

ORIGINAL ARTICLE

Central Sensitization and Postoperative Improvement of Quality of Life in Total Knee and Total Hip Arthroplasty: A Prospective Observational Study

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Background: While total knee arthroplasty (TKA) and total hip arthroplasty (THA) lead to excellent clinical outcomes, some patients experience residual surgical site pain and reduced satisfaction. This prospective observational study investigated the prevalence of preoperative and postoperative residual central sensitization (CS) after TKA and THA. The influence of residual CS on the improvement in quality of life (QOL) was also investigated. **Methods:** The participants were 40 patients who underwent TKA and 47 patients who underwent THA. CS was measured using the central sensitization inventory (CSI) questionnaire. Knee symptoms were evaluated using the Knee Injury and Osteoarthritis Outcome Scales (KOOS), and hip symptoms were evaluated using the Japanese Orthopedic Association Hip-disease Evaluation Questionnaires (JHEQ). General QOL was evaluated using EuroQOL (EQ-5D-5l). Regression analysis was performed to estimate factors related to low QOL after surgery. **Results:** Preoperatively, 47.5% of TKA patients and 66.0% of THA patients were CS positive ($P=0.083$), which reduced to 10.0% ($P=0.042$) and 25.5% ($P=0.202$), respectively, 3 months after surgery. Although the improvements in KOOS subscales and EQ-5D-5l scores in TKA patients with residual CS were significantly lower than in those without residual CS, residual CS status had no effect on JHEQ subscales and EQ-5D-5l scores in THA patients. Regression analysis indicated that EQ-5D-5l was negatively correlated with CSI in the TKA group ($P=0.017$). In contrast, CSI was not correlated with EQ-5D-5l in the THA group ($P=0.206$). **Conclusion:** Postoperative QOL improvement was achieved 3 months after THA regardless of residual CS status. In contrast, preoperative CS was negatively associated with the improvement in QOL after TKA.

Key Words: central sensitization; quality of life; total hip arthroplasty; total knee arthroplasty

INTRODUCTION

Both total knee arthroplasty (TKA) and total hip arthroplasty (THA) are established surgical procedures for severe knee and hip osteoarthritis that lead to excellent outcomes and patient satisfaction.¹⁻⁴ However, despite favorable clinical outcomes, there remain discrepancies between postoperative subjective and objective scales, with patient-

based outcome scores and satisfaction being relatively low in some cases.⁵⁻⁷ Some patients reportedly experience residual surgical site pain and chronic postsurgical pain (CPSP).⁸ A systematic review reported that 8.0–26.5% of TKA recipients and 4.8–20.5% of THA recipients reported postoperative residual pain.⁹

As one of the key causative factors of CPSP, central sensitization (CS) is a potential therapeutic target.¹⁰ CS influences

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sensitivity and the spread of pain via enhanced responsiveness of nociceptors.^{11–14} Despite the high prevalence of CS in end-stage OA, estimated as 20%,¹⁵ the relationship between the severity of CS and recovery after surgery and clinical outcomes remains unclear. Furthermore, postoperative satisfaction among THA recipients is reportedly superior to that of TKA recipients.^{16–18} The influence of CS or other related intrinsic psychological background factors on postoperative clinical outcomes following TKA and THA is not fully understood.¹⁹

This study aimed to investigate the prevalence of preoperative and postoperative residual CS after TKA and THA. Furthermore, the influence of residual CS on improvements after surgery was also investigated. We hypothesized that residual CS is more common in TKA patients than in THA patients and leads to inferior postoperative outcomes.

MATERIALS AND METHODS

Patients

We prospectively enrolled patients who underwent primary TKA or primary THA at our institution between January 2018 and March 2019. Inclusion criteria for TKA were patients with Kellgren-Lawrence grade 3 and 4 who underwent primary TKA for end-stage knee OA, regardless of their age. Also, the inclusion criteria for THA were primary or secondary hip OA with Kellgren-Lawrence grade 3 and 4 with no dislocation or acute hip fracture. Patients who underwent revision surgery and those with joint infection, lateral type knee osteoarthritis, osteonecrosis of the femoral head, undertreatment of rheumatoid arthritis or psychiatric disease, and any malignancy, were excluded. Finally, a total of 40 TKA patients (6 men and 34 women) and 47 THA patients (1 man and 46 women) were included. This study was performed in accordance with the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards. All participants gave their written informed consent, and the study was conducted with the approval of the Ethics Committee of Hirosaki Memorial Hospital (2018–01).

