ARAŞTIRMA MAKALESİ / *Research Article*

Frequency of Central Post-Stroke Pain and Its Impact on Quality of Life

İnme Sonrası Santral Ağrının Sıklığı ve Yaşam Kalitesine Etkisi

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Abstract

Objective	This study aims to determine the frequency of central post-stroke pain (CPSP) in a patient population with stroke as well as investigating the relationship between CPSP and patients' clinical/demographic characteristics, pain intensity, functional status, and quality of life.
Methods	The study included 150 patients, who had a stroke and were aged 18 years and above. Demographic data of the patients, time since onset, and etiology, localization of the cerebral lesion, affected side, ambulation status, and Brunnstrom stages were recorded. Douleur neuropathique 4 questions (DN4) were used to assess the presence of CPSP. Visual Analog Scale (VAS) was used for pain intensity, functional ambulation scale (FAS) was used for ambulation status, Barthel Index (BI) was used for functional status, and the stroke impact scale (SIS) was used for quality of life.
Results	The mean age of the patients was 67±11.5 years, 54.7% was male, and 45.3% was female. CPSP was evaluated in 15.3% of patients. There was no significant difference between the affected side of the body and age, gender, time since onset, BI scores, and ambulation status of patients according to their CPSP status (p>0.05). There was no statistically significant difference between SIS sub-parameter scores and the presence of CPSP (p>0.05). In correlation analysis, a significant relationship was found between Barthel Indexes and all SIS domains except memory and emotion (p <0.01).
Conclusion	CPSP can be seen with varying frequency in stroke patients. In our study, the negative effect of the presence of CPSP on quality of life was not demonstrated.
Keywords	central post-stroke pain; quality of life; stroke impact scale

Öz

Amaç	*Bu çalışma, inmeli bir hasta popülasyonunda inme sonrası santral ağrı (İSSA) sıklığını belirlemeyi ve İSSA ile hastaların klinik/demografik özellikleri, ağrı şiddeti, fonksiyonel durumu ve yaşam kalitesi arasındaki ilişkiyi araştırmayı amaçlamaktadır.*
Yöntemler	*Çalışmaya 18 yaş ve üzeri inme geçirmiş 150 hasta dahil edildi. Hastaların demografik verileri, inme sonrası geçen süre, etiyoloji, serebral lezyonun lokalizasyonu, etkilenen taraf, ambulasyon durumu ve Brunnstrom evreleri kaydedildi. İSSA varlığını değerlendirmek için Douleur nöropatik 4 (DN4) ölçeği kullanıldı. Ağrı şiddeti için görsel analog skala (VAS), ambulasyon durumu için fonksiyonel ambulasyon skalası (FAS), fonksiyonel durum için Barthel İndeksi (BI) ve yaşam kalitesi için inme etki skalası (SIS) kullanıldı.*
Bulgular	*Hastaların yaş ortalaması 67±11,5 yıl, %54.7'si erkek, %45.3'ü kadındı. İSSA hastaların %15.3'ünde saptandı. Hastaların İSSA durumlarına göre etkilenen taraf ile yaş, cinsiyet, inme sonrası geçen süre, BI skorları ve ambulasyon durumları arasında anlamlı fark yoktu (p>0.05). SIS alt parametre puanları ile İSSA varlığı arasında istatistiksel olarak anlamlı fark yoktu (p>0.05). Korelasyon analizinde Barthel İndeksleri ile bellek ve duygu dışındaki tüm SIS alt parametreleri arasında anlamlı bir ilişki bulundu (p<0.01).*
Sonuç	*İSSA, inme hastalarında değişken sıklıkta görülebilmektedir. Bizim çalışmamızda İSSA varlığının yaşam kalitesi üzerine olumsuz etkisi gösterilememiştir.*

