

Original Article

Does the preoperative presence of central sensitization affect sleep quality and pain after total knee arthroplasty?

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ABSTRACT

Objectives: This study aims to investigate the presence of central sensitization before total knee arthroplasty (TKA) in patients with knee osteoarthritis, to explore its relationship with sleep quality after this surgery, and to evaluate postoperative pain intensity, neuropathic pain, anxiety, depression, and functional status.

Patients and methods: Between May 2022 and May 2023, a total of 31 patients (8 males, 23 females; mean age: 68.1±2.8 years; range, 62 to 73 years) who underwent a radiographic examination, had Stage 3-4 osteoarthritis based on the Kellgren-Lawrence classification, and had TKA indications at the discretion of the orthopedic surgeon were included in this single-center, one-group, quasi-experimental, prospective study. The Central Sensitization Inventory (CSI) and International Physical Activity Questionnaire-Short Form (IPAQ) were used to evaluate patients scheduled for TKA due to osteoarthritis of the related joint. The Visual Analog Scale (VAS), painDETECT, the Pittsburgh Sleep Quality Index (PSQI), the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), and the Hospital Anxiety and Depression Scale were applied to all patients preoperatively and at one and three months postoperatively.

Results: The postoperative PSQI, VAS, and painDETECT scores were significantly higher in those with central sensitization compared to non-central sensitization group after surgery ($p<0.001$). The CSI score had a positive correlation with the PSQI, VAS, and painDETECT scores, and a negative correlation with the preoperative IPAQ score ($p<0.05$).

Conclusion: Our study results suggest that, in patients with knee osteoarthritis waiting for TKA, central sensitization status has an adverse impact on postoperative pain and sleep quality.

Keywords: Arthroplasty, central sensitization, knee osteoarthritis, neuropathic pain, sleep quality.

Knee osteoarthritis is one of the most common joint diseases in patients over 65 years and its incidence increases with age.^[1] The primary complaints related to knee osteoarthritis are pain, decreased joint mobility, and functionality. As the condition progresses, sleep disturbances may develop with the addition of rest pain to the symptoms.^[2] Although total knee arthroplasty (TKA) is considered to be a cost-effective intervention for patients with end-stage knee osteoarthritis, both in terms of pain reduction and increased activity score,^[3] about 8 to 20% of the patients have persistent postoperative pain.^[4] In addition, sleep disturbances can be

observed at a rate reaching 50% in the postoperative period; however, the relationship between TKA and sleep quality has not yet been fully elucidated.^[5,6]

The presence of neuropathic pain or central sensitization before treatment may be related to the chronicity of pain after TKA.^[7] Although there is a study reporting that sleep disturbances increase after TKA, the majority of studies in the literature have shown an improvement in sleep quality in the post-TKA period.^[8] In addition to researchers indicating a positive correlation between pain intensity and sleep quality after TKA,^[9] there are also those who suggest that

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there is no such relationship.^[10] To the best of our knowledge, no studies are known to have investigated the relationship between preoperative central sensitization and postoperative sleep quality in patients with knee osteoarthritis. In the present study, we aimed to investigate the presence of central sensitization before TKA in patients with knee osteoarthritis, to explore its relationship with sleep quality after this surgery, and to evaluate postoperative pain intensity, neuropathic pain, anxiety, depression, and functional status.

PATIENTS AND METHODS

This single-center, one-group, quasi-experimental, prospective study was conducted at Ankara City Hospital, Department of Orthopedics and Traumatology between May 2022 and May 2023. The study included literate patients who underwent a radiographic examination, had Stage 3-4 osteoarthritis based on the Kellgren-Lawrence classification, and had TKA indications at the discretion of the orthopedic surgeon. Exclusion criteria were as follows: (i) central and peripheral nervous system diseases that may cause neuropathic pain, (ii) rheumatological diseases that may cause secondary osteoarthritis, (iii) a previous diagnosis of central sensitization, and (iv) mental disorders that would prevent the patient from participating in active treatment and cause a lack of insight and judgment. Finally, 31 patients (8 males, 23 females; mean age: 68.1 ± 2.8 years; range, 62 to 73 years) who met the inclusion criteria were recruited. Written informed consent was obtained from each patient. The study protocol was approved by the Ankara City Hospital Clinical Research Ethics Committee (Date: 09.03.2022, No: E-1-22-2378). The study was conducted in accordance with the principles of the Declaration of Helsinki.

