İnme Alt Gruplarında Diurnal Varyasyonun Değerlendirilmesi; Bir Üniversite Hastanesinin Deneyimleri

Evaluation of Diurnal Variation in Stroke Subtypes; Experiences of a University Hospital

İbrahim Çaltekin[1], Erdal Demirtaş[2]
1Yozgat Bozok Üniversitesi Tıp Fakültesi, Acil Tıp Kliniği, Yozgat, Türkiye
2Cumhuriyet Üniversitesi Tıp Fakültesi, Acil Tıp Kliniği, Sivas, Türkiye

ÖZ

GİRİŞ ve AMAÇ: *Bu çalışmada inme alt tiplerinde diurnal varyasyonun uyku ve uyanıklık dönemi, aylık ve mevsimsel değişimler ile korelasyonu olup olmadığını incelemeyi amaçladık.*

YÖNTEM ve GEREÇLER: *İnme tanısı alarak takip ve tedavisi yapılan 18 yaş üstü tüm hastalar çalışmamıza dahil edilmiştir ve retrospektif olarak değerlendirilmiştir. İnme alt tipleri Oxfordshire Community Stroke Project (OCSP) sınıflandırmasına göre değerlendirilmiş ve hastaların kliniklerine göre; total anterior sirkülasyon infarktı (TASİ), posterior sirkülasyon infarktı (POSİ), parsiyel anterior sirkülasyon infarktı (PASİ), laküner infarkt (LAİ) grupları oluşturulmuştur. Ayrıca bu yapılan sınıflandırmaya göre hangi anatomik bölgenin tutulumu olduğu difüzyon ağırlıklı beyin manyetik rezonans görüntüleme sonuçlarından teyit edilmiştir. Hangi diurnal döngüde hangi grubun daha fazla etkilenim gösterdiği de tespit edilmiştir.*

BULGULAR: *Uyku ve uyanıklık periyodları incelendiğinde; TASİ grubunda bulunan hastaların, POSİ ve LAİ gruplarındaki hastalara göre uyku dönemde başvuru oranlarının daha sık olduğu tespit edildi ve bu durum istatistiksel olarak anlamlı bulundu (p=0.045). Diğer grupların arasında herhangi bir istatistiksel anlamlı farklılık bulunmadı (p>0.05). Mevsimsel değişkenler incelendiğinde ise yine gruplar arasında istatistiksel olarak anlamlı bir fark tespit edilmedi (p>0.05). Ancak sonbahar ve kış döneminde yüzde olarak başvurularda bir artış olduğu saptandı.*

TARTIŞMA ve SONUÇ: *Genellikle daha ciddi bir tutulumun ve daha ciddi morbiditenin gözlendiği TASİ grubunda, POSİ ve LAİ guplarındaki hastalara göre inme gelişiminin uyku döneminde daha sık gerçekleştiği tespit edilmiştir..*

Anahtar Kelimeler: *diurnal varyasyon, inme, acil servis*

ABSTRACT

INTRODUCTION: *In this study, we aimed to investigate whether the diurnal variation of stroke subtypes is correlated with the asleep and awake periods and monthly and seasonal changes.*

METHODS: *All patients over the age of 18 who were diagnosed with a stroke, treated, and followed up were included in our study and evaluated retrospectively. Stroke subtypes were evaluated according to Oxfordshire Community Stroke Project (OCSP) classification and grouped as total anterior circulation infarction (TACI), posterior circulation infarction (POCI), partial anterior circulation infarction (PACI), lacunar infarction (LACI) according to the patients' clinics. In addition, according to this classification, the anatomic location of the involvement was confirmed from the results of diffusion-weighted brain magnetic resonance imaging. It was also determined which group was more affected in which diurnal cycle.*

RESULTS: *When asleep and awake periods were examined, it was found to be statistically significant that the patients in the TACI group had more frequent hospital admission rates in the sleep period than the patients in the POCI and LACI groups (p=0.045). There was no statistically significant difference between the other groups (p>0.05). When the seasonal variables were examined, no statistically significant difference was found between the groups (p>0.05). However, there was an increase in the percentage of hospital admissions in the autumn and winter.*

DISCUSSION AND CONCLUSION: *It was determined that stroke development was more frequent during the asleep period in the patients in the TACI group, which usually had more serious involvement and more serious morbidity, than the patients in the POCI and LACI groups.*

Keywords: *diurnal variation, stroke, emergency medicine*

İletişim / Correspondence:
Dr.Öğrt.Üyesi İbrahim Çaltekin
Acil Tıp Kliniği, Yozgat Bozok Üniversitesi Tıp Fakültesi, Yozgat, Türkiye,
E-mail: drcaltekin@gmail.com
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INTRODUCTION

Ischemic stroke is defined as the disruption of blood flow and feeding of the brain as a result of an obstruction in an artery of the brain (1). Moreover, stroke is one of the most serious causes of morbidity, causing disability (2). When all of the reasons for mortality are examined, stroke is the second most common reason after cardiovascular causes. As the patient age increases, there is an increase in the emergency department admissions which may result in mortality (3).