INTRODUCTION

Stroke is a rapidly-developing manifestation, characterized by disturbances in cerebral function and high morbidity and mortality.[1,2] Various types of post-stroke pain develop in these patients. One of them is the central neuropathic pain, with sensory deficits, caused by a lesion that affects spinothalamic pathways in the brain. Although its pathophysiology is still not fully understood, it may develop in 40-50% of central post-stroke pain (CPSP) patients within 1-2 months after stroke; however, it may develop 6 months later in some of the patients.[3] There is a limited number of epidemiological studies related to CPSP, and its reported frequency was in the range of 1-35% depending on the heterogeneity in the studies.[4-9] The epidemiological studies have shown that the cognitive disorders developed after stroke have a negative impact on the quality of life (QOL) of the patients.[10]

Various scales are used in the evaluation of participative functionality and QOL in patients with stroke. Among them, the Nottingham Health Profile (NHP) and the Short Form-36 (SF-36) are generic scales used to assess the quality of life and may have major ceiling and floor effects in patients with stroke. However, the stroke impact scale (SIS) is a stroke-specific quality of life scale, which parametrically assesses the emotion, memory, thinking, and social role function dimensions of quality of life. This scale consists of 8 domains and 59 items to assess the post-stroke quality of life perceived by the patients and caregivers. It's a versatile scale that can be useful for assessments in clinical practice and research.[11]

There is a limited number of studies that show the relationship between CPSP presence and QOL, functional status, and pain intensity in patients with stroke.

In this study, we determined the frequency of CPSP in patients with stroke as well as its relationship with clinical and demographic characteristics, pain intensity, QOL, and functional status.

MATERIAL and METHODS

This was an observational study and the study population consisted of 150 patients with stroke who received rehabilitation care and were hospitalized in tertiary medical center between June 2015 and September 2015. Participants were informed about the study, and informed consent forms were collected. The study was approved by clinical research ethics committee. Individuals older than 18 years of age who have had a stroke were included in the study. Patients with aphasia, cognitive dysfunction (presence of dementia, person-time-place disorientation, etc) active psychiatric disease, complex regional pain syndrome, subarachnoid hemorrhage, arteriovenous malformation, tumor, stroke due to traumatic brain injury, spinal cord injury, and history of multiple sclerosis, the presence of neglect, and with a known diagnosis of neuropathic pain were excluded from the study.

The demographic characteristics of the patients; age, gender, profession, level of education, lifestyle, marital status, weight and height, time since onset, stroke etiology, dominant side, affected side, risk factors for stroke (age, gender, hypertension, diabetes mellitus, smoking, cardiovascular disease, stroke history, family history), ambulation status, and Brunnstrom stages were recorded. Presence of thalamic-extrathalamic lesion was determined using magnetic resonance imaging.

FAS was used to assess the ambulation status of patients, and VAS was used to assess the pain intensity. The functional status of the patients was assessed by the Barthel index (BI). In our study, to estimate the probability of CPSP, Douleur neuropathique 4 questions (DN4) questionnaire was used. It consists of 10 items, seven items related to pain characteristics (i.e. sensory and pain descriptors) are based on an interview with the patient, and 3 items are based on the clinical examination.[12]

To assess the quality of life, the SIS 3.0 was used. This scale has 59 items and 8 domains (strength, hand function, acti-

vities of daily living, useful activities of daily living, mobility, communication, emotion, memory and thinking, participation). Besides, the combination of the strength, hand function, activities of daily living, and mobility domains are evaluated as the composite physical dimension.[11] The patients are asked to assess their difficulty in completing each item within the last 1 week on a five-point Likert-type scale. On the scale, 1 point indicates that the patient had failed to perform the item, and 5 points indicate that the patient had no difficulty in completing the item. Also, there is a visual analog scale related to the perception of post-stroke general improvement (0: No improvement, 100: Full recovery). It takes approximately 15-20 minutes to complete the scale. In all patients included in the study, the domains of SIS were evaluated separately.

