

ORIGINAL ARTICLE

ÖZGÜN ARAŞTIRMA

NON-MOTOR SYMPTOMS IN STROKE PATIENTS

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ABSTRACT

INTRODUCTION: Recognition of any symptoms that may develop after stroke improves the quality of life of the patient and their relatives and is associated with a good prognosis. In our study, we aimed to investigate the frequency and characteristics of non-motor symptoms in post-stroke patients.

METHODS: Patients who had a stroke in the last 1 year and recovered well or with mild disability (mRS 0-2) and healthy volunteers as the control group were included in our study. The "Turkish Version of the Non-Motor Symptoms Scale" (NMSÖ-TR) questionnaire consisting of 30 questions was applied to the subjects who met the inclusion criteria, and the results were compared between the two groups.

RESULTS: In our study in which 54 stroke and 116 healthy volunteers were evaluated, the mean age of the stroke group was 59 (36-86) and 39 patients (72.2%) were women. In healthy volunteers, the mean age was 53 (24-77) and 61 (52.6%) were female. The mean NMSS scores were 6 (1-24) in the stroke group and 9 (0-24) in healthy volunteers, and no significant difference was found between the two groups. The most common non-motor symptoms in the stroke group were nocturia (67%), urinary urgency (48%), feeling sad (48%), incomplete bowel emptying (39%), amnesia (37%), Decreased/increased libido (37%), problems with sex (37%). Statistically significant dysphagia (31.5%, p: 0.011) and unpleasant sensation in your legs at night/craving to move (50%, p: 0.041) were detected more frequently in the stroke group.

DISCUSSION AND CONCLUSION: Post-stroke non-motor symptoms can be observed frequently, even if patients show a good recovery process. The treatment process to be guided by the early detection of these symptoms in the rehabilitation process is important for an increase in the quality of life and a better prognosis.

Keywords: Stroke, non-motor symptoms, life quality.

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İNME HASTALARINDA NON-MOTOR SEMPTOMLAR

ÖZ

GİRİŞ ve AMAÇ: İnme sonrası gelişebilecek her türlü semptomun tanınması, hasta ve yakınların yaşam kalitesini artırır ve iyi prognozla ilişkilidir. Biz de çalışmamızda inme sonrası hastalardaki non-motor semptomların sıklığını ve özelliklerini araştırmayı amaçladık.

YÖNTEM ve GEREÇLER: Çalışmamıza son 1 yıl içinde inme geçiren, iyi veya hafif engelle (mRS 0-2) iyileşen hastalar ve kontrol grubu olarak sağlıklı gönüllüler alındı. Çalışmaya alınma kriterlerini karşılayan olgulara 30 sorudan oluşan "Non-Motor Semptomlar Ölçeği Türkçe Versiyonu" (NMSÖ-TR) anketi uygulandı ve sonuçlar iki grup arasında karşılaştırıldı.

BULGULAR: 54 inme ve 116 sağlıklı gönüllünün değerlendirildiği çalışmamızda inme grubunda ortalama yaş 59 (36-86) ve 39 hasta kadındı (%72.2). Sağlıklı gönüllülerde ise ortalama yaş 53 (24-77) ve 61 olgu (%52.6) kadındı. NMSÖ skor ortalamaları inme grubunda 6 (1-24), sağlıklı gönüllülerde 9 (0-24) olup, her iki grup arasında anlamlı farklılık saptanmadı. İnme grubunda en sık gözlenen non-motor semptomlar noktüri (%67), idrara sıkışma (%48), üzgün hissetme (%48), bağırsakların tam boşalamaması (%39), unutkanlık (%37), cinsel istekte azalma/artma (%37), cinsel ilişkiye girmekte zorluktu (%37). İnme grubunda istatistiksel olarak anlamlı derecede disfaji (%31.5, p: 0,011), geceleri bacaklarınızda hoş olmayan duyu hissi/hareket isteği (%50, p: 0,041) daha sık saptandı.

TARTIŞMA ve SONUÇ: İnme sonrası non-motor semptomlar hastalar iyi iyileşme süreci sergileseler bile sıklıkla izlenebilmektedir. Rehabilitasyon sürecinde bu semptomların erken tespiti ile yön verilecek tedavi süreci hayat kalitesinde artış ve daha iyi prognoz için önemlidir.

Anahtar Sözcükler: İnme, non-motor semptomlar, hayat kalitesi.

