggest that the admission rate of patients with ischemic stroke to the emergency department and neurology clinic decreased, especially at the beginning of the pandemic. It can be interpreted that patients and their relatives preferred to stay at home during the presence of ischemic stroke symptoms because they were afraid of COVID-19 transmission. Within the scope of quarantine measures, the number of admissions to the emergency department for patients with TIA and minor stroke such as patients with myocardial infarction decreased as the physicians and media advised to stay at home (19-21). On the contrary, ischemic and hemorrhagic CeVD patients with more severe symptoms continued to be admitted to the hospital and transferred to tertiary health institutions during the pandemic. In contrast to the increase in hospitalizations due to hemorrhagic CeVD we observed, another study evaluating the three-month pandemic period reported a decrease of 11.5% (9). Changes have also been reported in

hospitalization due to the subtypes of ischemic stroke during the pandemic. There was not much difference in the percentage of patients hospitalized during the pandemic since cortical findings such as aphasia, loss of vision, and dominant hand weakness, which were common in stroke due to large vessel disease, led to severe disability. Nevertheless, the rate of large vessel disease may have increased relatively due to other subtypes with decreased hospital admission, albeit no change in number (8). In our study, while there was no decrease in the number of strokes due to large vessel disease, there was an increase in the number of lacunar infarctions and a decrease in the rate of cardioembolic stroke. In similar studies, hospitalizations due to lacunar infarction generally decreased in the pandemic. The increase in the rate of patients with small vascular disease hospitalized in our clinic during the pandemic could be explained by the fact that the neurology clinics of the second-line hospitals, which normally hospitalize these patients in our region, were transformed into COVID-19 pandemic clinics and their referral to tertiary institutions increased because these patients could not be hospitalized in the second-line hospitals.

Especially at the beginning of the pandemic, there was a decrease in the number of treatments for acute stroke with the hospitalizations due to stroke. In a multicenter study, it was revealed that the number of IV tPA administrations decreased and door-to-needle times almost doubled (22). As a result of delays in hospital access and treatment processes, many studies demonstrated a decrease in IV tPA and EVT administrations during the pandemic (23-25). On the other hand, in a study evaluating the 9-month period after the first wave of the pandemic (March 13 - May 18, 2020), an increase was observed in the number of acute strokes and IV tPA and EVT numbers remained the same (18). In a similar study, it was reported that acute stroke hospitalizations decreased, EVT rates were higher, and IV tPA rate decreased in the second wave (October-December 2020) compared to the previous year; however, it was similar in other months (26). In our hospital, there was no decrease in IV tPA and EVT administrations. Nevertheless, despite the prolongations in symptom-to-door, door-to-consultation, door-to-needle, and door-to-groin times among patients undergoing acute endovascular or systemic thrombolysis treatment, they did not reach a

statistically significant level. In a similar study, symptom-to-door time was demonstrated to be prolonged from 105 to 248 minutes and symptom-to-needle/groin time from 217 to 365 minutes in patients with proximal vascular occlusion (27). A significant prolongation of 12 minutes (50 vs. 62 minutes, $p < 0.01$) was reported for the door-to-groin time in another study involving data from 17 stroke centers (28). In our data, the door-to-groin times were prolonged from 85 minutes to 100 minutes; however, this difference was not statistically significant ($p > 0.05$). The reason for this prolongation could be the increase in the general intensity of the emergency department during the pandemic and the delays in the diagnosis process caused by the institutional and individual measures taken for the safety of healthcare workers.

On the other hand, the current data indicated that more severe patients presented during the pandemic. In a study conducted during the lockdown period, NIHSS scores at admission were found to be significantly higher compared to before the pandemic (28). In our study, NIHSS scores at admission were found to be statistically high during the pandemic. Similarly, hospitalizations in the intensive care and stroke unit were more common during the pandemic. Nevertheless, it was observed that the length of hospital stay was significantly shortened during the pandemic. This was probably because the responsible physicians hesitated while admitting patients with stroke due to COVID-19 transmission and the need for beds increased due to the pandemic. Accordingly, although there was a more severe patient group during the pandemic, efforts were made to shorten the length of hospital stay by accelerating the examination and treatment processes. Similarly, patients with stroke admitted during the pandemic period were found to have high NIHSS scores at the time of discharge in our study. The in-hospital mortality rate was similarly higher compared to the period before the pandemic. The data in the current literature indicated that the mortality rate in patients with acute stroke increased during the pandemic period (29,30).

The incidence of CeVD in admitted patients with COVID-19 was reported to be 2.8-5.4% (31,32). In a study including 457 stroke centers in seventy countries, 3.3% of patients who presented with acute stroke were reported to be COVID-19

positive (10). Similarly, the COVID-19 test was positive in 1.8% of the patients hospitalized with stroke in our clinic. There was no clear information that the prevalence of stroke increased in patients with asymptomatic COVID-19.

The primary limitation of our study was that it was conducted in a single center and the number of patients was relatively low.

As a result, the COVID-19 pandemic negatively affected the management of acute stroke globally. This study revealed the characteristics of patients with acute stroke before and during the 14-month pandemic. The duration of acute stroke treatment was delayed due to reasons occurring before and during hospitalization. The severity of stroke in patients hospitalized with the diagnosis of acute stroke during the pandemic was higher compared to the period before the pandemic. Poor clinical outcomes and high mortality rates were observed due to the heavy load of stroke.

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Ethics

Ethics Committee Approval: The study was approved by Clinical Research Ethics Committee of Ondokuz Mayıs University (Date: 09.07.2021, Number: 2021/345).

Informed Consent: The authors declared that informed consent was not obtained from the patients because of the retrospective study design.

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