

Pain at Rest as a Predictive Factor of Chronic Pain Related to Central Sensitization in Patients With Hip Osteoarthritis

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Abstract

Background

Central sensitization (CS) has been identified as a factor that induces chronic pain in patients with osteoarthritis (OA). Although there are some reports of CS in knee OA, studies on CS in hip OA are lacking. We aimed to evaluate chronic pain related to CS in patients with hip OA using the CS Inventory (CSI). Additionally, we aimed to clarify the characteristics of patients with pain related to CS.

Methods

A total of 100 patients scheduled to undergo total hip arthroplasty (THA) for hip OA were retrospectively reviewed. We investigated the CSI score as an assessment of the extent to which the patients had pain related to CS. Additionally, we assessed the relationships between the CSI score and clinical factors, including age, duration of pain, degree of pain at rest and on activity, by using the visual analogue scale (VAS) and the Harris Hip Score.

Results

The mean CSI score was 19.54 ± 11.25 points. Twenty-one percent of the patients with a score of ≥ 30 were diagnosed as having chronic pain related to CS. The CSI score correlated significantly only with the VAS pain score at rest ($r = 0.348$, $P < 0.001$). Fifteen patients were diagnosed with CS syndromes (CSSs) in the assessment of CSI Part B. The mean CSI score was significantly higher in patients diagnosed with CSSs (30.00 ± 12.50) than in patients without a CSS (17.70 ± 10.00 ; $P < 0.001$).

Conclusion

Twenty-one percent of the patients scheduled to undergo THA for hip OA were diagnosed with chronic pain related to CS, which might influence the clinical results after THA. As the VAS pain score at rest was significantly correlated with the CSI score, pain at rest might be a predictive factor of chronic pain related to CS in patients with hip OA.

Background

Osteoarthritis (OA) is a heterogeneous disease, characterised by progressive cartilage loss, subchondral bone remodelling, osteophyte formation, and synovial inflammation, with resultant joint pain and increasing functional disability. Patients with persistent pain due to OA complain of multiple symptoms that cannot be explained solely by structural changes. It has been reported that there is a poor correlation between structural and inflammatory changes in OA and pain levels.[1] Although the determinants of pain in OA are poorly understood, they are believed to involve multiple interactive pathways that are best

explained by a biopsychosocial framework, which includes biological, psychological, and social factors. [2, 3]

We have occasionally encountered cases of patients with OA who complain of severe pain at rest. Previous research suggests that OA-related pain at rest and on activity are weakly correlated.[4, 5] However, the mechanism of the discrepancy between pain at rest and pain on activity remains unclear.

In 2011, the International Association for the Study of Pain defined central sensitization (CS) as increased responsiveness of nociceptive neurons in the central nervous system to normal or subthreshold afferent input. CS results from persistent, intense nociceptor stimulation that triggers changes in the central pain transmitting neurons, leading to alterations in pain presentation and perception, and centrally mediated symptoms, such as fatigue and mood disorders.[6] Over the last several decades, many authors have reported CS as one of the mechanisms underlying various chronic pain disorders, including headache, whiplash pain, musculoskeletal pain, low back pain, visceral pain, vulvodynia, prostatitis, etc.[7] CS has also been reported as a chronic pain factor in patients with OA.[8, 9] Patients with chronic pain with a CS component have been reported to be resistant to conservative treatment, including traditional pain medication and physiotherapy.[10–12] Moreover, preoperative central modulation of pain is associated with poor outcomes after total knee arthroplasty.[13] Thus, surgeons should be attentive to patients with suspected CS involvement before surgery, as such patients might be at risk for unfavourable outcomes. However, evidence regarding the identification of CS is scarce, especially in patients with hip OA.

Therefore, we aimed to evaluate chronic pain related to CS in patients with hip OA before total hip arthroplasty (THA). Furthermore, we aimed to clarify the predictive factors of chronic pain related to CS in patients with hip OA by evaluating the characteristics of patients with and without CS involvement. It might be unknown factors which induce poor outcome after THA.

Methods

Ethical approval was obtained from our Institutional Review Board, and the study was performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. The requirement for informed consent was waived because of the retrospective study design.