INTRODUCTION

Annually, more than 12 million people worldwide suffer a stroke. 68% of affected individuals are under the age of 70. Globally, over 101 million people currently living are estimated to have experienced stroke (1). In line with these data, stroke is the second leading cause of death and a major cause of disability worldwide (2). Post-stroke symptoms negatively affect the quality of life of both patients (3) and caregivers (4). In this regard, a rehabilitation process to be guided by the identification of any post-stroke symptoms can directly improve the quality of life of the patient and the patient relatives.

Post-stroke symptoms can be classified as motor and non-motor (pain, mood, sleep, sexual dysfunction, and symptoms related to the gastrointestinal, urinary, and cardiovascular systems). Post-stroke motor and sensory symptoms constitute the most common complaints by patients (5). Scales developed for diagnosing stroke based on the easy identification of motor symptoms, such as FAST (Face-Arm-Speech-Time), can be shown as an example in this regard (6). Contrary to the focus on motor symptoms, non-motor symptoms (NMS) are often likely to be underdiagnosed or untreated for reasons such as aphasia, neglect, or cognitive impairment. A study evaluating pain in stroke patients reported that more than half of the patients had pain and more than one-third did not

receive treatment, among which more than two-thirds experienced central pain (7).

Among psychiatric complaints, post-stroke depression constitutes one of the most common NMS, occurring in one-third of stroke patients (8). Post-stroke depression is accompanied by anxiety in 39% of female patients and 26% of male patients (9). Dysphagia, associated with an increased risk of aspiration after stroke and stroke-associated mortality, can be observed in half of the patients (10). In addition, constipation can be seen at a rate of 48% (11), sexual dysfunction at 55% (12), sleep disorders at 78% (13), urinary system dysfunction (most commonly nocturia) at 94% (14), left-sided heart failure as a cardiovascular complication secondary to autonomic involvement at 31% (15), and forgetfulness at 25% (16).

Although studies summarized above question post-stroke symptoms, there is no epidemiological study in which NMSs are investigated thoroughly. In our study, we aimed to investigate NMS frequency and characteristics by questioning all NMSs in post-stroke patients.

METHODS

Our study was designed prospectively and conducted in the stroke outpatient clinic of our hospital between March – June 2022. In our study,

in which two groups were formed with stroke patients and healthy volunteers, patients with a disease duration of 1-12 months and a diagnosis of ischemic stroke or cerebral hemorrhage who recovered well or with mild disability were included in the patient group. Exclusion criteria for both groups included a previous diagnosis of common neurological diseases (Parkinson's disease, epilepsy, dementia, multiple sclerosis, neuromuscular diseases), endocrinological diseases (diabetes, hypo/hyperthyroidism), psychiatric diseases, or history of drug use (antipsychotic, antidepressant, anticholinergic), and inability to answer questions. In addition, acute-subacute duration (<1 month), diagnosis of different stroke types (transient ischemic attack, subarachnoid, subdural or epidural hemorrhage), aphasia, and moderate or severe disability were also among the exclusion criteria for the stroke group. Age, gender, vascular risk factors [hypertension (HT), hyperlipidemia (HL), coronary artery disease (CAD), smoking, alcohol], and etiological subtypes of stroke (Bamford classification) were recorded in all patients. The Turkish version of "the Non-Motor Symptoms Questionnaire" (NMSQ-TR) consisting of 30 questions was applied to all cases (Appendix).

Written permission was obtained from Ankara City Hospital Clinical Researches Ethics Committee (Date: 06.04.2022 Number: E1-22-2530) prior to the study. Our study was carried out in accordance with the "Helsinki Declaration" following research and publication ethics. Also, signed informed consent was obtained from the cases included in the study.

Statistical analysis: All data were analyzed using the statistical package program (SPSS)

Version 17. In the study, descriptive statistics were expressed as categorical variables n (%) and continuous variables as median (min-max). The "Mann Whitney-U test" was used to compare two independent groups. Fisher's Exact Test and Chi-Square test were used to compare categorical variables. $p < 0.05$ level was considered statistically significant.

