



# The Relationship Between Pain Level and Quality of Life And Sleep Disorder in Patients with Central Post-Stroke Pain

## İnme Sonrası Santral Ağrılı Hastalarda Ağrı Şiddeti ile Yaşam Kalitesi ve Uyku Bozukluğu Arasındaki İlişki

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Abstract / Öz

**Introduction:** Stroke is the third most common cause of death and the first cause of disability worldwide. Central post-stroke pain (CPSP) resulting from the dysfunction or primary lesion of the central nervous system after stroke is a common syndrome.

**Methods:** A total of 75 (31 female and 44 male) patients with ischemic stroke were included in the study. Of the patients, 28 (12 women and 16 men) experienced central pain within 1 year after ischemic stroke.

**Results:** The pain assessment of the patients was performed using the Leeds Assessment of Neuropathic Symptoms and Signs (LANSS) pain scale and the Visual Analog Scale (VAS). The European Quality of Life-5 Dimensions (EQ-5D) and EQ-5D VAS life quality assessment conducted in the group with central pain indicated a statistically significant correlation in the quality of life (QoL) in both measurements as the VAS level increased ( $p \leq 0.001$  and  $p \leq 0.001$ , respectively). Similarly, it was identified that the QoL (EQ-5D and EQ-5D VAS) was lower in the group with  $LANSS \geq 12$  than the group with  $LANSS < 12$  ( $p \leq 0.006$  and  $p \leq 0.016$ , respectively). Statistically significant data were obtained in the group with CPSP as the VAS score increased and in cases with  $LANSS \geq 12$  according to the Epworth Sleepiness Scale ( $p \leq 0.001$  and  $p \leq 0.002$ , respectively). When the groups with the Epworth score between  $< 11$  and  $\geq 11$  were compared, the daytime sleepiness ratio was found to be significantly higher in the group with  $LANSS \geq 12$  ( $p \leq 0.018$ ). A positive significant correlation was detected between the VAS score and the daytime sleepiness ratio ( $p \leq 0.001$ ).

**Conclusion:** The present study demonstrated that CPSP had a clearly negative effect on the QoL of patients with stroke. It is important for the literature to emphasize that it is possible to improve the comfort of patients with a correct diagnosis and treatment of sleep disorders, depression, and anxiety accompanying CPSP.

**Keywords:** Central post-stroke pain, leeds assessment of neuropathic symptoms and signs, visual analog scale, quality of life, sleep disorder

**Amaç:** İnme, dünyada en yaygın üçüncü ölüm nedeni ve birinci özür-lülük nedenidir. İnme sonrası santral sinir sisteminin disfonksiyon ya da primer lezyonundan kaynaklanan, inme sonrası santral ağrı (İSSA), sık görülen bir sendromdur.

**Yöntemler:** Çalışmamıza 31 kadın, 44 erkek olmak üzere toplam 75 iskemik inme hastası dahil edildi. 28 tanesi (12 kadın, 16 erkek) iskemik inme sonrası 1 yıl içinde santral ağrı gelişen hastalardı. Hastaların ağrı değerlendirilmesi, The Leeds Assessment of Neuropathic Symptoms and Signs (LANSS) ağrı skalası ve Visual Analogue Scale (VAS) ile yapıldı.

**Bulgular:** Santral ağrısı olan grupta yapılan European Quality 5 Dimension (EQ5D) ve EQ5D VAS yaşam kalitesi değerlendirmesi, VAS derecesi arttıkça yaşam kalitesinde, her iki ölçümde istatistiki olarak anlamlı korelasyon gösterdi ( $p=0,001$ ,  $0,001$ ). Aynı şekilde  $LANSS \geq 12$  olan grupta,  $LANSS < 12$  olan gruba göre yaşam kalitesinin (EQ5D ve EQ5D VAS) düşük olduğu saptandı ( $p=0,006$ ,  $0,016$ ). İSSA olan grupta, VAS puanı arttıkça ve  $LANSS \geq 12$  olanlarda Epworth Uyukluluk Ölçeği'ne göre istatistiki olarak anlamlı verilere ulaşıldı ( $p=0,001$ ,  $0,002$ ). Epworth skoru  $< 11$  ile  $\geq 11$  olan gruplar karşılaştırıldığında;  $LANSS \geq 12$  olan grupta gündüz uyukluluk oranı anlamlı düzeyde daha yüksek bulundu ( $p=0,018$ ). VAS puanı ile gündüz uyukluluk oranı arasında pozitif anlamlı korelasyon saptandı ( $p=0,001$ ).

**Sonuç:** Bu çalışma ile İSSA'nın inme hastalarında yaşam kalitesi üzerine belirgin negatif etkisi olduğu gösterilmiştir. İSSA'ya eşlik eden uyku bozuklukları, depresyon ve anksiyetenin doğru tanı ve tedavisi ile hastaların konforunun artırılabilirliğinin vurgulanması literatür açısından önem arz etmektedir.