Patients

A total of 100 consecutive patients diagnosed with hip OA who were scheduled to undergo THA between November 2018 and September 2019 were retrospectively included in this study. Patients who were not diagnosed with hip OA and/or previously underwent a hip surgery on the same laterality were excluded.

For all patients, data of age, sex, and clinical assessments (the duration of hip pain (in months), severity of pain, and clinical scores) were collected at a preoperative outpatient clinic one month before surgery.

The severity of OA-related pain at rest and on activity was assessed using a numeric visual analogue scale (VAS). The severity was also evaluated clinically by the Harris Hip Score (HHS).

Assessment of CS involvement

Researchers have proposed various possible mechanisms to clarify the existence of a CS component using technological developments such as (functional) magnetic resonance imaging, quantitative sensory testing, and the measurement of cytokine and neurotransmitter levels.[8, 9, 14–16] In addition, the CS Inventory (CSI) was recently developed as a comprehensive screening tool with high reliability and reproducibility to identify the existence of a CS component.[17, 18] The CSI is a simpler and more cost-effective detection method than other previously developed methods. The CSI comprises 2 parts: A and B. Part A is composed of 25 self-reported items that are scored from 0 to 100 points. Part A is designed to evaluate symptoms associated with CS. Part B screens for previous diagnoses of one or more specific disorders, including seven separate CS syndromes (CSSs) (e.g., fibromyalgia, chronic fatigue syndrome, temporomandibular joint disorder, irritable bowel syndrome, migraine or tension headaches, multiple chemical sensitivities, and restless leg syndrome). CS involvement is strongly suggested in these seven disorders, and a comprehensive disease concept, known as CSS, has been proposed.[19, 20] Thus, the CSI was used as measure of CS involvement in the present study.

We provided an explanation of the Japanese version of the CSI (both parts A and B) to the patients, and the patients completed the CSI by themselves. Tanaka et al. reported that the Japanese version of the CSI is a useful and psychometrically sound tool, comparable to the English version, for assessing CSSs in Japanese patients with musculoskeletal disorders.[21] The CSI Part A score was divided into five categories with increasing severity: subclinical (0–29), mild (30–39), moderate (40–49), severe (50–59), and extreme (60–100). As Neblett et al. reported that a CSI score over 30 might be indicative of the presence of CS,[22] we determined the number of patients with a CSI score of 30 points or above, as well as those with a score of 40 points or above. The CSI Part B was also completed to evaluate the prevalence of CSSs in the patients. Furthermore, the prevalence of patients with one or more CSSs was investigated.

Statistical analyses

Results are expressed as the mean and the standard deviation of the mean unless otherwise indicated. A sample size calculation was performed based on the study's main objective, which was to evaluate the correlation between CSI scores and significant variables. The minimum power level was set at 0.95. It was determined that we needed to include 97 patients to satisfy the expected effect size. Therefore, our sample size of 100 patients was deemed adequate. The relationships between the CSI score and age, duration of hip pain, VAS pain at rest, VAS pain on activity, and HHS were evaluated using the Spearman's correlation coefficient. In addition, CSI scores in patients with and without CSSs were compared using the Mann-Whitney U test. All statistical analyses were performed using Statistical Package for the Social Sciences software (version 25.0, IBM, NY, USA). P values < 0.05 were considered to indicate statistical significance.

Results

Patient demographics and clinical assessments are summarised in Table 1. The mean age was 63.92 ± 11.60 years, and there were 15 men and 85 women. All patients had hip OA, categorised as advanced and terminal stage on preoperative plain radiography. The mean duration of hip pain was 50.45 ± 53.09 months. The mean VAS score was 3.15 ± 2.73 for pain at rest and 6.06 ± 2.48 for pain on activity. The mean VAS score was significantly higher for pain on activity than for pain at rest ($P < 0.01$).