Statistical Analysis

IBM SPSS Statistics 22 (IBM SPSS, Turkey) program was used for analyzing the findings of the study. The Shapiro-Wilks test was used for assessing the normal distribution of the parameters in the evaluation of study data. In addition to the descriptive statistical methods (Mean, Standard deviation, Frequency), the Student t-test was used for intergroup comparison of parameters with normal distribution in the quantitative data, and Mann-Whitney U-test was used for the intergroup comparison on parameters that have no normal distribution. Pearson correlation analysis was used for investigating the relationships between parameters with a normal distribution, and Spearman's Rho correlation analysis was used for investigating the relationships between parameters without normal distribution. And, Chi-square test, Continuity (Yates) Correction, and Fisher Exact test were used for the comparison of qualitative data. $P<0.05$ was accepted as the level of significance.

RESULTS

The study included 150 patients with stroke, of which 82 were male and 68 were female. The mean age of the patients was 67±11.5 (36-91) years.

The demographic and clinical characteristics of the patients are summarized in Table 1.

Table 1: The distribution of demographic characteristics of patients

		Min-Max	Mean±SD
Age (year)		36-91	67.04±11.55
BMI (kg/m2)		16.43-47	26.81±4.51
Time since onset (month)		2-66	8.85±12.3
		N	%
Gender	Female	68	45.3
	Male	82	54.7
Occupation	Active	46	30.7
	Retired	46	30.7
	Housewife	58	38.7
Educational status	Illiterate	31	20.7
	Lettered	8	5.3
	Primary school	82	54.7
	Middle school	10	6.7
	High school	10	6.7
	Postgraduate	9	6
Marital status	Single	8	5.3
	Married	110	73.3
	Widow	32	21.3
Life style	Alone	37	24.7
	Nuclear family	113	75.3
Dominant side	Right	141	94
	Left	9	6
Stroke type	Ischemic	117	78
	Haemorrhagic	33	22
Time since onset group	1 month- 1 year	120	80
	Over 1 year	30	20

BMI indicates body mass index; Min, minimum; Max, maximum; SD, standart deviation

Their functional status was assessed with BI, and patients' mean BI score was found to be 32.7±22.6 (0-100). Of the patients, 68 (45.3%) had been affected on the right side, and 82 had been affected on the left. The location of the lesion was thalamic in 20 (13.3%) patients, whereas it was

extrathalamic in 130 (86.7%) of the patients.

Patients with and without CPSP were compared in terms of demographic and clinical characteristics (Table 2). In terms of the CPSP frequency, 23 out of 150 patients were found to have central pain (15.3%). There was no significant difference between the groups in the comparison of SIS domains between patients with and without CPSP (Table 3). The patient's functional status, age, time since onset, VAS, affected bodyside, and quality of life were compared (Tables 4-5). A significant correlation was found between the Barthel Indexes of the patients and all domains of SIS, except memory and emotion ($p<0.01$ Table 4). In the comparison of age and quality of life of the patients, a significant correlation was found between activities of daily living domains of SIS ($p<0.01$ Table 4). In the comparison of duration of stroke and quality of life of the patients, a significant correlation was found between time since onset and SIS domains (communication, mobility, recovery from the stroke) ($p<0.01$ Table 4). In the comparison of VAS scores and the quality of life of the patients, a significant correlation was found between VAS and the emotion domain of SIS ($p<0.05$ Table 4). And, in the comparison of the affected body side and quality of life of the patients, a significant correlation was found with the memory, communication, and mobility domains of SIS ($p<0.01$ Table 5).