**Anahtar Kelimeler:** İnme sonrası santral ağrı, the leeds assessment of neuropathic symptoms and signs, visual analogue scale, yaşam kalitesi, uyku bozukluğu

## Introduction

Stroke is the third most common cause of death and the first cause of disability in the world. It has a significant share in both hospitalization and health expenditures in industrialized countries (1).

The pain caused by the dysfunction or primary lesion of the central nervous system after stroke is called post-stroke pain, and it is one of the reasons for central neuropathic pain (2, 3). Central post-stroke pain (CPSP) is a common syndrome after stroke and is observed in approximately one out of three patients with post-stroke pain (4). It was first described by Dejerine and Roussy in 1906 as the pain occurring spontaneously after thalamic stroke (5). Thus, the expression of thalamic pain is sometimes used instead of CPSP. However, the researchers then comprehensively described the characteristics of the pain caused by extrathalamic lesions (6).

Central post-stroke pain is characterized by pain and sensory abnormalities in the body (when other reasons for significant nociceptive, psychogenic, or peripheral pains are excluded) after cerebrovascular lesion of the somatosensory system (7). Symptom onset is often gradual, coinciding with the improvement of perceived sensory loss and the appearance of dysesthesia. The pain is

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frequently severe and unrelenting, with pain-free episodes not exceeding a few hours (8). The prevalence of CPSP has been reported to be 7.3% (7).

The quality of life (QoL) is lower by 40% a year after stroke onset than before a stroke. As pain is known to affect recreational activities, vocational status, and quality of sleep, it can have a major role on QoL, mood, and rehabilitation outcome (9). In our study, the QoL and sleep quality were evaluated comparatively according to the presence and level of pain in patients with ischemic stroke with and without central pain.

## Methods

The study was conducted on patients with ischemic stroke who were followed up by our Neurology Clinic. Ethics Committee approval was received for this study from the Ethics Committee of Sakarya University (28.02.2017-71522473/050.01.04/67). Consent was obtained from the patients to participate in the study.

Patients diagnosed with ischemic stroke; aged between 30 and 85 years; with thyroid and parathyroid diseases; using corticosteroid and hormone replacement therapy; with malnutrition, cancer diagnosis, psychiatric treatment use, and chronic renal and liver diseases; without motor dysfunction due to an orthopedic discomfort, and who acknowledged their participation were included in the study.

There were 75 (31 female and 44 male) patients with ischemic stroke included in the study. While 28 patients experienced central pain within 1 year after ischemic stroke, 47 (19 female and 28 male) patients did not experience central pain in 1 year following an ischemic stroke. Patients were separated into two groups as thalamic and extrathalamic in terms of ischemic stroke localization.

The pain assessment of the patients was performed using the Leeds Assessment of Neuropathic Symptoms and Signs (LANSS)

pain scale and the Visual Analog Scale (VAS). The life quality assessment was performed by the European Quality of Life-5 Dimensions (EQ-5D) and EQ-5D VAS. Moreover, the Beck Anxiety Inventory (BAI), the Beck Depression Inventory (BDI), and the Epworth Sleepiness Scale (ESS) were applied to the patients.

In groups with and without central pain, gender, age, and infarct location were compared. In the group with central pain, with the LANSS values <12 and ≥12 and according to the VAS values, QoL was assessed by EQ-5D and EQ-5D VAS. Among the same groups, comparisons were made by the BAI and BDI scores with the Epworth sleep score values of <11 and ≥11 (daytime sleepiness).

## Statistical Analysis

The Fisher-Freeman-Halton test, independent samples t-test, one-way analysis of variance, Kruskal-Wallis H test, chi-square test, and correlation analyses were used in the assessment of data depending on the type and purpose of the characteristics. A p<0.05 was considered statistically significant. Statistical analysis was made using the Statistical Package for Social Sciences version 18.0 for Windows (IBM Inc.; Armonk, NY, USA).

## Results

While the lowest age was 32 years and the highest age was 87 years, the average age in the group with central pain was 64.04±12.9 years, and the average age in the group without central pain was 62.8±13.9 years.

While 15 (53.6%) patients had thalamic infarct and 13 (46.4%) patients had extrathalamic infarct in the group with central pain, 7 (14.9%) patients had thalamic infarct and 40 (85.1%) patients had extrathalamic infarct in the group without central pain.

Gender and age distributions were found to be similar in the groups with and without central pain (p≤0.836 and p≤0.701, respectively). The rate of the cases with thalamic infarct was significantly higher in the group with central pain (p≤0.001).

