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Comparison of treatment durations before Covid-19 pandemic, pre- and post-vaccination periods in acute ischemic stroke patients in a Turkish tertiary hospital

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Abstract

Objective: This study aimed to compare the frequency of admission to hospital in patients with acute ischemic stroke before the COVID 19 pandemic, during the pre-vaccination period, and after the start of vaccination for COVID 19, and to evaluate the time window period between symptom onset to door time, door to CT scan time, door to needle time, and door to puncture time. In addition, it aimed to investigate the effects of the COVID-19 pandemic on the admission, evaluation, and initiation of acute treatment of patients with acute ischemic stroke. *Methods:* Patients presenting with acute ischemic stroke between March 2019 - December 2019 (pre-pandemic), March 2020 - December 2020 (pre-vaccination pandemic period), and March 2021 - December 2021 (post-vaccination pandemic period) were included in the study. NIHSS was calculated by accordance with the neurological examination findings of the patients, cranial CT for the exclusion of bleeding and CT angiography images for the large vessel occlusions were performed, and the vital signs of the patients were recorded. IV tPA treatment was applied within the first 4.5 hours, and mechanical thrombectomy (MT) was performed in patients with large vessel occlusion. *Results:* Three hundred nineteen patients were included in the study. The times from symptom onset to emergency admission and from symptom onset to CT scan were found to be similar in all periods. The time from symptom onset to examine by a neurologist was found to be significantly longer in the vaccination period compared to the pandemic period. It was observed that the time from the door to needle time and the time from examine by a neurology doctor to needle time was statistically significantly shorter during the pandemic period ($p<0.05$). *Conclusion:* In our study in a tertiary hospital in Turkey, it was determined that the number of patients who was admitted with acute stroke clinic during the pandemic period was similar to other years and there was no delay in the initiation of treatment during the pandemic period. Door to needle times, as well as the time taken by the neurologist to examine and initiate IV-tPA treatment, were found to be shorter in the pre-vaccination pandemic period than in the pre-pandemic and post-vaccination periods.

Keywords: Acute stroke, COVID-19, pandemic, IV-tPA, mechanical thrombectomy

INTRODUCTION

Since December 2019, SARS-CoV-2 (Severe Acute Respiratory Syndrome-Coronavirus 2), which is the causative agent of "Coronavirus Disease 2019 (COVID-19)" with severe respiratory failure, has caused the death of millions of people worldwide. There are many publications on the impact of the Covid-19 pandemic on the management of acute stroke patients. There have been reports of a decrease in stroke admissions, delays in admission to the hospital, and consequently a decrease in reperfusion treatments due to both patients' fears and social and logistical barriers.[1-4] Due to its features of being easily transmitted and lethal characteristics, it is aimed to reduce the admission of patients to the hospital during this process unless it is very necessary. On the other hand, the necessity of protective equipment in the hospital,

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the necessity of decontamination procedures, the necessity of examining each patient coming to the emergency room for COVID-19, have led to the reduction of imaging tests unless necessary.[5-8]

For this reason, it was predicted that there may be decrease/delay in the admissions of patients with acute neurological symptoms to the hospital and the delays in the examination and treatment of the patients due to the health personnel trying to stop the spread of the virus. In this study, it was aimed to compare the frequency of admission to the hospital, the time of admission to the emergency room and evaluation, examination and initiation of reperfusion therapy in patients with acute ischemic stroke before the COVID-19 pandemic, during the pre-vaccination and post vaccination period. It was aimed to investigate the effects of the COVID-19 pandemic on the management of acute ischemic stroke patients by comparing these three different periods.

METHODS

Patients who were admitted to the Marmara University Training and Research Hospital emergency department with acute ischemic stroke between March 2019 – December 2019 (pre-pandemic), March 2020 – December 2020 (pre-vaccination pandemic period), and March 2021- December 2021 (post-vaccine pandemic period) were included in the study. The United States National Institutes of Health Stroke Scale (NIHSS) was recorded by the attending neurologist on arrival of all patients presenting with acute stroke symptoms. Routine biochemistry tests were sent to all patients at the time of admission, and cranial CT, cranial and cervical CT-Angiography imaging were performed. In all patients presenting with wake-up stroke, diffusion-weighted magnetic resonance imaging (DAG-MRI) and fluid attenuated inversion recovery (FLAIR) imaging scan were included. Symptom onset time of all patients, onset to door time, and door to evaluation by a neurologist time were recorded. In addition, door to – CT scan time, door to– needle time, door to– puncture times of all patients were also calculated.