Changes in hormonal status, catecholaminergic system, sympathetic nerve activity, and basal metabolism develop as a result of diurnal variation (4). It is known that diurnal variation, which also includes periods of sleeping and waking, makes changes in the frequency of stroke development just like in cardiovascular and endocrine events. It is also known that there is an increase in the frequency of stroke development in the patients during morning hours (5).

The effect of diurnal variation of stroke patients on asleep and awake periods or morning and night periods has been investigated in many studies (6, 7). However, it is not clear whether stroke subtypes are affected or how often they are affected. In this study, we aimed to investigate whether the diurnal variation of the stroke subtypes is correlated with asleep and awake periods and monthly and seasonal changes.

METHODS

This study was performed between 01.01.2018-01.01.2019 in the Emergency Department of Bozok University Faculty of Medicine, which is a tertiary health care institution where all the stroke patients, including those who received thrombolytic therapy, were accepted. Patients admitted with a stroke clinic were evaluated retrospectively. The study was approved by the local institutional ethics committee.

All patients over the age of 18 who were diagnosed with a stroke, treated and followed up were included in our study. The symptom onset time of the patients was divided into 2 subgroups (asleep: 00.00-06:59, awake: 07:00-23:59) using the 24-hour daily time zone asleep and awake period, which was obtained from the file records and it showed a diurnal variation. Monthly and seasonal changes at the time of hospital admission were also evaluated. Stroke types are divided into groups in various classifications and clinically Oxfordshire Community Stroke Project (OCSP) classification was used in our study. The stroke subtypes of the patients were evaluated according to OCSP classification and total anterior circulation infarction (TACI), posterior circulation infarction (POCI), partial anterior circulation infarction (PACI), lacunar infarction (LACI) groups were formed (8, 9). In addition, the anatomic location of the involvement according to this classification was confirmed from the results of the diffusion-weighted image (DWI) of the brain magnetic resonance imaging (MRI). It was also determined which group was more affected in which diurnal cycle. Additional diseases as hypertension (HT), diabetes mellitus (DM), hyperlipidemia (HL), and atrial fibrillation (AF) have been identified in these subtypes which could develop simultaneously in some cases. A blood pressure of 140/90 mmHg and above or chronic drug intake for HT, a blood sugar before fasting that is greater than 126 mg/dL, a blood sugar greater than 200 mg/dl at any time, or HbA1c $\geq$ 6.5% for DM, total cholesterol > 200 mg/dl, LDL > 160 mg/dl values for HL, detecting AF rhythm on electrocardiography (ECG) or 24-hour Holter follow-up for AF, were used to identify the presence of additional diseases.

The patients whose records of sleep periods during the onset of symptoms could not be identified or were unknown were excluded from the study. Furthermore, the patients whose clinical, examination, and imaging results were missing or file records could not be reached, were also excluded from the evaluation. The patients with hemorrhagic stroke, subarachnoid hemorrhage or intracranial mass were also excluded.

Statistical Analysis

Statistical analysis was performed using SPSS (version 20, SPSS, Chicago, IL). The data were expressed as mean ± SD and in percentile. The distribution of the variable data was determined using visual (histograms, probability plots) and analytical methods (Kolmogorov-Smirnov/Shapiro-Wilk's test). The Mann-Whitney U test was utilized for the non-parametric numerical data while the Student t-test was adopted for the parametric numerical data. Categorical data were compared through the use of Chi-square test or Fisher's exact tests. The significance between the OCSP

classification groups was evaluated by using post-hoc comparison test. A p-value of less than 0.05 was considered significant.

