RESEARCH ARTICLE / *Araştırma Makalesi*

Establishing a Stroke Center During the COVID-19 Pandemic: First-year Experiences

COVID-19 Pandemisi Sırasında İnme Merkezi Kurmak: İlk Yıl Deneyimleri

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Abstract

Objective	This study examines the data of patients of ischemic stroke who underwent intravenous thrombolytic therapy and/or mechanical thrombectomy a newly opened hospital in our country during the COVID-19 pandemic.
Materials and Methods	The files of 85 consecutive patients who were hospitalized in the Stroke Centre of Bursa City Hospital with a diagnosis of acute ischemic stroke between January and December 2020 who underwent intravenous thrombolytic therapy and/or mechanical thrombectomy were retrospectively reviewed.
Results	Symptom-to-door times (p<0.001) and symptom-to-recanalization/reperfusion times (p=0.005) were significantly higher in those referred from another hospital compared with those first admitted to our hospital. The modified Rankin scale score in the third month was significantly lower in the non-referred group than in the referred group (p=0.046). We found high age (p=0.032), high National Institutes of Health stroke scale/score at admission (p<0.001) and high symptom-to-recanalization time (p=0.046) were risk factors associated with bad outcomes.
Conclusion	This work contributes to the literature and provides reference data for new stroke centers that are candidates for service by sharing our first experiences with a newly established stroke center during the pandemic.
Keywords	Stroke Center; Pandemic; Experiences

Öz

Amaç	*Bu çalışmada, COVID-19 pandemisi sırasında ülkemizde yeni açılan bir hastanede intravenöz trombolitik tedavi ve/veya mekanik trombektomi uygulanan iskemik inmeli hastaların verilerinin incelenmesi amaçlandı.*
Gereç ve Yöntemler	*Ocak 2020-Aralık 2020 tarihleri arasında Bursa Şehir Hastanesi İnme Merkezi'nde akut iskemik inme tanısı ile yatırılan ve intravenöz trombolitik tedavi ve/veya mekanik trombektomi uygulanan ardışık 85 hastanın dosyaları retrospektif olarak incelendi.*
Bulgular	*Hastaların ilk semptomdan kapıya kadar geçen süre (p<0,001) ve semptom-rekanalizasyon/reperfüzyon süresi (p=0,005) başka bir hastaneden sevk edilen grupta, direkt olarak hastanemize başvuran gruba göre anlamlı olarak daha uzundu. 3. aydaki mRS skoru sevk edilmeyen grupta, sevk edilen gruba göre anlamlı derecede düşüktü (p=0.046). İleri yaşın (p=0,032), başvuruda yüksek NIHSS'un (p<0,001) ve semptomdan rekanalizasyona kadar geçen sürenin uzun olmasının (p=0,046) kötü sonuçla ilişkili olduğunu bulduk.*
Sonuç	*Pandemi sürecinde yeni kurulan bir inme merkezi olarak ilk deneyimlerimizi paylaşarak literatüre katkıda bulunmak ve hizmete aday yeni inme merkezleri için referans veri sağlamak istedik.*

INTRODUCTION

Stroke is a disease that exacerbates mortality and morbidity worldwide. The most common type of stroke is ischemic, which disrupts blood circulation to an area of the brain, resulting in neurological dysfunction. Regardless of the stroke type, the management of acute stroke treatment is highly time dependent.

Intravenous (IV) thrombolytic therapy and/or mechanical thrombectomy (MT) have been used in acute ischemic stroke treatments and have shown benefits to appropriate patients. Following the National Institute of Neurological Disorders and Stroke (NINDS) study, IV thrombolytic therapy was initially suggested for use within the first 3 h of stroke. Then, after the European Cooperative Acute Stroke Study (ECASS)-3 study was conducted in 2008, the recommendations arrived at a set time interval of 3–4.5 hours.[1,2] However, there is an outstanding need for more effective treatments, owing to the narrowness of the treatment window, the fact that it does not provide sufficient benefits for long-segment occlusions affecting proximal arteries. Today, endovascular stroke treatment in anterior circulation proximal vessel occlusions is recommended with a high level of evidence based on the results of nine randomized controlled studies. According to the results of studies published in recent years, the treatment window was extended up to 24 h in patients selected according to the results of multimodal imaging methods. Although treatment can be applied within the first 6 h, each 30-min delay in recanalization reduces functional recovery by 30%. Hence, rapid diagnosis, assistance, and transport are very important during the pre-hospitalization period. According to the most recent guidelines, a door-to-needle time of less than 60 min is targeted.[3]

