

# The impact of COVID-19 ischemic stroke in the emergency department

Acil serviste COVID-19'un iskemik inme üzerindeki etkisi

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## **OBJEKTIVE(S)**

The aim of this study is to investigate the number and characteristics of ischemic stroke patients admitted to the emergency department before and during the COVID-19 pandemic, to determine the impact of the pandemic on a disease with high mortality and morbidity, and to support the development of preventif strategies.

# **METHODS**

This single-center, retrospective cohort study, included patients diagnosed with ischemic stroke and transient ischemic attack who presented to the emergency department between March 2018 and March 2022. We classified patients into two groups, pre-pandemic and pandemic, each covering a two-year periods. We compared the numbers, admission characteristics and outcomes of the patients.

#### RESULTS

A total of 1,632 patients were included in the study, including 915 patients in the pre-pandemic period and 717 patients in the pandemic period. During the pandemic period, there was a 21.6% decrease in the number of stroke cases (n:915 vs. n:717). The median National Institutes of Health Stroke Scale at admission was similar (4 vs. 4, p = 0.071). The rate of thrombectomy was higher in the pandemic group (p < 0.001). The rate of hospitalization was lower in the pandemic group (p < 0.001), but there was no difference in 28-day mortality (p = 0.100).

## DISCUSSION

During the COVID-19 pandemic, we observed a decline in the number of strokes, as a result of people in seeking medical care. The implementation of health policies and educational campaigns is essential to ensure timely access to health care and minimize morbidity and mortality in future pandemic.

## **KEYWORDS**

COVID-19, emergency department, ischemic stroke, thrombectomy

## AMAÇ

Bu çalışmanın amacı, pandeminin yüksek mortalite ve morbiditeye sahip hastalıklar üzerindeki etkisini belirlemek ve önleyici stratejilerin geliştirilmesini sağlamak amacıyla COVID-19 pandemisi öncesinde ve sırasında acıl servise başvuran iskemik inme hastalarının sayısını ve özelliklerini araştırmaktır.

## YÖNTEM

Bu tek merkezli, retrospektif kohort çalışmasına Mart 2018 ile Mart 2022 arasında acil servise başvuran iskemik inme ve geçici iskemik atak tanısı almış hastalar dahil edildi. Hastaları ikişer yıllık dönemleri kapsayan pandemi öncesi ve pandemi dönemi olmak üzere iki gruba ayırdık. Hastaların sayıları, başvuru özellikleri ve sonuçlarını karşılaştırdık.

## BULGULAR

Çalışmaya pandemi öncesi dönemde 915 hasta ve pandemi döneminde 717 hasta olmak üzere, 1632 hasta dahil edildi. Pandemi döneminde inme olgularının sayısında %21,6 oranında azalma görüldü (n:915 vs. n:717). Hastaların Ulusal Sağlık İnme Ölçeği ortanca değerleri benzerdi (4 vs. 4, p = 0,071). Trombektomi oranı pandemi döneminde daha yüksekti (p < 0,001). Hastaneye yatış oranı pandemi döneminde daha düşüktü (p < 0,001), ancak 28 günlük mortalitede bir farklılık yoktu (p = 0,100).

## SONUÇ

COVİD-19 pandemisi döneminde, hastaların tıbbi bakım alma konusundaki tereddütleri nedeniyle inme sayılarında ciddi bir azalma saptandı. İleride yaşanabilecek pandemilere yönelik hazırlanacak sağlık politikaları ve eğitim kampanyalarının uygulanması sağlık hizmetine erişimi sağlamak, morbidite ve mortaliteyi en aza indirmek için oldukça önemlidir.

## ANAHTAR KELİMELER

Acil Servis, COVID-19, iskemik inme, trombektomi

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he COVID-19 disease caused by the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) originated from Wuhan, China, and led to a global health crisis (1). According to the World Health Organization (WHO), there have been approximately 768 million confirmed cases, and 6.9 million deaths due to COVID-19 (2). Numerous studies have been published indicating that COVID-19 significantly increases the number of thromboembolic events, which have a significant impact on mortality (3-5). This has been attributed to inflammation and endothelial damage caused by the virus, resulting in a procoagulant state (6-7). It is now known that the devastating effects of COVID-19 are not solely due to a viral infection, but rather to a systemic procoagulant process endothelial damage triggered by (8-9). Venous particularly thromboembolism, pulmonary embolism, accounts for the majority of these thromboembolic complications (10-11). In addition, studies have shown the development of arterial thrombotic complications such as ischemic stroke and myocardial infarction (5,12).