In this study, COVID-19 PCR swab samples were collected from all participants using flocked swabs, and swab was first taken from the nasopharynx and then from the oropharynx with the same swab, placed in the containing tubes and delivered to the laboratory. After vortexing the vNAT tubes for 5 seconds, they were loaded into the realtime PCR device using amplification kits. The results were obtained from the device and analyzed for all of patient during the pre-vaccination and pandemic COVID -19.

Statistical reviews

NCSS (Number Cruncher Statistical System) 2007 (Kaysville, Utah, USA) program was used for statistical analysis. Descriptive statistical methods (mean, standard deviation, median, frequency, percentage, minimum, maximum) were used while evaluating the study data. The conformity of the quantitative data to the normal distribution was tested with the Shapiro-Wilk test and graphical examinations. Kruskal-Wallis test and Dunn-Bonferroni test were used for comparisons between groups of more than two quantitative variables that did not show normal distribution. Fisher-Freeman-Halton exact test was used to compare qualitative data. Statistical significance was accepted as $p<0.05$.

RESULTS

In this study, the data of patients who were admitted to the emergency department of Marmara University Training and Research Hospital and diagnosed with acute stroke between March 2019-December 2019, March 2020-December 2020, March 2021-December 2021 were retrospectively analyzed. A total of 319 cases, 49.8% (n=159) male, 50.2% (n=160) female, were included in the study. The ages of the subjects participating in the study ranged from 29 to 96, with a mean age of 69.42±13.88 years (Table 1).

When the treatments given to the subjects participating in the study were examined; it was observed that 61.1% (n=195) received IV tPA, 20.1% (n=64) had thrombectomy, 18.8% (n=60) had received both IV tPA and thrombectomy (Table 1).

It was observed that 30.7% (n=98) of the cases was treated in 2019, 37% (n=118) in 2020, and 32.3% (n=103) in 2021 (Table 1).

When the arrival NIHSS scores of the cases were examined by years, the NIHSS scores of the cases in 2021 were significantly higher than those in 2019 ($p=0.011$; $p<0.05$) (Table 2).

The gender, age, follow-up and lesion localization of the cases did not show any statistically significant difference according to years ($p>0.05$) (Table 2).

When the duration of the cases from the onset of symptoms to examined by a neurologist is compared; the duration of the cases in 2021 was found to be significantly longer than those in

Table 1: Distributions of descriptive characteristics

		n (%)
Gender	**Male**	159 (49.8)
	Female	160 (50.2)
Age	*Mean±SD*	69.42±13.88
	Median (Min-Max)	72 (29-96)
Treatment	**tPA**	195 (61.1)
	Thrombectomy	64 (20.1)
	tPA + Thrombectomy	60 (18.8)
Years	**2019**	98 (30.7)
	2020	118 (37.0)
	2021	103 (32.3)

tPA: Tissue plasminogen activator

2020 (p=0.003; p<0.01) (Table 3).

The time from CT scan to examination by a neurologist according to years was examined, and as a result of paired comparisons; the duration of the cases in 2019 was found to be significantly longer than those in 2020 and 2021 (p=0.007; p=0.001; p<0.01) (Table 3).

When the times from door-to-needle time are compared, the duration of the cases in 2019 was significantly longer than in 2020; but shorter than in 2021 (p=0.001; p=0.038; p<0.05) (Table 3).