Our study examined the data of patients having ischemic stroke who underwent IV thrombolytic therapy and/or MT after applying to the emergency department of a newly opened hospital in our country. We also compared the clinical results of patients who had applied directly to our center to those who had been transferred from an external institution, owing to the new center's regional referral status, to evaluate whether the transfer from another center had caused irreparable delays in acute stroke management.

MATERIALS and METHODS

The files of 85 consecutive patients who were hospitalized at the Stroke Centre of Bursa City Hospital with a diagnosis of acute ischemic stroke between January and December 2020 who underwent IV thrombolytic therapy and/or MT were retrospectively reviewed. Other ischemic stroke patients were excluded. The hospital began accepting patients in July 2019, whereas the stroke center was functional by December 2019.

Patient complaints, demographics, risk factors, Alberta Stroke Program Early Computed Tomography (ASPECT) scores on cranial computed tomography (CT), National Institutes of Health Stroke Scale (NIHSS) scores at admission, and modified Rankin Scale (mRS) scores at discharge and at 90 days–third month were recorded. Additionally, information concerning treatment-related complications and time periods of admittance within the day (24-h time format, 07:00–15:00, 15:00–23:00, 23:00–07:00), the time from symptom onset to hospital admission (symptom–door time), and the time between hospital admission to the initiation of reperfusion treatment (IV thrombolytic and/or MT) (e.g., door-to-needle time, door-to-groin puncture time) were retrospectively reviewed and analyzed from medical files.

The patients were divided into three groups with respect to the treatment modalities applied: IV thrombolytic therapy, MT, and combined therapy. Cranial CT, diffusion magnetic resonance (MR) imaging, cranial CT angiography, and/or MR angiography findings of the patients were recorded. An mRS score of <2 was considered to be a good result. Additionally, patients who applied directly to our hospital and those transferred from other centers were compared. The identification of hemorrhages causing clinical worsen-

ing on cranial CTs after treatment was defined as a symptomatic intracranial hemorrhage.

Ethics committee approval was obtained from Bursa City Hospital Ethics Committee with the decision number 2021-7/3, and informed consent was obtained from all patients or their legal heirs before the procedure, carried out in accordance with the principles of the Helsinki Declaration.

Statistical Analysis

All analyses were performed using SPSS v21 (SPSS Inc., Chicago, IL, USA). For the normality check, the Shapiro–Wilk test was used. Data were given as mean±standard deviation or median (minimum–maximum) for continuous variables according to normality of distribution and frequency (percentage) for categorical variables. Normally, distributed variables were analyzed with the independent samples t-test. Non-normal distributed variables were analyzed with the Mann–Whitney U test. The distribution of categorical variables was analyzed using the Pearson chi-square or Fisher's exact tests. Repeated measurements were compared via the Wilcoxon Signed Ranks test for ordinal data or the McNemar test for nominal data. Multiple logistic regression analysis (forward conditional method) was performed to determine significant risk factors of bad outcomes (≥2 mRS score). The statistical significance value was accepted as $p<0.05$.

RESULTS

We included 85 patients (43 males and 42 females) in our study; the mean age was 67.36±13.03 (range 32–95) years. The most common time interval at admission was the 15:00–23:00 time period (Table 1).