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Stroke is one of the leading causes of disability worldwide (13). Approximately 12 million people worldwide experience their first stroke attack each year (14). In Türkiye, the annual incidence of ischemic stroke has been reported to be 93.2-108.6 per 100,000 population (15). The majority of ischemic strokes are caused by thromboembolic processes such as large artery atherosclerosis, cardioembolic and small artery occlusion (16). Despite the studies showing an increase in thromboembolic complications associated with COVID-19, several studies have been published showing a decrease in ischemic strokes and transient ischemic attacks (TIAs) during the pandemic (17-19). However, large-scale studies on this topic in Türkiye are lacking. In this study, our primary objective is to determine the impact of the COVID-19 pandemic on the number of cases of ischemic stroke and transient ischemic attack (TIA) presenting to the emergency department by comparing the pre-pandemic and pandemic periods. Our secondary objectives are to assess the impact on time to presentation, hospitalization rates, and mortality rates.

# **Materials and Methods**

This retrospective cohort study included cases presenting with stroke to the emergency department (ED) of our university hospital between March 2018 and March 2022. Our ED is a stroke center located in Izmir, the third largest city in Türkiye. Cases diagnosed with ischemic stroke or TIA based on clinical findings and radiological imaging were included. Patients with hemorrhagic stroke or missing demographic and clinical data were excluded.

Patients were categorized into pre-pandemic and pandemic groups based on the date of the first confirmed COVID-19 case in Türkiye (March 11th, 2020). The study compared differences in the number of admissions clinical severity at admission, time from symptom onset to presentation and treatments administered. Demographic data, comorbidities, risk factors for ischemic stroke, admission dates, time from symptom onset to presentation to the ED, National Institutes of Health Stroke Scale (NIHSS) scores at admission, radiological findings, treatments administered, patient outcomes (discharge, admission to stroke unit, death) and 28day mortality data were obtained from electronic patient records in the hospital information management system. Patients diagnosed with TIAs were recorded as having a, NIHSS score of "0" on admission. For ischemic strokes, patients with admission NIHSS score <5 were classified as having a mild strokes, while patients with an NIHSS score ≥5 were classified as having a moderate and severe strokes. When comparing admission times, patients were divided into two groups based on the target thrombolysis time of 4.5 hours, categorized as early and late admissions.

# Statistical analysis

Data were analyzed by using SPSS Statistics for Windows, Version 29.0 (IBM SPSS Statistics for Windows, Version 29.0. Armonk, NY: IBM Corp). The normal distribution of the variables was tested using the Kolmogorov-Smirnov test. Numerical data that conformed to the normal distribution were presented as mean and standard deviation, while those that did not conform to the normal distribution were presented as median and interquartile range. The Mann-Whitney U test was used to compare non-parametric numerical data. Chisquare and Fisher's exact tests were used to compare categorical data. Data was analyzed with a 95% confidence interval, and p <0.05 was considered statistically significant.

# Results

In total, 2006 patients with stroke were admitted to the ED. Of these them, 228 (11.3%) patients were excluded because of hemorrhagic stroke and 146 (7.2%) patients were excluded because of missing data. A total of 1632 patients with ischemic stroke were included in the analysis. Of those patients, 934 (%57.2) were male and the median age was 72 years. The distribution of stroke subtypes among these patients over different time periods is shown in Figure 1.

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Figure 1. Distribution of patients according to stroke subgroups in different periods

The total number of patients admitted to the ED in the pre-pandemic period was 263,000 with 915 ischemic strokes (0.34%), whereas the total number of patients in the pandemic period was 161,000 with 717 ischemic strokes (0.44%). There was a 38.8% reduction in the total number of patients

presenting to the ED, and a 21.6% reduction in the number of stroke cases.

The demographics characteristics and risk factors of the patients were shown in Table 1.