Interventions

All patients received TKA with the same surgeon using a standard technique and while under spinal anesthesia. A conventional, posterior-stabilizing, cemented knee system (Stryker Triathlon; Stryker, Mahwah, NJ, USA) was used in all patients. For up to three days after surgery, 500 mg of paracetamol and/or 50 mg of tramadol hydrochloride were prescribed for pain control, as needed. The patients were allowed to walk using a walker from day one and to perform gradually increasing range of motion in-bed exercises.

Outcome measures

Demographics data of all patients involved in the study were collected. Central sensitization was evaluated with the Central Sensitization Inventory (CSI) and physical activity was assessed by the International Physical Activity Questionnaire-Short Form (IPAQ). The patients were also evaluated with the Visual Analog Scale (VAS) for pain before TKA as well as at one and three months after surgery, the painDETECT for neuropathic component of knee osteoarthritis-pain, Pittsburgh Sleep Quality Index-21 item version (PSQI), Western Ontario McMaster Universities Osteoarthritis Index (WOMAC) standard edition. The Hospital Anxiety and Depression Scale (HADS) was finally used to screen patients for anxiety and depression with this survey.

Central sensitization inventory: This tool is used, most specifically in cases of chronic pain and central sensitization syndromes to assess for presence of a central sensitivity. It measures two constructs: Part A is a 25-item Likert type scale on the frequency of symptoms. All questions were evaluated using a 0 (never) to 4 (always) scale. The total score can be 0 to 100 and a higher score equals greater central sensitization. Patients with a score of 40 or above are classified as having central sensitization. Part B is designed to establish whether the patient has a pre-existing diagnosis of central sensitization syndrome.^[11] The Turkish version of CSI has a study indicating its validity and reliability.^[12]

International Physical Activity Questionnaire-Short Form: This is an assessment to estimate the total physical activity of patients as part of daily living in metabolic equivalent of task (MET)-min/week. It comprises seven questions related to physical activity performed within the past seven days.^[13] A previous study has been undertaken to analyze the validity and reliability of IPAQ in Turkish.^[14]

Visual Analog Scale: A 10-cm VAS was given to all patients to detect their knee pain intensity. This was a 0 to 10 point Likert type scale; with 0 meaning no pain, and 10 representing the worst imaginable level of pain.

painDETECT: This assessment tool is designed to identify the existence and aspects of neuropathic pain. Scores at or below 12 indicate no neuropathic pain, while scores of 19 or above suggest a high likelihood of neuropathic pain, and scores between 12 and 19 indicate uncertainty. The Turkish version

of painDETECT has been previously examined in terms of validity and reliability.^[15]

Pittsburgh Sleep Quality Index: This inventory is used to evaluate sleep quality and disturbances within the past one month. The total score is obtained by summing the score of each of the following seven components: subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medication, and daytime dysfunction. The total score ranges from 0 to 21, and high scores indicate poor sleep quality.^[16]

A previous study has been undertaken to analyze the validity and reliability of PSQI in Turkish.^[17]

Western Ontario McMaster Universities Osteoarthritis Index: This specialized questionnaire is designed for individuals with hip or knee osteoarthritis. It contains 24 items divided into three subscales assessing pain, stiffness, and physical function. The maximum possible score is 20 for pain, 8 for stiffness, and 68 for physical function. Higher scores indicate more severe or worse symptoms, maximal limitations, and poor health.^[18] The Turkish