A significant difference was found between

Table 2: Comparison of Descriptive Characteristics by Years

		Years			p
		2019 (n=98)	**2020 (n=118)**	**2021 (n=103)**	
Gender	**Male**	51 (52.0)	57 (48.3)	51 (49.5)	[a]*0.867*
	Female	47 (48,0)	61 (51,7)	52 (50,5)	
Age	*Mean±SD*	67.65±14,34	70.81±13,33	69.50±14,01	[b]*0.292*
	Median(Min-Max)	69,5 (29-91)	73 (34-96)	72 (35-95)	
NIHSS	Mean±SD	9.46±5,62	9.81±4,83	11.25±4,96	***[b]0.011****
	Median(Min-Maks)	8 (1-25)	9 (2-22)	11 (2-24)	
Follow-up	**Ex**	1 (1.0)	1 (0.9)	2 (1.9)	[a]*0.258*
	Transferred	3 (3.1)	6 (5.1)	10 (9.7)	
	Discharge	61 (62.2)	76 (65.0)	53 (51.5)	
	ICU	33 (33.7)	34 (29.1)	38 (36.9)	
ACA	**Absent**	94 (95.9)	113 (97.4)	102 (99.0)	[a]*0.399*
	Present	4 (4.1)	3 (2.6)	1 (1.0)	
MCA	**Absent**	11 (11.2)	16 (13.8)	5 (4.9)	[a]*0.075*
	Present	87 (88.8)	100 (86.2)	98 (95.1)	
PCA	**Absent**	92 (93.9)	114 (98.3)	100 (97.1)	[a]*0.234*
	Present	6 (6.1)	2 (1.7)	3 (2.9)	
Brainstem	**Absent**	92 (93.9)	104 (89.7)	99 (96.1)	[a]*0.184*
	Present	6 (6.1)	12 (10.3)	4 (3.9)	
Cerebellum	**Absent**	95 (96.9)	114 (98.3)	100 (97.1)	[a]*0.821*
	Present	3 (3.1)	2 (1.7)	3 (2.9)	

ICU: Intensive care unit, ACA: Anterior cerebral artery, MCA: Middle cerebral artery, PCA: Posterior cerebral artery
[a]*Fisher Freeman Halton Test*
[b]*Kruskal Wallis Test & Dunn Bonferonni Test*
**p<0,05*

Table 3: Comparison of durations and treatments by years

		Years			*p*
		2019 (n=98)	**2020 (n=118)**	**2021 (n=103)**	
Symptom onset time to door	***Mean±SD***	91.58±73,52	90.12±91.06	92.53±132.59	[b]*0.892*
	Median (Min-Max)	66 (7-347)	63 (6-695)	67 (10-1288)	
Symptom onset time to neurologist	***Mean±SD***	160.68±77,21	142.88±101.30	162.05±178.52	[b]***0.004****
	Median (Min-Max)	150 (40-405)	125 (15-820)	112 (20-1140)	
Symptom onset time to CT	***Mean±SD***	117.69±72.37	125.25±110.88	141.90±116.47	[b]*0.295*
	Median (Min-Max)	96 (22-397)	97 (25-972)	105 (15-780)	
CT to neurologist	***Mean±SD***	42.99±41.52	25.54±24.77	17.26±15.78	[b]***0.001****
	Median (Min-Max)	29.5 (3-187)	15 (1-130)	10 (2-71)	
Door to needle time	***Mean±SD***	143.19±48.88	114.65±64.20	161.57±165.10	[b]***0.001****
	Median (Min-Max)	137 (49-263)	108.5 (36-571)	117 (58-1088)	
Neurologist to needle time	***Mean±SD***	74.81±39.26	61.7±48.08	80.07±63.70	[b]***0.009****
	Median (Min-Max)	70 (10-174)	50 (5-438)	65 (9-386)	
Neurologist to puncture time	***Mean±SD***	134.30±137.83	116.00±72.10	168.09±65.54	[b]***0.001****
	Median (Min-Max)	110 (0-663)	92 (18-320)	159.5 (37-380)	
Door to puncture time	***Mean±SD***	205.57±151.03	169.83±96.93	132.88±67.92	[b]***0.009****
	Median (Min-Max)	169.5 (1-726)	135 (47-437)	130 (15-375)	
Treatment	**tPA**	49 (50.0)	89 (75.4)	57 (55.3)	[a]***0.001****
	Thrombectomy	16 (16.3)	22 (18.6)	26 (25.2)	
	tPA+ Thrombectomy	33 (33.7)	7 (5.9)	20 (19.4)	

CT:Computed tomography, tPA: Tissue plasminogen activator
[a]*Fisher Freeman Halton Test*
[b]Kruskal Wallis Test & Dunn Bonferonni Test
*p<0,05

the time from examine by a neurologist to the administration of IV tPA (p=0.009; p<0.01). As a result of the pairwise comparisons made in order to determine the source of the difference; The duration of the cases in 2020 is significantly shorter than those in 2019 and 2021 (p=0.017; p=0.045; p<0.05) (Table 3).