RESULTS

A total of 130 patients, 72 (55.4%) males and 58 (44.6%) females with stroke, were included in the study. The mean age of the patients was 71.75 ± 11.24, and the mean age by gender was 69.86 ± 11.67 in male patients and 74.1 ± 10.3 in female patients. Fifteen (11.5%) patients were admitted in the asleep period (00:00-06:59) and 115 (88.5%) patients were admitted in the awake period (07:00-23:59). It was found that there were 30 (23.1%) hospital admissions in the winter, 27 (20.8%) admissions in the spring, 29 (22.3%) admissions in the summer, and 44 (33.8%) admissions in the autumn. When OCSP groups were evaluated; 33 (25.4%) patients were in the TACI group, 23 (17.7%) were in the POCI group, 47 (36.2%) were in the PACI group and 27 (20.8%) were in the LACI group (Table 1).

Table 1. Variables of the study

			Mean±Standart deviation	
age			71,75±11,24	
gender	**male**	**age**	69,86±11,67	
	female	**age**	74,1±10,3	
			count	**%**
gender	**men**		72	55,4%
	women		58	44,6%
hour	**00:00-06:59 (asleep period)**		15	11,5%
	07:00-00:00 (awake period)		115	88,5%
month	**january**		8	6,2%
	february		7	5,4%
	march		8	6,2%
	april		7	5,4%
	may		12	9,2%
	june		7	5,4%
	july		9	6,9%
	august		13	10,0%
	september		15	11,5%
	october		14	10,8%
	november		15	11,5%
	december		15	11,5%
season	**winter**		30	23,1%
	spring		27	20,8%
	summer		29	22,3%
	autumn		44	33,8%
OCSP	**TACI**		33	25,4%
	POCI		23	17,7%
	PACI		47	36,2%
	LACI		27	20,8%

OCSP (Oxfordshire Community Stroke Project)
TACI(total anterior circulation infarctions); POCI(posterior circulation infarctions); PACI(partial anterior circulation infarctions); LACI(lacunar infarction)

Moreover, when asleep and awake periods were examined, it was found to be statistically significant that the patients in the TACI group had more frequent hospital admission rates in the asleep period than the patients in the POCI and LACI groups (p=0.045). There was no statistically significant difference between the other groups (p>0.05) (Table 2) (figure 1). When the seasonal variables were examined, no statistically significant difference was found between the groups (p>0.05). However, there was an increase in the percentage of hospital admissions in the autumn and winter.

Table 2. Statistical evaluation of asleep awake status according to OCSP classification

	OCSP								p
	TACI		POCI		PACI		LACI		
00:00-06:59	8	24,2%[b,c]	1	4,3%[a]	5	10,6%	1	3,7%[a]	**0.045**
07:00-23:59	25	75,8%	22	95,7%	42	89,4%	26	96,3%	

OCSP (Oxfordshire Community Stroke Project)
TACI(total anterior circulation infarction); POCI(posterior circulation infarction); PACI(partial anterior circulation infarction); LACI(lacunar infarction)
**Chi-Squre Test.*
aThere was a significant difference with compared TACI in post-hoc comparison.
bThere was a significant difference with compared POCI in post-hoc comparison.
cThere was a significant difference with compared LACI in post-hoc comparison.
**p values with statistical significance (p < 0.05) are shown in bold*

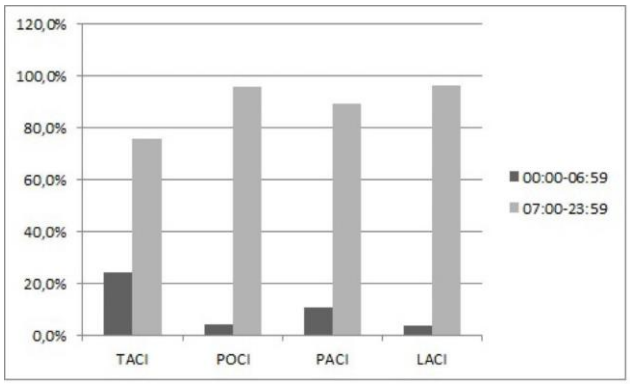

Figure 1. The evaluation of the symptom onset time according to the OCSP classification

When additional diseases of the patients were examined, some of them were found simultaneously, and HT in 22 patients, DM in 13 patients, HL in 13 patients, AF in 11 patients, were found in TACI group; HT in 14 patients, DM in 10 patients, HL in 4 patients, AF in 4 patients were found in POCI group; HT in 34 patients, DM in 18 patients, HL in 8 patients, AF in 4 patients, were found in PACI group; HT in 18 patients, DM in 6 patients, HL in 5 patients, and AF in 4 patients, were found in LACI group (Table 3).