RESULTS

In our study, in which 54 stroke and 116 healthy volunteers were evaluated, the mean age of the stroke group was 59 (36-86) and 39 (72.2%) patients were female. In healthy volunteers, the mean age was 53 (24-77) and 61 (52.6%) were female. There was a significant difference in age and gender distribution between the two groups. Vascular risk factors, except for CAD, were more common in the stroke group. The type of stroke was ischemic in 50 patients (92.6%) and hemorrhagic in 4 (7.4%) patients. The mean NMSQ score was 6 (1-24) in the stroke group and 9 (0-24) in healthy volunteers, and no significant difference was noted between the two groups ($p:0.215$) (Table 1). The most common NMSs observed in the stroke group were nocturia ($n=36$, 67%), urinary incontinence ($n=26$, 48%), depression ($n=26$, 48%), incomplete bowel movement ($n=21$, 39%), forgetfulness ($n=20$, 37%), decreased/increased sexual desire ($n=20$, 37%), and difficulty in sexual intercourse ($n=20$, 37%). In the stroke group, dysphagia ($p=0.011$) and restless legs syndrome ($p=0.041$) were observed more frequently at a statistically significant rate. There was no statistically significant complaint at a higher frequency in the control group (Table 2).

Table 1. Characteristics of stroke and control group.

	Stroke (n=54)		Control (n=116)		p
	%	Median (min-max)	%	Median (min-max)	
Age		59 (36-86)		53 (24-77)	0.007*
Female/Male	72.2/27.8		52.6/47.4		0.015
Vascular Risk Factors					
HT	51.9		14.7		<0.001
HL	13		0.9		0.001
CAD	4.3		7.4		0.467
AF	9.3				0.003
Smoking	28		6.8		0.001
Alcohol	9.3		1.8		0.034
Stroke Type Ischemia/Hemorrhage	92.6/7.4				
NMSQ score		6 (1-24)		9 (0-24)	0.215*

Chi-square test was used to compare categorical variables. * The "Mann Whitney-U test" was used to compare two independent groups.

Table 2. Comparison of NMSQ answers of stroke and control group.

Sorular	Stroke (n=54)	Control (n=116)	p
	%	%	
Stream of saliva	25.9	13.8	0.053
Taste/Odor Change	9.3	13.8	0.403
Dysphagia	31.5	14.7	0.011
Nausea/vomiting	13	16.4	0.565
Constipation	31.5	28.4	0.586
Fecal incontinence	14.8	5.2	0.067*
Feeling of not completely emptying the intestines	38.9	38.8	0.99
Urinary urgency	48.1	60.3	0.135
Nocturia	66.7	57.8	0.268
Pain	33.3	42.2	0.268
Weight loss	14.8	9.5	0.314
Forgetfulness	37	49.1	0.14
Indifference to the surrounding	29.6	36.2	0.4
Hallucination	5.6	10.3	0.393*
Lack of attention	33.3	37.9	0.562
Feeling sad	48.1	56.9	0.287
Fear/Anxiety/Panic	33.3	37.9	0.562
Increase/decrease in sexual desire	37	48.3	0.17
Difficulty having sexual intercourse	37	40.5	0.666
Vertigo/Dizzy	40.7	50	0.26
Fall	14.8	20.7	0.362
Somnolence	13	12.1	0.869
Difficulty sleeping	29.6	40.5	0.171
Fearful dreaming	9.3	17.2	0.171
Talking/acting in sleep	16.7	18.1	0.819
Restlessness/need to move legs at night	50	33.3	0.041
Edema in the legs	18.5	25	0.349
Excessive sweating	25.9	26.7	0.913
Diplopia	24.1	25	0.896
Delusion	11.1	9.5	0.742

Fisher's Exact Test and Pearson Chi-Square* test were used.

DISCUSSION AND CONCLUSION

Stroke is an important global public health problem of the 21st century, both due to its high mortality and morbidity and associated post-stroke disability (1). Studies showing the negative effects of stroke on patients and caregivers point out the importance of early effective rehabilitation (17). However, they mostly focus on motor impairments, which occur at a high rate of 82% following stroke (18). In our study, we investigated the NMSs that may be associated with the quality of life and prognosis in post-stroke patients.

Gastrointestinal symptoms (excessive salivation, dysphagia, constipation, incomplete bowel movement, and symptoms such as nocturia, weight loss, restless legs syndrome, and delusion were more frequently observed among stroke patients. This frequency was also statistically significant in dysphagia and restless legs syndrome. The degree of post-stroke symptoms correlates with the rate of ischemic cerebral blood flow (19). Therefore, each patient may develop a

different degree of symptoms depending on the affected brain area and the severity of the stroke. In addition, symptoms can be observed more prominently in the acute-subacute period following stroke and in elderly patients (7,8). The limited number of patients in our study, and the inclusion of only healthy or mildly disabled, middle-aged, and chronic cases may have contributed to the insignificance of other NMSs in question.