A significant difference was found between the time from examined by a neurologist to the puncture time of the cases according to years (p=0.001; p<0.01). The duration of the cases in 2021 is significantly longer than in 2019 and 2020 (p=0.001; p=0.003; p<0.01) (Table 3).

A significant difference was found when the door to puncture time was compared (p=0.009; p<0.01). As a result of the pairwise comparisons made in order to determine the source of the difference; door to puncture time in 2019 was significantly longer than in 2021 (p=0.006; p<0.01) (Table 3).

When the treatments applied to the patients were compared, IV tPA administration to cases in 2020 is higher than in 2019 and 2021. Treatment with IV tPA + thrombectomy in 2020 is lower than in 2019 and 2021 (p=0.001; p<0.01) (Table 3).

When the time from symptom onset to emergency admission and the time from symptom onset to CT scan were compared according to years, no statistically significant difference was observed (p>0.05) (Table 3).

DISCUSSION

Over the years, advances in the hyperacute treatment of stroke and treatment results have revealed the slogan "time is brain" and supported its importance. However, with the onset of the COVID-19 pandemic, a call to "stay at home" was made. As a result, it is thought that patients' fears of in-hospital virus contamination, maintaining

social distance, and the need to reduce the additional workload of health authorities are thought to cause a decrease or delay in hospital admissions even in emergency situations due to warnings.

In our study, it was aimed to investigate the effect of the COVID-19 pandemic on acute stroke admissions and management. For this reason, we compared the data of acute stroke admissions and treatment applied in our clinic before the pandemic, during the pandemic period and the start of vaccination.

Various studies have reported a worldwide decline in stroke cases during the COVID-19 pandemic. [6,8-10] During the pandemic period, it was expected that the duration of examination and reperfusion treatments of acute stroke patients would be shortened with the decrease in all applications to the emergency services and the patient load in the emergency services. However, the evaluation of patients for COVID-19 during their first admission, as well as disinfection of the imaging areas after the patient's contact, revealed that there may be delays in the periods.

Contrary to what was expected in our study, the number of patients presenting with acute stroke clinic during the pandemic period was found to be similar compared to other years, and no statistically significant difference was found in the time from symptom onset to coming to the emergency department. This suggests that patients do not delay their admission to the emergency department in the presence of a serious clinical picture such as acute stroke during the pandemic period.

The fact that there was no statistically significant difference in the time from the onset of symptoms to the CT scan in our study indicates that there was no delay in the initial evaluation and subsequent cranial CT scan during the patient's admission to the emergency department during the pandemic period.

It was found that the time from symptom onset to examination by a neurologist was significantly longer in the pandemic period after vaccination compared to the pre-vaccination pandemic period. Similarly, the time between patients' admission to the emergency room and IV tPA administration (door to needle time) and the time from examination by a neurologist until IV tPA was administered were found to be statistically significantly shorter in the pre-vaccination pandemic period. This situation can be associated with the fact that the number of admission to emergency services was decreased, the additional workload of physicians and assistant healthcare workers decreased in this period and the processing was faster.

In a study conducted in Canada, pre-pandemic and pandemic acute stroke admission were compared, unlike our study, prolongation in the hospital admission process and logistic delays in acute reperfusion treatments were found in the pandemic process, and the negative effects of the pandemic on acute stroke management were noted.[11] In a different study conducted in Canada, although no change was observed in the time from symptom onset to hospital admission, a prolongation was found in door to needle time and also in patients who underwent IV tPA and/or MT during the pandemic period.[12] In various studies, although the time from symptom onset to admission to the emergency department was found to be longer in the pandemic period compared to the pre-pandemic period, no difference was found between door to-CT time, door to needle time, and door to MT times. [13-15]