Table 1
Patients' demographics and clinical assessments (N = 100)

	Mean (SD) or N = %
Sex	Male:15, Female:85
Age (years)	63.92 (11.60)
Tönnis grade	0:0 1:0 2:23 3:77
Duration of hip pain (months)	50.45 (53.09)
VAS pain at rest	3.15 (2.73)
VAS pain on activity	6.06 (2.48)
HHS	47.4 (12.99)
CSI score	19.54 (11.25)
CSI: Central Sensitization Inventory, VAS: Visual Analogue Scale, HHS: Harris Hip Score, SD: standard deviation	

The mean CSI score was 19.54 ± 11.25 (Table 1). The classification of CS severity level according to the scoring in CSI Part A is shown in Table 2. Seventy-nine patients were classified as subclinical (score: 0–29), 16 were classified as mild (score: 30–39), 3 were classified as moderate (score: 40–49), 2 were classified as severe (score: 50–59), and none were classified as extreme (score: 60–100). Twenty-one percent of the patients had a score of 30 or more points, and 5% of the patients had a score of 40 or more points. Prevalence rates of CSS diagnoses according to CSI Part B are shown in Table 3. Fifteen percent of the patients were diagnosed with one or more CSSs. The variables associated with the CSI score among all patients are shown in Table 4. The CSI score significantly correlated with the VAS score for pain at rest ($r = 0.348$, $P < 0.001$). However, other factors, including age, duration of hip pain, VAS score for pain on activity, and HHS, were not significantly associated with the CSI score. Additionally, the CSI score was significantly higher in patients with one or more CSSs (30.00 ± 12.50) than in patients without a CSS diagnosis (17.70 ± 10.00 ; $P < 0.001$) (Table 5).

Table 2
The classification of CS severity level according to the CSI
Part A score

CSI score	N = %
Subclinical (0–29)	79
Mild (30–39)	16
Moderate (40–49)	3
Sever (50–59)	2
Extreme (60–100)	0
30 or above	21
40 or above	5
CSI: Central Sensitization Inventory, CS: Central Sensitization	

Table 3
The prevalence rates of CSSs and the number of
patients with at least one CSS

CSS Diagnoses	N = %
Restless leg syndrome	0
Chronic fatigue syndrome	0
Fibromyalgia	0
Temporomandibular joint disorder	3
Migraine or tension headaches	3
Irritable bowel syndrome	3
Multiple chemical sensitivities	1
Neck injury including whiplash	4
Anxiety or panic attacks	1
Depression	5
Number of patients with at least one CSS	15
CSSs: Central Sensitization Syndromes	

Table 4
Variables associated with the CSI score among all patients with hip osteoarthritis

	Age	Duration of hip pain	VAS pain at rest	VAS pain on activity	HHS	CSI score
Age	—					
Duration of hip pain	-0.158	—				
VAS pain at rest	-0.109	0.173 *	—			
VAS pain on activity	-0.170	0.014	0.392 ***	—		
HHS	0.010	0.057	-0.211 *	-0.255 *	—	
CSI score	-0.185	0.159	0.348 ***	0.180	-0.155	—
VAS: Visual Analogue Scale, HHS: Harris Hip Score, CSI: Central Sensitization Inventory; Data are Spearman's rho correlation coefficients. Statistically significant P values (< 0.05) are underlined.						
*P < 0.05, **P < 0.01, ***P < 0.001						

Table 5
The relationship between parts A and B of the CSI: comparison of the mean CSI part A score between patients with and without CSSs on part B

	N = %	Mean CSI score (SD)
No CSSs	85	17.70 (10.00)
CSSs	15	30.00 (12.50) ***
CSSs: Central Sensitization Syndromes, CSI: Central Sensitization Inventory, SD: standard deviation; Statistically significant P values (< 0.05) on Mann-Whitney U tests are underlined.		
*P < 0.05, **P < 0.01, ***P < 0.001		

Discussion

This study was evaluated chronic pain related to CS in patients with hip OA before THA and evaluated the characteristics of patients with and without CS involvement to identify the predictive factors of chronic pain related to CS. In the present study, 21% and 5% of the included patients who were scheduled to undergo THA had CSI scores of at least 30 and 40 points, respectively. CSI scores between 30 and 39 points are classified as mild and considered to indicate the presence of CS.[22] Furthermore, a CSI score of 40 or more points are considered as the best predictors of patients with CSSs. Pain with a CS component, as determined by the CSI, has been reported to influence the clinical outcome in OA, for both conservative and operative treatments. Kim et al. found that patients with high CSI scores (≥ 40) before knee arthroplasty report more severe postoperative pain intensity.[23] Additionally, Benett et al. reported

that patients with CSI scores ≥ 40 before vertebral fusion surgery exhibit higher patient-reported disability scores after surgery.[24] THA is recognised as a feasible treatment for hip OA, with great advantages in terms of early rehabilitation and recovery in the activities of daily living.[25] However, about 10% of the patients who undergo THA complain of persistent pain and poor outcomes at long-term follow-up.[26, 27] Although the patient satisfaction after THA correlates best with pain,[28] the causes of pain after THA might be multifactorial and remain unclear. To our best knowledge, no study has reported THA clinical outcomes in patients with CS-related pain. From our results, it should be noted that a certain number of patients with hip OA have CS-related pain, which might influence postoperative outcomes.