Although some NMSs were observed more frequently in the control group, it was not statistically significant. Even in an illness such as Parkinson's, in which NMSQ is applied and NMSs are observed more prominently, some symptoms emerged at a higher rate in the control group (20), which may be attributed to the fact that NMSs such as GIS, sleep and mood disorders are common in the normal population, and that they are undiagnosed and untreated especially when mild (21-23).

GIS is among the systems that can be

significantly affected after a stroke, the pathophysiology of which is caused by the disruption of the connections between the central nervous system and the GIS. Aspiration during a swallow exam, bilateral hemisphere infarction, stroke severity (NIHSS>12), use of bolts, use of anticholinergic drugs, need for toilet assistance, advanced age, and middle cerebral artery infarction constitutes independent risk factors for post-stroke GIS complications (24). GIS symptoms such as dysphagia (30-70%), constipation (7-55.2%), bleeding (1.5-7.8%), fecal incontinence (5-40%), excessive saliva, and delayed bowel movement can be observed after stroke (25-34). In our study, the risk of GIS symptoms was not assessed due to the absence of examination to evaluate swallowing, the inclusion of patients only with good functionality, the exclusion of imaging findings, and anticholinergic drug use being an exclusion criterion. In addition, bleeding associated with GIS symptoms was not included in the NMSQ questions. However, all of the GIS symptoms questioned were more common in the stroke group. This frequency was statistically significant in terms of dysphagia and nearly significantly higher in terms of increased salivation, which is one of the indirect symptoms of dysphagia.

Available studies have shown that dysphagia can be observed in more than half of stroke patients, increasing the risk of malnutrition, dehydration, aspiration pneumonia, and death (10). Our results, on the other hand, showed that even stroke patients with a good prognosis can exhibit these symptoms twice as high compared to healthy individuals when examined without using additional testing or diagnostic methods. In stroke, dysphagia occurs with the disruption of the connections of the motor cortex and/or motor fibers with the brainstem and/or cranial nerves due to supratentorial and/or brainstem damage (35). It is most commonly seen in strokes affecting the middle cerebral vascular area, with a higher incidence in hemorrhagic stroke (36). Lateral medullary syndrome (Wallenberg's syndrome), associated with the vascular area of vertebral arteries and/or posterior inferior cerebellar arteries, is typically a brainstem vascular syndrome (37). The affected arterial vascular territories were out of the scope of our study. Since the number of hemorrhagic stroke patients was as few as 4, no comparison could be made

with ischemic stroke patients in terms of the prevalence of dysphagia.

Available studies have revealed a close relationship between stroke and sleep disorders (SD). In a study evaluating 200 stroke patients in terms of sleep disorders, SD was found in 78% of the patients, with 42% being severe, 20% moderate, and 16% moderate-severe, which is independent of the type of stroke and localization (13). Apnea is the most common sleep disorder associated with stroke and is seen in more than half of stroke patients (38). A bidirectional relationship exists between sleep disorders and stroke. In addition to the high prevalence of SD in stroke patients; sleep apnea (39) increases the risk of stroke twice as much while other SDs increase the risk at a rate of 20%. Therefore, they are involved in the cryptogenic etiology of stroke (40). Its pathogenesis involves oxidative stress secondary to increased sympathetic activity associated with SD, increased inflammation and prothrombotic factors, endothelial dysfunction, atherosclerosis, and arrhythmia. This bidirectional relationship is also associated with the fact that patients often present with vascular risk factors such as obesity, diabetes, hypertension, and heart rhythm disorders, which are risk factors for stroke, as is the case with sleep apnea. Other non-apnea sleep disorders frequently accompanying stroke include REM sleep behavior disorder, periodic limb movement disorder (PLMD), restless legs syndrome (RLS), and insomnia. In our study, the feeling of restlessness in the legs at nighttime or an increase in the desire to move the legs while resting, suggesting RLS and PLMD, were found significantly higher. No significant difference was noted in other questioned insomnia, parasomnia (fearful dreaming, sleep talking or movement), and somnolence symptoms. In addition, the fact that the investigation of the fundamental symptoms of sleep apnea (snoring, witnessed apnea, and excessive daytime sleepiness) was limited to somnolence and acted as a hindrance in terms of detection.