There was a significant difference between the VAS average of 3.25±0.96 of the patients with LANSS<12 and the VAS average of 7.1±1.25 of the patients with LANSS≥12 in the group with central pain (p≤0.001). According to this result, the VAS severity of those with LANSS of ≥12 was higher.

As a result of the EQ-5D and EQ-5D VAS life quality assessment conducted in the group with central pain, there was a significant positive correlation between both values (p≤0.001), and both measurements indicated a statistically significant correlation in the QoL as the VAS level increased (p≤0.001 and p≤0.001, respectively). Similarly, it was identified that the QoL (EQ-5D and EQ-5D VAS) was lower in the group with LANSS≥12 than in the group with LANSS<12 (p≤0.006 and p≤0.016, respectively) (Table 1).

There was no statistically significant difference between the groups with and without CPSP in terms of the ESS point average (p≤0.522). In the assessment performed in two separate groups as the Epworth score (daytime sleepiness condition) <11 and ≥11, there was no significant difference between the cases with and without CPSP (p≤0.744). Statistically significant data were obtained in the group with CPSP as the VAS score increased and in cases with LANSS≥12

**Table 1. The comparison of the quality of life and EQ-5D in patients with stroke with CPSP with LANSS and VAS**

	LANSS<12		LANSS≥12		VAS	
	n	n	p	n	p	
EQ-5D	4	24	0.006	28	0.001	
EQ-5D VAS	4	24	0.016	28	0.001	

LANSS: leeds assessment of neuropathic symptoms and signs; VAS: visual analog scale; EQ-5D: European quality of life-5 dimensions

**Table 2. The comparison of the Epworth Sleepiness Scale in patients with stroke with CPSP with LANSS and VAS**

CPSP	LANSS<12		LANSS≥12		VAS	
	n	n	p	n	p	
Epworth sleepiness score	4	24	0.002	28	0.001	
Epworth score<11	4	11	0.018	15	0.001	
Epworth score≥11	0	13		13		

CPSP: central post-stroke pain; LANSS: leeds assessment of neuropathic symptoms and signs; VAS: visual analog scale

according to the ESS ( $p \leq 0.001$  and  $p \leq 0.002$ , respectively). When the groups with the Epworth score  $< 11$  and  $\geq 11$  were compared, the daytime sleepiness rate was found to be significantly higher in the group with  $\text{LANSS} \geq 12$  and as the VAS score increased ( $p \leq 0.018$  and  $p \leq 0.001$ , respectively) (Table 2).

The BAI and BDI values of the groups with and without CPSP did not indicate a significant change ( $p \leq 0.731$  and  $p \leq 0.249$ , respectively), and the anxiety and depression levels of both groups were found to be similar. In the group with CPSP, it was identified that the anxiety level determined with the BAI scale was significantly higher in cases with  $\text{LANSS} \geq 12$  than in those with  $\text{LANSS} < 12$  ( $p \leq 0.007$ ), and there was no significant difference in terms of the depression level ( $p \leq 0.406$ ). A significant positive correlation was found between the anxiety and depression levels in the group with central pain according to the VAS, BAI, and BDI ( $p \leq 0.000$  and  $p \leq 0.001$ , respectively). In other words, as the VAS level increases, the anxiety and depression levels of patients increase significantly.

## Discussion

Neuropathic pain is the pain that causes sensory symptoms and findings caused by a lesion in the peripheral or central nervous system or in both of them. It is divided into central and peripheral neuropathic pain. Post-stroke pain is one of the causes of central neuropathic pain (2, 3). Although there remain some mysteries as to the pathophysiology of CPSP, it is believed to be caused by stroke in the region of the thalamus and extrathalamic areas. The thalamus is a relay station for sensory information from all over the body (10). In our study, the patient group who had central pain after ischemic stroke was divided into two groups as thalamic and extrathalamic.

In most of the patients with stroke, central pain develops in the first month after stroke; however, it may also develop  $\geq 6$  months after stroke in some patients (11). Patients who experienced central pain within 1 year after stroke were included in the study.

Although central pain after stroke was originally described as "thalamic pain," it is currently recognized that strokes involving the sensory tracts in various brain regions can produce pain similar to central pain (12).

In some studies, higher pain intensities have been reported when the lesions were located in the brainstem or thalamus than in other areas; however, in another study, the symptoms and severity of CPSP in thalamic versus extrathalamic stroke did not differ (9). Of the 75 patients with ischemic stroke, 28 had CPSP in our study. The rates of the 15 (53.6%) patients with thalamic infarct were similar with the rates of the 13 (46.4%) patients with extrathalamic infarct. There were only 7 (14.9%) patients with thalamic infarct in the group of 47 patients without CPSP. In other words, thalamic lesions are observed more frequently in the group with CPSP than in the group without CPSP ( $p \leq 0.001$ ); moreover, the frequency of thalamic and extrathalamic lesions was found to be similar in the group. This situation will become clearer in future studies to be conducted with more patients with CPSP.