Surgical Procedures for TKA

Cruciate-substitute TKAs were performed using the measured resection technique without a navigation system. A medial parapatellar approach was used to expose the knee. Femoral osteotomy was done using an intramedullary guide. The tibial osteotomy was done using an extramedullary guide with a varus/valgus of 0° and a slightly posterior slope. The gap distance was measured with a tensor. The soft tissue

balance was adjusted for straight alignment with minimized medial soft tissue release in a step-by-step manner such that the medial and lateral gap difference was less than 3 mm at both full extension and 90° flexion. Finally, the components were implanted using a cementless technique.

Surgical Procedures for THA

Antero-lateral approach THAs were performed without a navigation system with the patient in the supine position. The target angles of cup insertion were 40° inclination and 15° anteversion (radiographic definition). The femur was placed in extension, external rotation, and adduction for femoral stem insertion. Intraoperative fluoroscopic images were captured to examine cup positioning, femoral component size, and alignment. Leg length was determined using the cup-head traction distance during traction in the neutral position. Anterior stability was assessed by measuring 20° extension and maximum external rotation. Posterior stability was assessed by measuring 90° flexion and maximum internal rotation.

The standard postoperative rehabilitation program involved weight bearing (as tolerated with a walking aid) starting from the day after surgery for both TKA and THA patients. All patients were allowed to perform full weight bearing and were discharged after ensuring stable/healed surgical wounds and adequate mobility to perform daily activities.

Evaluation of Central Sensitization

CS was evaluated using the central sensitization inventory (CSI).²⁰ This self-report questionnaire exhibits satisfactory psychometric strength, clinical utility, and initial construct validity. The complete version comprises 25 items. However, we also used a shorter version consisting of nine items (CSI-9) that was locally available. Scores were assigned from 0 (best) to 4 (worst) for each item. The maximum total score was 100 points for the full version of the CSI and 36 points for CSI-9, wherein a higher score indicates more severe CS. CSI-9 has been validated using Spearman's correlation coefficient ($r=0.91$) with respect to the full version of CSI.²¹ Based on this previous report,²¹ we assigned patients to the CS group if they scored 10 points or higher on CSI-9.

Patient Satisfaction

To further evaluate the health-related quality of life (HR-QOL) of patients, we used EuroQoL-5-dimensions 5-levels (EQ-5D-5l) in the form of self-reported questionnaires.²² Among generic scales, the EQ-5D-5l has been widely used

to measure HR-QOL in patients with OA.^{23,24} The EQ-5D-5/ self-report questionnaire measures five domains of HR-QOL, namely mobility, self-care, usual activities, pain/discomfort, and anxiety/depression.²² Each of the five domains is assessed by a single question with three response levels (no problem, some problems, and extreme problems). These results are coded and converted to a useful score with the help of tables of values.²⁵ The EQ-5D-5/ scoring algorithm was first developed using time trade-off-based preference scores for a sample of these health states from a representative sample of the UK general population²²; the Japanese version of the EQ-5D-5/ has also been validated against the English version.²⁵ This EQ-5D-5/ algorithm is used worldwide and can yield scores ranging from -0.111 to 1.000, wherein negative scores represent health states worse than being dead, 0 represents being dead, and 1.00 represents a state of complete health.

Evaluation of Knee Symptoms

TKA patient-reported outcome measures were evaluated using the Knee Injury and Osteoarthritis Outcome Scales (KOOS).^{26,27} KOOS consists of 42 knee-related items, and each item is scored from 0 to 4. Summed scores in five subscales (symptoms, pain, activities of daily living, sports, and QOL) are converted to 100 points as the best condition. Due to limitations with respect to postoperative activity, KOOS sports items were not considered in this study.

Evaluation of Hip Symptoms

Patient-reported outcomes were evaluated using the Japanese Orthopedic Association Hip-Disease Evaluation Questionnaires (JHEQ) for THA patients.²⁸ The JHEQ is a validated self-administered questionnaire for evaluating the quality of life of Asian patients with hip diseases. JHEQ has three subscales, i.e., pain, movement, and mental condition, and the scores for each range from 0 (worst) to 28 (best) points. The total score of the JHEQ ranges from 0 (worst) to 84 (best) points.