Table 1. Summary of patients' characteristics

Age (years), mean ±SD	67.36 ± 13.03
Gender, n (%)	
Male	43 (50.59)
Female	42 (49.41)
Heart diseases, n (%)	39 (45.88)
Diabetes mellitus, n (%)	22 (25.88)
CVA history, n (%)	12 (14.12)
TIA history, n (%)	5 (5.88)
Hypertension, n (%)	54 (63.53)
Hyperlipidemia, n (%)	13 (15.29)
Smoking, n (%)	19 (22.35)
Alcohol, n (%)	4 (4.71)
Type of admission, n (%)	
Referred from another hospital	40 (47.06)
Directly to our hospital	45 (52.94)
Time period at admission, n (%)	
07:00 - 15:00	31 (36.47)
15:00 - 23:00	39 (45.88)
23:00 - 07:00	15 (17.65)
NIHSS at admission,	14 (4 - 26)
Symptom-to-door time (min), median (min., max.)	120 (20 - 360)
Door-to-recanalization time (min)), median (min., max.)	90 (12 - 350)
Symptom-to-recanalization time (min)), median (min., max.)	201 (60 - 450)
Door-to-needle time(min)), median (min., max.)	80 (20 - 270)
Door-to-groin time (min)), median (min., max.)	107.5 (28 - 350)
Hemorrhage, n (%)	17 (20.00)
Symptomatic	4 (4.71)
Asymptomatic	13 (15.29)
Modified Rankin Scale, median (min.-max.)	
Discharge	5 (0 - 6)
3rd month	4 (0 - 6)
Modified Rankin Scale (Discharge), n (%)	
Good outcome (< 2)	17 (20)
Bad outcome (≥ 2)	68 (80)
Modified Rankin Scale (3rd month), n (%)	
Good outcome (< 2)	26 (30.59)
Bad outcome (≥ 2)	59 (69.41)
Mortality, n (%)	
Before discharge	20 (23.53)
3rd month	29 (34.12)

SD: Standard deviation, TIA: Transient ischemic attack, CVA: Cerebrovascular accident
Data are given as mean ± standard deviation or median (minimum - maximum) for continuous variables according to normality of distribution and as frequency (percentage) for categorical variables

We divided patients into two groups according to their first admission. Symptom-to-door time (p<0.001) and symptom-to-recanalization/reperfusion time (p=0.005) were significantly higher in those referred from another hospital compared with those first admitted to ours. Door-to-recanalization time was significantly higher in those directly applying to our hospital compared with referred patients (p<0.001). There was no significant difference between groups with regard to mRS score at discharge (p=0.478), but the mRS score in the third month was significantly lower in the non-referred group than in the referred group (p=0.046). There was no significant difference between the discharge and third-month mRS scores in the referred group (p=0.227), whereas the third-month mRS score was significantly lower than the discharge mRS score in the non-referred group (p=0.001). However, the difference in the increase of mortal cases was found to be significantly higher in the referred group (p=0.016) (Table 2, Figure 1,2).

We performed multiple logistic regression analysis to determine the significant factors of bad outcomes (mRS score ≥2). We found that high age (p=0.032), high NIHSS at admission (p<0.001), and high symptom-to-recanalization time (p=0.046) were risk factors associated with bad outcomes. Other variables included in the model, such as admission type (p=0.615), gender (p=0.164), symptom-to-door time (p=0.229), door-to-recanalization time (p=0.337), treatment (p=0.719), and hemorrhage after treatment (p=0.287), were found to be insignificant (Table 3).

Table 2. Summary of patients' characteristics with regard to groups

		Admission		
		Referred (n=40)	Non-referred (n=45)	
Age		68.52 ± 13.08	66.33 ± 13.04	0.442
Gender	Male	17 (42.50%)	26 (57.78%)	0.234
	Female	23 (57.50%)	19 (42.22%)	
Time at admission	07:00 - 15:00	14 (35.00%)	17 (37.78%)	0.732
	15:00 - 23:00	20 (50.00%)	19 (42.22%)	
	23:00 - 07:00	6 (15.00%)	9 (20.00%)	
NIHSS at admission		14 (7 - 26)	12 (4 - 24)	0.491
Symptom-to-door time, min		160 (60 - 360)	60 (20 - 240)	<0.001
Door-to-recanalization/reperfusion time, min		60 (12 - 240)	110 (30 - 350)	<0.001
Symptom-to-recanalization/reperfusion time, min		210 (117 - 450)	180 (60 - 350)	0.005
Hemorrhage		10 (25.00%)	7 (15.56%)	0.415
Symptomatic		3 (7.50%)	1 (2.22%)	0.421
Asymptomatic		7 (17.50%)	6 (13.33%)	
Modified Rankin Scale	Discharge	5 (0 - 6)	5 (0 - 6)	0.478
	3rd month	4 (0 - 6)	3 (0 - 6)	0.046
p (within variables)		0.227	0.001	
Mortality	Before discharge	10 (25.00%)	10 (22.22%)	0.964
	3rd month	17 (42.50%)	12 (26.67%)	0.191
	p (within variables)	0.016	0.500	