RLS and PLMD are usually observed as concurrent sleep disorders (80-90%) (41). Their pathophysiology involves a disruption in the dopaminergic system in the brain stem due to the positive response they exert against dopaminergic drugs (42). In a study evaluating post-stroke RLS and PLMD in the literature, the lesion was found to be most commonly located in the pons (43). In

another study in which 137 stroke patients were evaluated, RLS was found in 12.7% of the patients, with the lesion being located in the basal ganglia/corona radiata at 30%, pons at 22%, thalamus at 14%, internal capsule at 12.5% and cortical at 1.9%. The results of this study suggest that subcortical lesion sites such as the pyramidal pathway and basal ganglia-brainstem axis, which are involved in motor functions and sleep-wake cycles, may lead to RLS symptoms in patients after ischemic stroke (44). In addition, frequent occurrences of post-stroke iron deficiency and anemia, major secondary causes of RLS, may play a role in the etiology. The results of our study have some limitations as we did not evaluate brain imaging and laboratory (iron, etc.) parameters and did not include any sleep tests.

One of the points that should be kept in mind is that further improvement can be observed in motor functions with the treatment of NMS, which has been proved in randomized controlled studies in which SSRIs are used in the treatment of depression (45-47). In our study, dopamine agonists are the first-line treatment in patients with RLS and PLMD with a significant frequency (48). Currently, there is no established medical treatment for dysphagia. Various treatment modalities, including a therapy team, are recommended, such as behavioral therapy, acupuncture, electrical or magnetic stimulation, and medications (49,50).

In conclusion, post-stroke NMS can be observed frequently, even if the patients exhibit a good recovery process. The treatment process, which will be guided by the early detection of these symptoms during rehabilitation, bears great importance in terms of increased quality of life and a better prognosis. There are some limitations in our study. The limited number of cases in the stroke group, the significant difference in age and gender between the groups, the failure to evaluate the relationship between stroke severity at admission, the duration of stroke diagnosis and symptoms, and the lack of imaging findings and treatment methods are among these limitations. Lastly, the NMSQ-TR scale we used is an adapted scale for Parkinson's disease, therefore a new scale should be developed for stroke patients with prospective studies to be conducted in this regard.

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Ethics

Ethics Committee Approval: The study was approved by Ankara City Hospital Clinical Researches Ethical Committee (Date: 06.04.2022, Number: E1-22-2530).

Informed Consent: The authors declared that informed consent was obtained from all cases included in the study.

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Appendix. The "Turkish Version of the Non-Motor Symptoms Scale" (NMSÖ-TR) Questionnaire.

1- Did you have stream of saliva during the day?	YES	NO
2- Is there a change or loss in taste or smell?	YES	NO
3- Have you encountered difficulty in swallowing food and drinks or choking?	YES	NO
4- Have you had nausea or vomiting?		
5- Did you encounter constipation (less than 3 stools per week) or stool output difficulties?	YES	NO
6- Have you experienced fecal incontinence?	YES	NO
7- Did you feel that your bowels were not completely emptied when you came out of the toilet?	YES	NO
8- Do you feel that you have enough urine to take it to the toilet?	YES	NO
9- Do you regularly urinate at night?	YES	NO
10- Do you suffer from unexplained pain?	YES	NO
11- Do you have unexplained weight loss?	YES	NO
12- Do you have difficulty remembering events that happened before or things you did or any complaints such as forgetting?	YES	NO
13- Have you lost interest in the events or things happening around you?	YES	NO
14- Do you hear sounds or see images that you know are not real?	YES	NO
15- Do you have difficulty concentrating?	YES	NO
16- Do you feel sad?	YES	NO
17- Do you feel scared, anxious or panicked?	YES	NO
18- Do you feel an increase or decrease in sexual desire?	YES	NO
19- Do you have difficulty in having sexual intercourse?	YES	NO
20- Do you have dizziness, feeling of lightheadedness when getting up from sitting or lying position?	YES	NO
21- Did you fall?	YES	NO
22- Did you have staying awake while working, driving or eating?	YES	NO
23- Do you have difficulty falling asleep or staying asleep at night?	YES	NO
24- Have you had intense, vivid or frightening dreams?	YES	NO
25- Do you talk or move while asleep?	YES	NO
26- Do you feel an unpleasant sensation in your legs at night or feel the need to move your legs while resting?	YES	NO
27- Is there swelling in your legs?	YES	NO
28- Have you had excessive sweating?	YES	NO
29- Have you had double vision?	YES	NO
30- Does some things seem to have happened to you even though others say they are not?	YES	NO
Total:		