Evaluation of Pain Catastrophizing

Pain catastrophizing was determined using the Japanese version of the Pain Catastrophizing Scale (PCS),²⁹ a 13-item self-report questionnaire that helps measure maladaptive thoughts regarding pain; each item is rated on a 5-point Likert-type scale (0=not at all; 4=all the time), and higher scores reflect a greater degree of pain-related catastrophizing. The PCS contains three dimensions of pain catastrophizing: rumination, helplessness, and magnification. Rumination

represents repeated pain-related thoughts, helplessness indicates the state of feeling helpless in dealing with a painful situation, and magnification represents an exaggeration of the perception of threat arising from pain; the Japanese version has been found to be valid and reliable.²⁹

Statistical Analysis

The survey items were measured before surgery and 3 months after surgery to evaluate the short-term outcomes and their correlation with preoperative CS status.⁹ Preoperative PCS, CSI, and EQ-5D-5/ scores were compared between the TKA and THA groups using the Mann-Whitney U test. The preoperative and postoperative prevalences of CS in TKA and THA patients were estimated. Among those with CS before surgery, patients were divided into the improved (I) group and the remained (R) group, based on the CS status 3 months after surgery. KOOS subscales, JHEQ subscales, and the EQ-5D-5/ scores of the I and R groups were compared using the Mann-Whitney U test. To investigate the association between postoperative EQ-5D-5/ scores and CS, linear regression analysis was performed with EQ-5D-5/ as the dependent variable, and age, sex, body mass index (BMI), bilateral surgery, CSI-25, PCS, and KOOS subscales or JHEQ subscales as independent variables. To avoid multicovariance, KOOS QOL and JHEQ mental scores were not included in the models. Data input and analysis were performed using IBM SPSS version 27.0 (IBM Corp., Armonk, NY, USA). A P-value of less than 0.05 was considered statistically significant.

RESULTS

The mean ages (with standard deviations) of TKA and THA patients were 71.5 ± 5.3 and 63.0 ± 7.5 years, respectively ($P=0.015$). The mean BMIs calculated from the patients' height and weight were $26.7 \pm 3.6 \text{ kg/m}^2$ in TKA patients and $24.5 \pm 4.0 \text{ kg/m}^2$ in THA patients ($P<0.001$). The patient demographic data are summarized in **Table 1**. There were no significant differences in terms of preoperative PCS or EQ-5D-5/ scores between the TKA and THA groups (**Table 1**). In contrast, CSI-25 and CSI-9 scores of the THA group were significantly higher than those of the TKA group. Preoperatively, 47.5% of the TKA group and 66.0% of the THA group ($P=0.083$) were CS positive; 3 months after surgery, these percentages had shrunk to 10.0% ($P=0.042$) and 25.5% ($P=0.202$), respectively. Among the 19 TKA patients with preoperative CS, 4 (21.1%) were included in the R group. Their KOOS pain, KOOS symptoms, and EQ-5D-

Table 1. Comparison of preoperative clinical conditions between total knee arthroplasty and total hip arthroplasty patients

	TKA	THA	P-value
Sample size	40	47	
Female, %	34 (85.0%)	46 (97.9%)	0.045
Age, years	71.5 ± 5.3	63.0 ± 7.5	0.015
Body mass index, kg/m ²	26.7 ± 3.6	24.5 ± 4.0	<0.001
Bilateral surgery	19 (47.5%)	10 (21.3%)	0.010
Pain catastrophizing scale	31.3 ± 12.0	28.6 ± 10.7	0.246
CSI-25	19.7 ± 10.6	23.8 ± 10.2	0.037
CSI-9	9.4 ± 5.1	11.6 ± 5.2	0.028
Patients with CS (CSI-9≥10)	19	31	
EQ-5D-5l	0.56 ± 0.16	0.53 ± 0.20	0.518

Data were compared using the Mann–Whitney U test or Fisher's direct test.
CSI, central sensitization inventory.