Data are given as mean ± standard deviation or median (minimum - maximum) for continuous variables according to normality of distribution and as frequency (percentage) for categorical variables

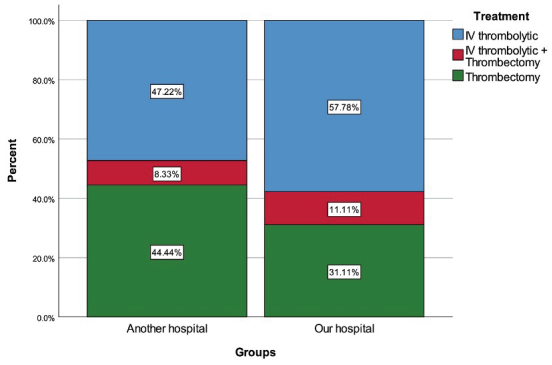

Figure 1. Distribution of treatments with regard to groups

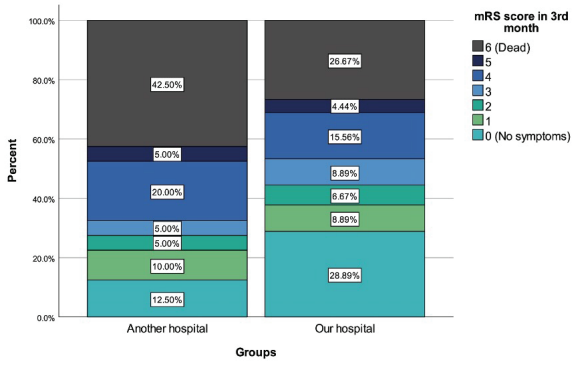

Figure 2. mRS scores at the 3rd month with regard to groups

Table 3. Significant factors of the bad outcome, multiple logistic regression analysis

	β coefficient	Standard Error	p	Exp(β)	95.0% CI for Exp(β)	
Age	0.052	0.024	0.032	1.054	1.005	1.106
NIHSS at admission	0.344	0.089	<0.001	1.411	1.184	1.681
Symptom-to-recanalization/reperfusion time	0.012	0.006	0.046	1.012	1.000	1.024
Constant	-9.204	2.552	<0.001	0.000		

Dependent Variable: Bad outcome (≥ 2 mRS score) in 3rd month. Nagelkerke R2=0.516; Correct prediction=81.18%
CI: Confidence Interval

DISCUSSION

The most important goal for clinical success in patients with acute ischemic stroke is to shorten the time until treatment. It has been reported that approximately 2M neurons and 14B synapses are lost every minute until reperfusion is achieved.[4] Although the treatment window is currently recommended to be 4.5 h with IV thrombolytic therapy and 6 h with anterior system MT, it is important to administer the treatment as early as possible. With this rule in mind, it is recommended that stroke patients be identified as early as possible during emergency services and that the door-to-needle time should not exceed 60 min.[3] In our study, the mean door-to-needle time in patients admitted to our hospital was 80 min, and the door-to-groin time was 107.5 min. The most important factors of the increase during this period include the fact that we were a newly established center, and the delays in the diagnosis stage were caused by the intensity caused by the pandemic.

Studies have shown that prolonged symptom-to-door or symptom-to-needle durations are associated with poor prognoses. It has also been reported that advanced age and high NIHSS at admission are associated with poor prognoses in patients undergoing reperfusion therapy.[5-9] Our study findings were similar to those in the extant literature, advanced age, high NIHSS at admission, and high symptom-to-recanalization time were found to be associated with poor prognoses (mRS score ≥2).