Demographic characteristics	Total	Pre-Pandemic	Pandemic	p
Age (Median, IQR)	72 (62-80)	73 (64-81)	71 (61-78)	<0.001
Sex (Male)	937 (57.4)	518 (56.6)	419 (58.4)	0.459
Risk Factors	n (%)	n (%)	n (%)	
Hypertension	1002 (61.4)	551 (60.2)	451 (62.9)	0.269
Diabetes	496 (30.4)	239 (26.1)	257 (35.8)	< 0.001
Hyperlipidemia	121 (7.4)	71 (7.8)	50 (7.0)	0.547
Malignancy	91 (5.6)	45 (4.9)	46 (6.4)	0.191
Smoking	221 (13.5)	86 (9.4)	135 (18.8)	< 0.001
Atrial Fibrillation	269 (16.5)	158 (17.3)	111 (15.5)	0.334
Coronary Artery Disease	515 (31.6)	256 (28.0)	259 (36.1)	<0.001
History of Stroke	286 (17.5)	168 (18.4)	118 (16.5)	0.316

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The gender distribution (male) did not differ between pre-pandemic and pandemic groups (p = 0.459). However, the data showed that the pandemic group was younger (73 vs.71 years, p <0.001, respectively). Smoking (p <0.001), presence of

diabetes mellitus (p <0.001) and coronary artery disease (p <0.001) were also higher patients in the pandemic group.

The clinical stroke characteristics of the patients are shown in Table 2.

Table 2. Clinic	al characteristic	s of patients	with ischemic stroke.
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Clinical characteristics	Total	Pre-Pandemic	Pandemic	
	n (%)	n (%)	n (%)	p
Transient ischemic attacks	168 (10.3)	95 (10.4)	73 (10.2)	
Mild Stroke	751 (46.0)	438 (47.9)	313 (43.7)	0.186
Moderate and Severe Stroke	713 (43.7)	382 (41.7)	331 (46.2)	
Onset-to-door time, ≤4,5h	612 (37.5)	324 (39.4)	288 (43.8)	0.083
	Median	Median	Median	
	(IQR 25-75)	(IQR 25-75)	(IQR 25-75)	
Onset-to-door time, h	6 (2.5-17.5)	6.5 (2.5-19.0)	5.5 (2.5-14.0)	0.112
NIHSS* on admission	4 (2-8)	4 (2-7)	5 (3-9)	0.071
NIHSS* at discharge/7th day	3 (1-6)	3 (1-5)	4 (2-8)	<0.001
*National Institutes of Health Stroke	Scale			

There was no significant difference in the distribution of stroke subgroups between groups. Although the median admission NIHSS scores were similar in both periods (p = 0.071), the discharge/7th-day NIHSS score was higher in the pre-pandemic group (p <0.001). The median time from symptom onset to ED admission was similar (6.5 vs. 5.5 hours, p = 0.112).

There was no difference in intravenous thrombolysis, but endovascular treatment was used more frequently in during the pandemic group. Comparing patient outcomes, the hospitalization rate for treatment was lower during the pandemic compared to the pre-pandemic group (p < 0.001). Mortality rates were similar in both periods (Table 3).

Table 3. Treatments and outcomes of patients with ischemic stroke.

Total	Pre-Pandemic	Pandemic	p
n (%)	n (%)	n (%)	
266 (16.3)	139 (15.2)	127 (17.7)	0.177
120 (7.4)	49 (5.4)	71 (9.9)	< 0.001
.386 (85.1)	830 (90.9)	556 (77.7)	<0.001
92 (5.6)	44 (4.8)	48 (6.7)	0.100
	<b>Total</b> <i>n</i> (%) 266 (16.3) 120 (7.4) 386 (85.1) 92 (5.6)	Total         Pre-Pandemic           n (%)         n (%)           266 (16.3)         139 (15.2)           120 (7.4)         49 (5.4)           386 (85.1)         830 (90.9)           92 (5.6)         44 (4.8)	Total         Pre-Pandemic         Pandemic           n (%)         n (%)         n (%)           266 (16.3)         139 (15.2)         127 (17.7)           120 (7.4)         49 (5.4)         71 (9.9)           386 (85.1)         830 (90.9)         556 (77.7)           92 (5.6)         44 (4.8)         48 (6.7)