Table 2: Comparison of the demographic characteristics of patients according to the presence of central post-stroke pain (CPSP)

		CPSP		P
		(+)	(-)	
		Mean±SD (Median)	Mean±SD (Median)	
Age (year)		63.83±10.89	67.62±11.61	10.148
BMI(kg/m²)		27.66±4.24	26.65±4.55	10.324
Time since onset (month)	15.22±21.08 (4)	7.69±9.62 (4)	20.110	
		n (%)	n (%)	P
Gender	Female	10 (14.7%)	58 (85.3%)	[3]1.000
	Male	13 (15.9%)	69 (84.1%)	
Occupation	Active	7 (15.2%)	39 (84.8%)	[4]0.840
	Retired	6 (13%)	40 (87%)	
	Housewife	10 (17.2%)	48 (82.8%)	
Educational status	Lettered or illeterate	10 (25.6%)	29 (74.4%)	[4]0.081
	Primary school	11 (13.4%)	71 (86.6%)	
	High school and above	2 (6.9%)	27 (93.1%)	
Marital status	Alone	4 (10%)	36 (90%)	[3]0.403
	Married	19 (17.3%)	91 (82.7%)	
Life style	Alone	4 (10.8%)	33 (89.2%)	[3]0.537
	Nuclear family	19 (16.8%)	94 (83.2%)	

[1]Student t Test [2]Mann Whitney U Test [3]Continuity (Yates) Correction [4]Chi-Square Test
p value relates to comparison between patients with and without CPSP.

Table 3: Comparison of patient's Stroke Impact Scale 3.0 (SIS) domains and total scores according to the presence of CPSP			
SIS domains	CPSP		P
	(+)	(-)	
	Mean±SD(Median)	Mean±SD(Median)	
Strength	13.32±10.54 (12.5)	16.14±17.6 (6.25)	0.884
Memory	65.68±29.03 (75)	73.08±24.63 (78.57)	0.448
Emotion	35.14±13.8 (33.33)	39.96±15.3 (38.88)	0.467
Communication	59.78±27.37 (57.14)	64.06±27.46 (64.28)	0.314
ADL/IADL	15.54±7.72 (20)	17.38±12.93 (20)	0.363
Mobility	8.09±7 (8.33)	9.07±13.9 (2.77)	0.427
Hand Function	0.65±3.13 (0)	3.43±12.8 (0)	0.374
Social Participation	2.17±6.06 (0)	5.07±13.51 (0)	0.784
Recovery	45.65±22.53 (50)	41.73±22.68 (40)	0.408
Composite physical domain	9.4±5.29 (9.4)	11.5±12.14 (8.12)	0.884
SIS total	27.33±8.49 (27.09)	29.99±11.58 (28.63)	0.448
Mann Whitney U Test ADL: activities of daily living, IADL: instrumental activities of daily living			

Table 4. Comparison of Functional status (Barthel Index), age, duration of stroke, Visual Analog Scale (VAS) and SIS domains										
SIS domains	**Barthel Index**		**[1]Age (year)**		**[1]BMI (kg/m2)**		**[2]Duration of stroke (month)**		**VAS**	
	r	**P**	**r**	**p**	**r**	**P**	**r**	**P**	**r**	**p**
Strength	0.583	**0.001***	-0.033	0.684	-0.008	0.926	0.034	0.682	0.065	0.433
Memory	0.071	0.388*	-0.113	0.169	0.051	0.532	0.141	0.085	-0.076	0.353
Emotion	0.033	0.693*	0.074	0.367	-0.061	0.455	-0.053	0.517	-0.170	**0.037***
Communication	0.248	**0.002***	-0.105	0.203	0.037	0.651	0.182	**0.025***	0.080	0.329
ADL/IADL	0.543	**0.001***	-0.215	**0.00***	0.020	0.804	0.063	0.441	0.088	0.285
Mobility	0.689	**0.001***	-0.090	0.275	0.086	0.294	0.235	**0.004***	0.121	0.141
Hand function	0.326	**0.001***	0.012	0.886	0.009	0.912	-0.110	0.181	-0.106	0.198
Social participation	0.294	**0.001***	0.034	0.679	-0.038	0.643	0.058	0.484	-0.082	0.318
Recovery	0.657	**0.001***	-0.136	0.098	0.122	0.137	0.225	**0.006***	0.100	0.223
Composite physical domain	0.736	**0.001***	-0.093	0.258	0.030	0.716	0.142	0.084	0.145	0.077
SIS total	0.550	**0.001***	-0.111	0.164	0.050	0.544	0.187	**0.022***	0.047	0.569
Spearman's Rho Correlation Analyse										

Table 5. Comparison of lesion localization and SIS domains.