TABLE 1
Comparison of the patients according to the presence or absence of central sensitization

	Central sensitization present (n=12)			Central sensitization absent (n=19)			p
	Mean±SD	Median	IQR	Mean±SD	Median	IQR	
Age (year)	67.5±3.7			68.4±2.1			0.42a
Body mass index (kg/m ²)	26.8±2.1			27.5±2.1			0.43a
IPAQ		3,780	2,455-3,909		6,366	2,700-8,520	0.08b
PSQI							
Preoperative	9.2±2.3			6.9±1.9			0.006^a
Month 1	14.9±3.9			6.4±1.7			<0.001^a
Month 3	8.5±3.2			3.2±1.4			<0.001^a
p ^c (post-hoc)		<0.001 (2>1=3)			<0.001 (3>1=2)		
HADS-anxiety							
Preoperative		6	3-11		6	3-6	0.38 ^b
Month 1		4	2-6		3	2-5	0.73 ^b
Month 3		3	0-4		3	1-4	0.36 ^b
p ^d (post-hoc)		<0.001 (2>1=3)			0.004 (1=2>3)		
HADS-depression							
Preoperative		3	2-6		4	2-5	0.84 ^b
Month 1		1	0-2		2	1-4	0.23 ^b
Month 3		1	0-3		2	1-3	0.34 ^b
p ^d (post-hoc)		0.004 (1>2=3)			<0.001 (1>2=3)		
VAS							
Preoperative	7.8±1.4			7.3±0.8			0.28 ^a
Month 1	5±1.8			4.2±1.1			0.18 ^a
Month 3	4.2±1.4			1.3±1.8			<0.001^a
p ^c (post-hoc)		<0.001 (1>2=3)			<0.001 (1>2>3)		
painDETECT							
Preoperative	11.1±4.1			9.0 ±2.6			0.13 ^a
Month 1	7.5±3.4			4.3±2.6			0.08^a
Month 3	6.5±3.5			1.2±2.0			<0.001^a
p ^c (post-hoc)		0.006 (1>2=3)			<0.001 (1>2>3)		
WOMAC							
Preoperative		54.6	37.5-64.8		43.66		0.10 ^b
Month 1		12	0-29		2		0.32 ^b
Month 3		5	0-22		2		0.70 ^b
p ^d (post-hoc)		<0.001 (1>2>3)			<0.001 (1>2>3)		

SD: Standard deviation; IQR: interquartile range; IPAQ: International Physical Activity Questionnaire-Short Form; PSQI: Pittsburgh Sleep Quality Index; HADS: Hospital Anxiety and Depression Scale; VAS: Visual Analog Scale; WOMAC: Western Ontario and McMaster Universities Arthritis Index; ^a Independent-samples t-test; ^b Mann-Whitney U test; ^c Repeated-measures test; ^d Friedman's test. In post-hoc analyses, the numbers indicate that; 1: Preoperative; 2: Month 1; 3: Month 3.

version of WOMAC has been previously investigated in terms of validity and reliability.^[19]

Hospital Anxiety and Depression Scale: This questionnaire, aimed at assessing anxiety and depression, consists of 14 items, evenly split with seven items each for depression and anxiety. Separately collected scores for depression and anxiety are noted as normal (0-7), borderline (8-10) and abnormal (11 and above).^[20] Aydemir et al.^[21] contributed the Turkish version of this scale to the literature by conducting Turkish validity and reliability analyses.

Statistical analysis

Power analysis and sample size calculation were performed using the G*Power version 3.0.10 software (Heinrich-Heine-Universität Düsseldorf, Düsseldorf, Germany). The sample size estimation was based on the postoperative CSI score from a previous study,^[22] giving 22 patients required per group at level of significance $\alpha=0.05$ and power $\beta=80\%$. In all, 34 patients were screened for eligibility and eventually 31 qualified by both the inclusion criteria as well as follow-up in the study.