It is hard to diagnose CPSP. In this process, it is beneficial to identify pain level with pain scales, such as the VAS and Numerical Rating Scale; however, there was no scale developed especially for CPSP (7). In our study, the pain assessment was performed us-

ing the LANSS and VAS in the group with CPSP, and it was identified that the VAS severity was higher in the group with  $\text{LANSS} \geq 12$  ( $p \leq 0.001$ ). In other words, both tests were correlated in indicating the level of pain.

There are many studies on the fact that the presence of CPSP impairs the life quality of patients. For example, in the study conducted with 100 patients with stroke by Kılıç et al. (13), CPSP was determined in 20 patients. While CPSP was evaluated by the LANSS, the QoL was evaluated by the Nottingham Health Profile (NHP). Central pain was related to a significant difference in the pain parameter of the NHP ( $p \leq 0.001$ ). In conclusion, CPSP is a complication that should not be ignored because it is not rare and has a negative impact on the QoL of patients with stroke. In a study conducted with 24 patients with CPSP, while pain was evaluated by the LANSS and VAS, the QoL was evaluated by the 36-item Short-Form Health Survey quality of life scale (SF-36 QoLS). The result showed that CPSP has a negative impact on the physical subscale score of the SF-36 QoLS in patients with stroke (9). In our study, the QoL of patients was assessed using the EQ-5D and EQ-5D VAS. In the assessments performed with both the LANSS and VAS, the level of pain and the QoL were statistically significant. It was observed that as the severity of CPSP increased, the QoL decreased in correlation with this. This condition did not indicate any difference between thalamic and extrathalamic groups. It is a fact that central pain has a negative effect on the QoL; however, it is possible to increase the QoL of patients with a correct diagnosis and treatment.

In many studies, it has been demonstrated that as CPSP affects the QoL, it also affects sleep quality. In the study conducted by Raffaelli et al. (14) with 601 patients with stroke with CPSP, half (50%) of the interviewed pain population could sleep in a restful way, 28.8% had some difficulty, and 21.8% could not sleep at all. A total of 199 patients were examined to identify sleep disorders in a 3-month period after cerebral infarct, and the nighttime sleep quality and excessive daytime sleepiness of the patients were evaluated by the Verran-Snyder-Halpernsleepscale and ESS. Bad nighttime sleep was reported in 88 (44.2%) patients, and excessive daytime sleepiness was reported in 28 (14.4%) patients. There was no significant relationship between post-stroke pain and post-stroke sleep disorders (15). In a study conducted with 3732 individuals aged  $\geq 65$  years, as a result of the assessment using the Pittsburgh Sleep Quality Index in cases with subjective bodily pain, it was observed that those with serious and very serious bodily pain had the highest values; moreover, higher values were identified in the group with mild bodily pain than in the group without any bodily pain. It is known that painful syndromes cause sleep disorders. CPSP is one of the serious painful syndromes (16).

In our study, there was no statistically significant result between the groups with and without CPSP in terms of bad nighttime sleep and excessive daytime sleepiness. However, it was identified in the group with CPSP that the nighttime sleep quality decreased as the VAS score increased ( $p \leq 0.001$ ). The nighttime sleep quality was worse in the group with  $\text{LANSS} \geq 12$  in the same group ( $p \leq 0.002$ ). In the assessment conducted according to excessive daytime sleepiness, the rate was higher in the group with  $\text{LANSS} \geq 12$  and as the VAS score increased ( $p \leq 0.018$  and  $p \leq 0.001$ , respectively).

In general, it is known that painful syndromes cause sleep disorders. CPSP is one of the serious painful syndromes (16). These sleep

disorders developing in patients with CPSP further deteriorate the QoL of patients.

Sleep disorders and functional disorders, such as depression and anxiety, are the important comorbid conditions accompanying CPSP (11). In our study, depression and anxiety were found at similar rates between the groups with and without CPSP; however, in the assessment using the LANSS and VAS in the group with CPSP, it was identified that the anxiety and depression levels increased as the level of pain increased. In other words, pain appears as a condition increasing depression and anxiety and deteriorating the QoL in this regard. The importance of the diagnosis and treatment of these diseases accompanying CPSP has been emphasized once again.

## Conclusion

Central post-stroke pain is a frequently observed syndrome among post-stroke pains. In addition to our study and in many studies, it has been shown that it has a remarkable negative effect on the QoL of patients with stroke. It is important for the literature to emphasize that it is possible to improve the comfort of patients with a correct diagnosis and treatment of sleep disorders, depression, and anxiety accompanying CPSP.

**Ethics Committee Approval:** Ethics Committee approval was received for this study from the Ethics Committee of Sakarya University (28.02.2017-71522473/050.01.04/67).

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