In a nationwide study in the Netherlands, it was reported that patients transferred from other hospitals to a comprehensive stroke center for endovascular thrombectomy experienced delays in treatment that worsened functional outcomes in patients.[10] In our study, nearly half of the patients who underwent reperfusion therapy were trans-

ferred from other centers. The mRS scores at the third month were higher in patients transferred from other hospitals. Symptom-to-door and symptom-to-reperfusion times were longer in patients transferred from other hospitals. Interestingly, reperfusion therapy was started after a longer time in patients who applied directly to our hospital (non-referred). Previous studies have shown that there is an inverse relationship between symptom-to-door and door-to-needle times, and it has been reported that patients who reach the hospital early have a longer door-to-needle time.[11,12] In our study, regarding patients transferred from other hospitals, there may have been a few primary factors that shortened door-to-needle times, including referrals of the patient after informing family for consent and those receiving accurate medical information from emergency medical services concerning the patient, those being prepared for the patient at arrival, and the fact that cranial imaging could be ordered at the first-admitting institution before transfer.

In the study of Reuter et al., it was reported that approximately 10% of acute ischemic stroke patients with the potential to undergo MT were admitted to the hospital at night (23:00–06:59).[13] In our study, 17.65% of patients who underwent reperfusion therapy were admitted to the hospital between 23:00 and 07:00. Considering the rate and number of patients, it can be suggested that patients who are likely to receive reperfusion therapy in our city, which has two stroke centers, may be alternately accepted by these centers at night (between 23:00 and 07:00). Therefore, the coordination of the provincial ambulance control command center can be effective with regard to the swiftness of treatment at both centers.

In a nationwide study in Germany, it was reported that the number of patients who received IV thrombolytic therapy in stroke units in 2019 was approximately 2.5 times the number of patients who underwent MT (IV thrombolytic therapy: 36,745, MT: 16,135 patients).[14] According to another study conducted in Italy, it was reported that 33% of all acute ischemic stroke patients could be suitable for IV thrombolytic therapy, 22% for IV thrombolytic therapy and MT, and 4% for MT.[15] In our study, 44 (52%) patients underwent IV thrombolytic therapy, 11 (13%) patients underwent IV thrombolytic therapy and MT, and 30 (35.2%) underwent mechanical thrombectomy. The high number of patients who underwent MT was caused by the high rate of large and proximal vessel occlusions and the fact that patients reached the hospital from an external center within a time interval of 4.5–6 h, which was suitable for MT.

In studies published in our country, data were mostly provided with regard to the thrombolytic therapy experiences of hospitals.[16,17] In a meta-analysis examining 2,349 cases related to thrombolytic therapy applications published in the past 10 years in our country, thrombolytic-related symptomatic hemorrhage was reported to occur in 5.6% of patients.[18] In our study, symptomatic hemorrhage was 4.3% in patients who received IV thrombolytic therapy. In the pool analysis that included NINDS rt-PA, ECASS, ECASS II, and ATLANTIS studies, it is understood that those who received treatment in the early period had a higher chance of recovery.[19] According to our experience, the clinical response was more satisfactory among patients to whom treatment was initiated within the first 3 h.

In developed countries, IV thrombolytic therapy is generally initiated in the primary stroke center, and patients who require MT are referred to a comprehensive stroke center; whereas, in our province, patients are referred directly to a comprehensive stroke center for both IV thrombolytic therapy and MT. Initiating IV thrombolytic therapy with the "drip and ship" method in capable hospitals and referring patients to a comprehensive stroke center may preserve times for these patients. The transfer of patients who can be treated with reperfusion directly to a hospital with an established stroke center by emergency medical services can also shorten the time until treatment.

Limitations

The most critical limitation of our study is that it was a single-center and retrospective study. Furthermore, our hospital was designated as a pandemic hospital by the Health Ministry after March 2020. This situation affected the arrival rates of stroke cases to the hospital and the durations of their diagnosis.

CONCLUSION

We strove to contribute to the literature and provide reference data for new stroke centers that are candidates for service by sharing our early experiences with recanalization treatments applied by our hospital, which was a newly established stroke center during the pandemic.

Conflict of interest statement

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Authors' Contributions

C.H., B.A., M.İ., S.B.: conceptualization, data collection, and writing, statistical analysis, and writing;
N.T., Y.Y., Ç.Ç., H.B., T.T., A.E., Ş.F., Ü.E., M.A.B., A.M., B.H.: conceptualization, data collection, supervision, and writing

Ethics committee approval

Ethics committee approval was obtained from Bursa City Hospital Ethics Committee with the decision number 2021-7/3.

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