Statistical analysis was performed using the IBM SPSS version 23.0 software (IBM Corp., Armonk, NY, USA). Normal distribution was evaluated by histogram, detrended normal, and Q-Q plot visualizations and coefficient of variation, skewness and kurtosis analyses, and the Shapiro-Wilk test. Continuous data were expressed in mean $\pm$ standard deviation (SD) or median and interquartile range (IQR), while categorical data were expressed in number and frequency. In the presence of normal data distribution, repeated measures test and paired samples t-test were utilized in the analysis of follow-up data within groups. If the data were not normally distributed, this assessment was undertaken with Friedman and Wilcoxon signed-rank tests. The comparison of the two groups was carried out by independent sample t-test for quantitative data in the existence of normally distributed data, otherwise by Mann-Whitney U test. The Spearman correlation test was utilized to investigate the correlation among the data. A p value of <0.05 was considered statistically significant.

RESULTS

According to HADS, three patients had abnormal and two had borderline scores for anxiety, and one patient had a borderline score for depression. In the

evaluation with CSI, the rate of patients with central sensitization was 38.7% ($n=12$). Table 1 presents the pre- and postoperative first- and third-month data of the patients with or without central sensitization. The sleep quality as measured by PSQI was particularly poorer in patients with preoperative central sensitization ($p=0.006$), and it remained after surgery resulting even a statistically significant difference compared to the group without central sensitization ($p<0.001$). The VAS and painDETECT scores at the third month were significantly higher in central sensitization group than non-central sensitized ($p<0.001$).

The correlation analysis of central sensitivity with pre- and postoperative scores indicated a significant positive relation between the CSI score and the PSQI (moderate correlation at preoperative term, strong correlation at one and three months), VAS (moderate correlation at one month, strong correlation at three months), and painDETECT (moderate correlation at one month, strong correlation at three months) scores. Additionally, the CSI score was negatively moderately correlated with preoperative IPAQ results. The findings of the correlation analysis can be seen in detail in

TABLE 2
Correlation analysis of the CSI score

IPAQ	rho	-0.475
Preoperative	p	0.007
PSQI	rho	0.443
Preoperative	p	0.013
PSQI	rho	0.806
Month 1	p	<0.001
PSQI	rho	0.788
Month 3	p	<0.001
VAS	rho	0.149
Preoperative	p	0.423
VAS	rho	0.481
Month 1	p	0.006
VAS	rho	0.781
Month 3	p	<0.001
PainDETECT	rho	0.204
Preoperative	p	0.271
PainDETECT	rho	0.592
Month 1	p	<0.001
PainDETECT	rho	0.756
Month 3	p	<0.001

CSI: Central Sensitization Inventory; IPAQ: International Physical Activity Questionnaire-Short Form; PSQI: Pittsburgh Sleep Quality Index; VAS: Visual Analog Scale. Spearman correlation.

Table 2. The CSI score showed no correlation with the HADS and WOMAC scores.

DISCUSSION

In the present study, we investigated the presence of central sensitization before TKA in patients with knee osteoarthritis and explored its relationship with sleep quality after this surgery. Our study results showed that patients with knee osteoarthritis who had central sensitization preoperatively had worse postoperative pain, higher neuropathic pain intensity, and poorer sleep quality. There was no significant difference in functional status between the groups with and without central sensitization; however, pain and sleep score differences were greater, notably at the postoperative third month. The patients with preoperative central sensitization had high sleep disturbance scores and low physical activity scores.