SIS domains	Lesion Localization		P
	Right	Left	
	Mean±SD (Median)	Mean±SD (Median)	
Strength	17±16.9 (12.5)	14.63±16.59 (6.25)	0.215
Memory	62.44±27.6 (64.28)	79.83±20.42 (89.28)	0.001**
Emotion	38.43±15.78 (36.11)	39.87±14.65 (40.27)	0.650
Communication	52.07±27.56 (42.85)	72.82±23.56 (73.21)	0.001**
ADL/IADL	16.18±14.14 (20)	17.87±10.51 (20)	0.346
Mobility	10.86±14.78 (8.33)	7.31±11.3 (2.77)	0.006**
Hand Function	3.97±13.92 (0)	2.2±9.88 (0)	0.664
Social Participation	4.87±14.17 (0)	4.42±11.39 (0)	0.545
Recovery	44.41±22.88 (40)	40.61±22.41 (40)	0.336
Composite physical domain	12±12.94 (9.23)	10.5±9.91 (8.12)	0.185
SIS total	27.8±12.94 (26.10)	31.06±9.3 (29.89)	0.007**
Mann Whitney U Test	**p<0.01	SD:Standart Deviation	

DISCUSSION

In our study, we found no significant difference in the QOL parameters between the groups with and without CPSP. Nonetheless, QOL was poorly affected by advanced age, poor functional status, right hemiplegia, and the presence of pain in both groups.

CPSP is a complication of stroke that causes difficulties in treatment and rehabilitation compared to the other types of pain.[13] In a study by Andersen et al., the CPSP prevalence was found as 8%.[3] In another study conducted by Lundstrom et al. with 147 patients, it has been reported that 4% of patients had CPSP.[14] McGowan et al. have reported that CPSP had been developed within 6 months in 25% of patients in their study conducted with 63 patients with stroke.[15] In their study carried out for post-stroke pain definition and pain classification, Widar et al. have found CPSP in 15 (35%) out of 43 patients with stroke.[8] In our study, CPSP was identified in 23 out of 150 patients (15.3%), which is consistent with the literature.

Looking at the studies that examine the CPSP prevalence according to age groups; Harno et al. have reported that central pain is more common in young patients with stroke,[16] whereas Andersen et al. has found no difference in terms of mean age between the groups with and without CPSP in their study conducted with 267 patients with stroke3. Similarly, Leijon et al found no difference in terms of mean age as well.[17] Also in our study, there was no difference in patients with CPSP in terms of mean age.

As is known, factors such as functional status, age, socioeconomic level, psychological status, the presence of pain, and level of education affect the QOL in stroke. In a study by Abubakar et al., where the quality of life was assessed in 62 patients with stroke, the functional status, measured by the modified Rankin Scale, and depression were found to be the independent factors that affect the quality of life.[18] In their study that investigated the quality of life and disability in stroke, Patel et al. have found a positive correlation between BI, Frenchay Activity Index, and SF36 physical activity subscale.[19] In a study by Baumann et al., where they have investigated the QOL in 94 patients with stroke and 62 caregivers, a significant difference was found between the sleep, affectivity, cognitive level, sensation, and pain level parameters of Newcastle Stroke-specific Quality of Life Measure (NEWSQOL).[20] Raju et al. have investigated the quality of life and affecting factors using the World Health

Organization Quality of Life Scale (WHOQOL-BREF) in 162 patients with stroke, and have found a negative relationship between anxiety, depression, and QOL, and a positive correlation between functional independence measure scores and QOL as well as reporting that advanced age, severe stroke and the presence of depression results in reduced independence.[21] In our study, 97.3% of the patients were moderately or highly dependent, and there was a significant positive relationship between the QOL parameters (strength, communication, activities of daily living, mobility, hand function, social participation, recovery from a stroke) and functional status of these patients. According to these results, poor functional status had a negative impact on the QOL in patients with stroke.