# Discussion

During the pandemic, many articles have been written about the reduction in ischemic stroke admissions the delayed admissions worldwide. However, no comprehensive study that conducted in our country. To the best of our knowledge, this is the most comprehensive study conducted in a tertiary stroke center in one of the largest cities in our country. In our study, we found a decrease in the number of ischemic strokes, but we found an increase in the frequency of ischemic strokes due to the decrease in the total number of patients admitted to the ED. Furthermore, we did not find a delay in the time from symptom onset to admission to the ED in ischemic stroke patients. We found an absolute increase in the use of mechanical thrombectomy, but we found a significant decrease in hospitalization rates.

Several studies have investigated the impact of the COVID-19 pandemic on stroke, and the majority of these studies reported a decrease in the number and incidence of strokes during the pandemic period (20–22). One of the most significant findings of our study is the 21.6% decrease in the

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number of stroke cases presenting to the ED. Although the total number of stroke cases has decreased, the proportion of stroke cases among all patients presenting to the ED has increased. This finding could be attributed to two main factors. First, when analyzing patient numbers, it is possible that the restrictions imposed by COVID-19 and the fear of infection led to a reduction in the number of stroke patients presenting to the ED. However, the more pronounced decrease in ED admissions for non-stroke conditions may explain the relative increase in the proportion of stroke cases. Secondly, despite the significant decrease in the total number of patients presenting to the ED, the increased thromboembolic complications due to from endothelial dysfunction caused by COVID-19 may have contributed to this relative increase.

In our study, similar to the current literature, there was no difference in patients' NIHSS scores on admission between the pre-pandemic and pandemic groups (20,23,24). However, NIHSS scores at discharge were higher in the pandemic group. Several parameters such as age at admission, comorbidities, infarct area size, time from symptom onset to admission to the ED, and treatments administered influence the clinical outcome of stroke patients. In our study, the higher prevalence of risk factors in stroke patients in the pandemic group combined with the shorter duration of hospitalization during the pandemic group may have contributed to this result.

The time from symptom onset to ED admission, defined as the last well-known time, plays a crucial role in the treatment planning for ischemic stroke. In our study, there was no significant difference in the time from symptom onset to admission to the ED between the two periods. Balucani et al. and Tanaka et al. reported that patients in the pandemic group in their study had late ED admission (21-25). However, there are also studies reporting the contrary (20,24,26).

While rates of intravenous thrombolysis were similar in both periods in our study, the use of mechanical thrombectomy was higher in the pandemic period. This increase may not be due to the impact of COVID-19, but rather to the global trend towards increased use of endovascular procedures in stroke patients, coupled with a limited number of centers capable of performing such procedures. Other studies have supported similar findings showing that the use of mechanical thrombectomy has not decreased despite a decrease in the number of patients (17,21,26). Our study also found that patient hospitalization rates decreased, similar to other studies on this topic (17,22). To reduce hospital transmission of COVID-19, fewer hospital admissions can be managed as outpatients cases, such as TIAs and mild strokes, which may explain this finding.

#### **Study limitations**

As there was no information on whether the stroke patients in our study had previously had COVID-19, it is difficult to draw definite conclusions about the exact cause of the relative increase in stroke incidence. Due to the retrospective nature of the study, unavailable data is an important limitation. In addition, the generalizability of the results is not given because the study was conducted at a single center and the population was limited.

## Conclusion

During the COVID-19 pandemic, a decrease in the total number of patients and the number of stroke cases presenting to the ED was observed. There was no significant difference in the admission NIHSS scores and the time from symptom onset to admission. Mortality rate did not change although the rate of mechanical thrombectomy increased during the pandemic period.

Although several factors may have contributed to the decline in stroke cases, the most important factor appears to have been the reluctance to seek medical care the pandemic. For diseases with high morbidity and mortality, such as stroke, the benefits of access to healthcare outweigh the risks of infection. Therefore, health policies should be developed to address potential pandemic periods, and education campaigns for the public and healthcare worker should be implemented..

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#### **Conflict of interest**

Authors declare no conflict of interest.

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