Multiple studies have identified patients with preoperative neuropathic pain or central sensitization to be at higher risk for the development of postoperative pain.^[7] Central sensitization has been associated with poor postoperative functional status, greater pain intensity, depression, and anxiety.^[23] It has been emphasized that, in hip and knee joint replacement surgery, the self-reported assessment of central sensitization, such as CSI, may be more optimal than the assessment of the pressure pain threshold.^[24] Similarly, we used CSI to determine central sensitization in our study. In a previous study evaluating the relationship between central sensitization and postoperative recovery, the former had a negative correlation with the amelioration in quality of life scores and pain activity in patients who underwent TKA.^[25] There are also other studies in the literature indicating high central sensitization levels, high pain intensity, and analgesic requirements after TKA.^[22,26] However, it has been suggested that high central sensitization levels have no effect on functional status.^[26] In the current study, the intensity of post-TKA pain and neuropathic pain was higher in patients who had central sensitization. The increase in pain intensity was observed to be significant at three months. No significant difference was found in functional status. As the central sensitization scores increased, pain and neuropathic pain intensity increased at one and three months. This finding demonstrates the necessity of evaluating central sensitization preoperatively for the treatment to be successful.

With future studies focusing on the addition of central sensitization to TKA, poor postoperative outcomes can be prevented.

In the literature, the majority of studies have shown that the treatment of knee osteoarthritis with TKA improves sleep quality, particularly through the reduction of pain at rest and at night.^[8] Sleep quality, which particularly deteriorates in the postoperative period, starts to improve from the third month.^[8] In addition to studies reporting a correlation between the VAS and PSQI scores after TKA,^[9] there are also those which did not detect a correlation between pain intensity and sleep quality.^[10] In a study including a patient group that underwent TKA and a control group, the PSQI scores were compared at the first postoperative month and there was a significantly superiority in the TKA group.^[27] In the literature, we found no evidence for preoperative central sensitization among patients undergoing TKA. However, in one study, the effect of preoperative sleep quality on postoperative findings was examined, and it was found to be interrelated with postoperative pain, function, and sleep quality.^[28] Unlike the literature, in our study, preoperative sleep quality was lower in the presence of central sensitization, and there was a significant difference compared to non-central sensitization group, particularly at the first postoperative month, which sustained through to the third month. In addition, as central sensitization scores increased, both pre- and postoperative sleep quality deteriorated. Although it has been shown that the presence of sleep disorder causes an increase in pain intensity and the sensitization of peripheral and central pain in healthy individuals, this situation is not as clear in individuals with chronic pain.^[29] Nevertheless, sleep disturbances constitute an important component of the disease cluster defined as central sensitization syndromes.^[30] In our study, we observed that the risk of postoperative sleep disturbances increased, if central sensitization was present preoperatively. Any intervention for central sensitization prior to TKA may reduce the risk of postoperative sleep disturbance development. In the presence of chronic pain and central sensitization, a multimodal treatment including exercise therapy is recommended.^[31] Although we found that the physical activity score was less in the central sensitization group, this difference did not reach statistical significance. However, a negative correlation was found between central sensitization scores and physical activity scores.

In these patients, a preoperative intervention could have changed their postoperative outcomes. The addition of increased physical activity or exercise therapy to treatment can help to intervene in not only central sensitization but also pain intensity and sleep disturbances. Thus, more successful TKA outcomes can be achieved. Future studies may shed light on this issue.

The main strength of our study is that it is the first to assess the effect of pre-TKA central sensitization on postoperative sleep disturbances. However, the study also had certain limitations. Using more objective assessment methods, such as polysomnography, to assess sleep quality could have provided stronger results. Another limitation is the lack of long-term postoperative evaluation beyond three months.

In conclusion, the presence of preoperative central sensitization adversely affects postoperative pain and sleep quality in patients with knee osteoarthritis who are scheduled for TKA. The evaluation of the presence of central sensitization and intervention before TKA may improve postoperative success. Nonetheless, there is still a need for further studies to explore treatment interventions for central sensitization.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

Author Contributions: Conception, design, supervision, data analysis, interpretation, literature review, manuscript writing: B.M.K.; Resources, materials, data collection, data analysis: U.Ö.; Design, resources, materials, data collection: İ.B.; Conception, resources, supervision: D.A.Ö. All authors critically revised and approved the final manuscript.

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