Moreover, we clarified that a significant relationship exists between pain at rest and CSI scores in patients with hip OA in this study. In patients with OA, pain on activity might be a common phenomenon, while pain at rest may sometimes occur with a variety of pain complaints (e.g., from a dull ache to a sharp, stabbing pain).[29] Since the presence and severity of joint pain correlate poorly with structural evidence of joint damage,[1] a variety of different mechanisms might contribute to the occurrence of pain in OA. Results of functional brain imaging studies suggest that pain at rest (or spontaneous pain) is associated with distinct patterns of abnormal brain activity.[30, 31] Creamer et al. reported that a relatively high pain at rest, but not on activity, was associated with decreased pain thresholds in patients with knee OA.[32] Lundblad et al. reported that high preoperative VAS pain at rest was associated with the presence of CS component and was also associated with less pain relief at 18 months after TKA.[4] Kadum et al. reported less functional improvement in patients who underwent total shoulder arthroplasty among those with higher preoperative pain at rest.[33] Despite differences in the targeted joints, pain at rest is considered to be more representative of a CS component than pain on activity. Based on the present study results, pain at rest might also be a predictor of CS-related pain in patients with hip OA.

The CSI was developed as a comprehensive screening tool for identifying the presence a CS component, as well as the presence of CSSs, with a high test-retest reliability.[17, 18] We used the CSI to indicate CS involvement because it is simpler, less expensive, and more non-invasive than previous methods. However, there are limited reports regarding the identification of CS using the CSI in patients with OA, and there are no reports regarding hip OA. Therefore, we evaluated the relationship between CSI Parts A and B to check the validity of the CSI score in patients with hip OA in this study. The patients diagnosed with one or more CSSs (30.00 ± 12.50) on Part B scored significantly higher on Part A than did those without a CSS diagnosis (17.70 ± 10.00 ; $p < 0.001$). Consequently, the CSI should be considered to be a valid scoring system to clarify the existence of a CS component in patients with hip OA. The present study has several limitations to acknowledge. First, although we determined the necessary sample size with a power analysis, the sample size was relatively small. Second, this study had a cross-sectional design. Although we have clarified that a certain number of patients with hip OA have a CS component in the current study, the relationship between preoperative CS component and postoperative clinical results remains unclear. A prospective longitudinal study will be needed to evaluate these relationships.

Conclusions

Twenty-one percent of the patients scheduled to undergo THA for hip OA had a CSI score of 30 or more points. Thus, a certain number of patients with hip OA have a CS component. Since CS might influence clinical outcomes, the existence of CS should be evaluated and noted. As the VAS score for pain at rest was significantly associated with the CSI score, pain at rest might be a predictive factor of chronic pain related to CS in patients with hip OA.

List Of Abbreviations

OA: osteoarthritis; CS: central sensitization; THA: total hip arthroplasty; VAS: visual analogue scale; HHS: Harris Hip Score; CSI: Central Sensitization Inventory; CSS: central sensitization syndrome;

Declarations

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Availability of data and materials

The datasets supporting the conclusions of this article are included within the article. The raw data can be requested from the corresponding author.

Authors' contributions

YO, KF, GI contributed to the conception and design the study. YO and KF wrote the manuscript. YO, KF, TK, MT, KaU, and NT participated in the data collection, and did the statistical analysis. GI and KeU edited the manuscript. MT supervised the study. All authors read and approved the final manuscript.

Ethical approval and consent to participate

This study was approved by the Ethics Review Board of Kitasato University (reference number: B 20-096). The study was performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. Written consent to participate was not applicable for this retrospective study.

Consent for publication

Not applicable

Competing interests

The authors declare that they have no competing interests.

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