Table 3. Chronic diseases of the OCSP classification groups

Chronic Disease	OCSP								
	TACI		POCI		PACI		LACI		
	Count(%)		Count(%)		Count(%)		Count(%)		total
HT	22	84,6%	14	77,8%	34	89,5%	18	85,7%	88
DM	1	3,8%	3	16,7%	4	10,5%	2	9,5%	10
HL	1	3,8%	0	0,0%	0	0,0%	1	4,8%	2
AF	2	7,7%	1	5,6%	0	0,0%	0	0,0%	3
HT	0	0,0%	0	0,0%	0	0,0%	0	0,0%	
DM	12	60,0%	7	58,3%	14	73,7%	4	40,0%	37
HL	4	20,0%	2	16,7%	3	15,8%	2	20,0%	11
AF	4	20,0%	3	25,0%	2	10,5%	4	40,0%	13
HT	0	0,0%	0	0,0%	0	0,0%	0	0,0%	
DM	0	0,0%	0	0,0%	0	0,0%	0	0,0%	
HL	8	80,0%	2	66,7%	5	71,4%	2	100,0%	17
AF	2	20,0%	1	33,3%	2	28,6%	0	0,0%	5
HT	0	0,0%	0	0,0%	0	0,0%	0	0,0%	
DM	0	0,0%	0	0,0%	0	0,0%	0	0,0%	
HL	0	0,0%	0	0,0%	0	0,0%	0	0,0%	
AF	3	100,0%	0	0,0%	0	0,0%	0	0,0%	3

OCSP (Oxfordshire Community Stroke Project)
TACI(total anterior circulation infarctions); POCI(posterior circulation infarctions); PACI(partial anterior circulation infarctions); LACI(lacunar infarction)
HT(Hypertension); DM(Diabetes Mellitus); HL(Hyperlipidemia);AF(Atrial Fibrillation)

DISCUSSION

Just like cardiovascular events, stroke events show diurnal variation over 24 hours. It has been reported in many studies that ischemic stroke patients have an increased peak once in the morning and a second in the evening. (1). In another study, the incidence of stroke was found to be highest between the times of 06:00-12:00 (10). Similarly, in our study, when all of the stroke patients were examined, it was seen that 88.5% of the admissions were between 07:00-23:59 hours.

The stroke types are divided into three main groups as ischemic, hemorrhagic, and subarachnoid hemorrhage (11). However, it is known that this classification has very serious diurnal differences (12). Therefore, the analysis of the subgroups in the OCSP classification of ischemic stroke showed more homogeneous results (8). Ripamonti et al. compared the asleep and awake periods with Trial of ORG 10172 in Acute Stroke Treatment (TOAST) classification in their study and determined a higher frequency of all subtypes in the asleep period (13). According to our OCSP classification subgroup analysis; stroke development was more frequent in the TACI group during the asleep period than in the POCI and LACI groups.

Decreased cerebral perfusion, which plays a role in the development of vasovagal syncope, increases significantly in the early morning hours and this circadian pattern also plays a significant role in the development of ischemic stroke (5, 14, 15). When our subgroups were examined; the fact that most of the cases occurred during the awake period, including this period of early morning times, can be considered as a result of this mechanism.

Stroke development is affected by external factors such as physical activity, immobilization,

feeding habits, and stress (16-18). In addition to these external factors, changes in the week cycle or climate are reported as factors. It is reported that the risk of stroke development increases both in the first and the last days of the week and in the months when the temperature decreases (19, 20). In our study, monthly and seasonal analyzes were performed and it was found that the admissions were significantly higher in the autumn and the winter months when the weather was cold.

However, HT, DM, HL, smoking, a history of stroke, antiplatelet, or anticoagulant drug use were identified as independent risk factors for stroke (21). In our study, a high rate of co-morbidities was found in the stroke subtypes, including some of these risk factors simultaneously. This has been shown once again that these independent risk factors increase stroke frequency and tendency.

There are some limitations to our study. The most important limitation is that our study was performed in a single-center and it was designed retrospectively. Another limitation is the fact that the onset of symptoms and the obtained data were dependent on the anamnesis and the file records. Similar prospective studies are needed such as this one in this regard.

CONCLUSION

To our knowledge, this is one of the few studies that analyzed stroke subgroups according to the OCSP classification of diurnal variation. It was determined that stroke development was more frequent during the asleep period in the patients in the TACI group, which usually had more serious involvement and more serious morbidity, than the patients in the POCI and LACI groups.

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