In a study conducted in 14 stroke centers in the USA, when the data of acute stroke patients before and during the pandemic were compared, the rate of IV tPA in the first 60 minutes during the pandemic period was found to be lower. It was observed that the delay was between imaging and bolus administration.[16] In a study conducted in 9 centers in the USA in which 676 acute stroke patients who underwent thrombolysis were evaluated, it was observed that there were delays in reperfusion treatments during COVID-19 compared to the pre-pandemic period.[17] In addition, there are studies in which acute ischemic stroke applications decreased during the pandemic period, the door to-needle time was prolonged during the pandemic period, and no change was observed in the door to-MT times.[18]

When the treatments applied to the patients are examined, the fact that IV tPA application to the cases in 2020 is higher than in 2019 and 2021, and IV tPA + MT application to the cases in 2020 is lower than in 2019 and 2021, which shows that interventional procedures were applied less in the pre-vaccination pandemic period. This result may be related to the fact that the number of patients transferred to our hospital from other centers during the pre-vaccination pandemic period may have decreased, and that radiological activities such as MT should be avoided except for the definite indications in the guidelines due to the risk of contamination. While some of the data from different centers show that there is a decrease in the patients treated with IV tPA

or MT during the pandemic period[19-21], some centers emphasize that the patients treated with reperfusion therapy have similar rates in the pre-pandemic and pandemic periods.[13,22-25]

In a retrospective study evaluating the data of 22 stroke centers in Italy, a significant decrease was found in stroke admissions during the pandemic period compared to the pre-pandemic period. While no change was observed in the rate of IV tPA administration during the pandemic period in the same study, a significant decrease was observed in the rate of patients who underwent thrombectomy, similar to our study. This is because; difficulty in providing the filtering and sterilization conditions of the rooms where interventional procedures are performed, the scarcity of endovascular surgeons who will perform the procedure, and the difficulty of transferring stroke patients to comprehensive stroke center due to the pandemic.[26,27]

In a multicenter study conducted in France, it was reported that there was a significant decrease in the rate of patients who underwent MT during the pandemic period, and that patients who were suitable for MT had a delay in transfer times to stroke centers that could perform thrombectomy within the therapeutic window.[27]

In a study of a private tertiary hospital, they found no significant change in the acute ischemic stroke care quality on the basis of in-hospital time-based measures: door-to-scan time, door-to-needle time, and door-to-groin time, between the pre-COVID-19 and COVID-19 periods.[28]

In a study comparing the first and second waves of the pandemic (June 1 - August 31, 2020 and June 1 - August 31, 2021), an improvement was found in the second wave between door-CT time and door-needle times. It was emphasized that time measurements in stroke care could be improved by reorganizing the system during unexpected global problems such as pandemics.[24]

Our study has some important limitations. The first is a retrospective study from a single center. The latter illustrates the effects of stroke treatment in an area severely affected by the pandemic and may not be representative of other areas where fewer cases of COVID-19 have been treated.

In conclusion, in our study, the number of patients presenting with acute stroke during the pandemic period was similar to other years and there was no significant difference in the time from the onset of the symptoms to the hospital admission according to years. This suggests that they do not delay their admission to the emergency department. Door to needle times, as well as the time taken by the neurologist to examine and initiate IV-tPA treatment, were found to be shorter in the pre-vaccination pandemic period than in the pre-pandemic and post-vaccination periods. These findings were interpreted as being due to reduced number of referral to the neurologists, in terms of coming to the emergency department, decrease in hospitalizations in wards and the cancellation of patient appointments in outpatient clinics during the pre-vaccination pandemic period.

As a result, although it was thought that acute stroke patients may delay their admission to the emergency department due to the risk of infection and that the pandemic may have negative effects on acute stroke management due to the reflection of the workload of COVID-19 patients on acute stroke. We found that there was no delay in treatment. It shows that this process is well managed in our hospital during the pandemic period. As acute stroke is a medical emergency and possibly carries a higher risk of death and disability than COVID-19, we must also warn and inform about the seriousness of medical emergency referrals and early intervention while warning about the pandemic. The strength of our study compared to other studies is that it included data covering the period after the start of vaccination for COVID-19, in addition to the data before the COVID-19 pandemic and during the pre-vaccination pandemic.

DISCLOSURE

Conflict of interest: None

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