Considering the studies that examine the quality of life in stroke and age, it is seen that QOL reduces with advanced age in general. Sharma et al. have reported that the QOL is lower in patients over 75 years of age, and have stated that these patients have more risk in terms of mortality.[22] Fernandez et al. have reported in their study conducted with 39 patients with stroke that social isolation increased as the age advances in the NHP.[23] Heikinheimo et al. have evaluated the QOL in 25 patients with stroke and reported that advanced age and poor functional status have a negative impact on QOL as well as reporting a negative correlation between advanced age and activities of daily living sub-parameter of NEWSQOL.[24] In our study, we also found a negative relationship between age and activities of daily living sub-parameter of stroke impact scale. It is observed that QOL is reduced as age increases.

There are some studies in the literature evaluating the relationship between the time elapsed after stroke and QOL. Kong et al. have found a correlation between age, time since onset, modified BI, and QOL in their study conducted with patients with stroke more than 1 year.[25] Kılıç et al. have evaluated the QOL in 100 patients with stroke and found a significant relationship between the time since onset and the NHP sub-parameters.[26] Guidetti et al. have assessed the QOL of 204 patients with stroke at 3rd and 12th months in their study, and have found a significant increase in mean strength, emotion, and recovery from stroke sub-scale scores of SIS.[27] In our study, a significant relationship was found between the time since onset and communication, mobility, and recovery from stroke domains.

The CPSP have been shown to adversely affect the QOL in many studies. In one study by Kwok et al., the presence of pain was found to have a negative impact on QOL.[28] In a recent study conducted by Tang et al. on 14 patients with CPSP, it was shown that the presence of pain caused by defective gamma-aminobutyric acid-ergic inhibition significantly negatively affects quality of life.[29] In another study carried out by Widar et al., the presence of pain in patients with stroke was found to have a negative correlation with sleep quality, physical condition, and mood status.[30] In our study, we also found a significant negative relationship between VAS scores and SIS emotion domain scores. The mood was deteriorating as the intensity of pain increases.
In the literature, among the studies that investigate the quality of life in stroke, there is one study that draws attention to the difference related to the affected side of the body. Wade et al., have reported in their study that the QOL was lower in the right hemiplegia group.[31] In the comparison of QOL patients with right and left hemiplegia in our study, the memory and communications domains of SIS were found to be higher in patients with left hemiplegia, as a result, QOL in this patient group is better compared to patients with right hemiplegia.

There are different scales for assessing the QOL in patients with CPSP. In the literature review, we haven't found any other study that uses SIS to assess the QOL in patients with CPSP. From this perspective, our work is valuable. In this study that we have assessed the CPSP, no significant difference was found between the patients with and without CPSP in terms of domains of SIS. This stems from the fact that stroke has a negative effect on the QOL, and SIS scores

in both groups were low.

In the present study, the main parameters that affect the QOL were poor functional status, post-stroke pain severity, advanced age, and the presence of right hemiplegia, which are consistent with the literature. Lower QOL also has a negative impact on the success and outcomes of rehabilitation.

Limitations

Since our study is a cross-sectional study, the long-term effects of CPSP on QOL could not be determined. Besides, these results are not representative of the entire stroke population since the stroke patients with cognitive impairment and speech problems were excluded from the research.

CONCLUSION

CPSP is one of the parameters that negatively affect the rehabilitation process and functional recovery in patients with stroke. It is of critical importance for clinicians to consider this condition and identify the presence of CPSP in the rehabilitation process. Implementation of specific and effective treatments for CPSP will have an important role in improving the quality of life of these patients.

Compliance with Ethical Standards

Conflict of Interest: The authors declare that they have no conflict of interest.

All procedures performed in studies involving human participants were following the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Additional informed consent was obtained from all individual participants for whom identifying information is included in this article.

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