Table 2. Comparison of knee symptoms and QOL after TKA

	I group n = 15	R group n = 4	P-value
KOOS Pain	40.6 ± 22.6	8.3 ± 15.9	0.027
KOOS Symptom	34.5 ± 18.9	−6.3 ± 17.1	0.002
KOOS ADL	28.9 ± 23.5	3.3 ± 10.7	0.062
KOOS QOL	32.5 ± 25.2	18.8 ± 17.7	0.411
EQ-5D-5l	0.32 ± 0.19	−0.04 ± 0.27	0.020

TKA patients with preoperative positive CS were divided into an improved (I) group and a remaining (R) group, based on the CS status 3 months after surgery. Scores were compared using the Mann–Whitney U test.

Table 3. Comparison of hip symptoms and QOL after THA

	I group n = 19	R group n = 12	P-value
JHEQ Pain	16.9 ± 7.2	14.2 ± 6.2	0.205
JHEQ Movement	13.6 ± 5.9	11.1 ± 6.4	0.306
JHEQ Mental	14.2 ± 7.5	11.8 ± 4.9	0.435
JHEQ Total	44.7 ± 16.2	37.0 ± 15.0	0.236
EQ-5D-5l	0.37 ± 0.27	0.27 ± 0.24	0.367

Data were compared using the Mann-Whitney U test.

5l scores were significantly lower than those of the I group (**Table 2**). Among the 31 THA patients with preoperative CS, although 12 (38.7%) were included in the R group, there was no significant difference between the I and R groups for the JHEQ subscale scores or EQ-5D-5l scores (**Table 3**). Regression analysis showed that, whereas the EQ-5D-5l scores were negatively correlated with CSI-25 in the TKA group ($P=0.017$), EQ-5D-5l scores were not correlated with CSI-25 in the THA group ($P=0.206$) (**Tables 4 and 5**).

DISCUSSION

Even though this was a short-term observational study, the preoperative CS, as evaluated using CIS-25, was negatively associated with the general QOL improvement after TKA. In contrast, satisfactory outcomes following THA were not associated with preoperative CS status. However, a certain number of patients did suffer CS after THA. Among TKA patients, 47.5% and 10.0% were CS positive before and after surgery, respectively. Furthermore, the 66.0% of preoperative

Table 4. Factors related to the postoperative EQ-5D-5l score of TKA patients

	β	P-value
Female	-0.31	0.021
Age	0.02	0.915
Body mass index	-0.07	0.641
Bilateral surgery	0.19	0.265
Preoperative CSI-25	-0.44	0.017
Preoperative PCS	0.24	0.110
Preoperative KOOS Pain	-0.23	0.445
Preoperative KOOS Symptoms	0.13	0.636
Preoperative KOOS ADL	-0.35	0.192

Linear regression analysis was performed with the postoperative EQ-5D-5l score as the dependent variable, and age, body mass index, pain catastrophizing scale (PCS), central sensitization inventory (CSI), and knee injury and osteoarthritis outcome scales (KOOS) as independent variables.

Table 5. Factors related to the postoperative EQ-5D-5l score of THA patients

	β	P-value
Female	0.01	0.985
Age	-0.07	0.614
Body mass index	-0.08	0.542
Bilateral surgery	0.36	0.010
Preoperative CSI-25	-0.20	0.206
Preoperative PCS	0.24	0.122
Preoperative JHEQ Pain	-0.17	0.363
Preoperative JHEQ Movement	-0.25	0.148

Linear regression analysis was performed with the postoperative EQ-5D-5l score as the dependent variable, and age, body mass index, pain catastrophizing scale (PCS), central sensitization inventory (CSI), and Japanese Orthopedic Association Hip-disease Evaluation Questionnaire (JHEQ) subscales as independent variables.

CS-positive THA patients had reduced to 25.5% by 3 months after surgery. These results suggested that postoperative residual CS was not rare, even though the widespread hyperesthesia and enhanced spatial summation were normalized following TKA.³⁰⁾ These results stress the need to consider early preoperative or perioperative intervention for CS.

Nearly half of all THA and TKA patients had preoperative CS, a frequency that is markedly higher than that in the general population. A previous epidemiological study showed that the prevalence of CS in the general population was 14.0% and was not correlated with their Kellgren–Lawrence grade.³¹⁾ However, knee OA patients who developed CS suffered from nocturnal knee pain and their sleep quality and general QOL diminished significantly.^{16,31,32)} The proportion of patients who are CS positive just before undergoing TKA is reportedly in the range 24–48%,^{33,34)} which is similar to that observed in our study. In contrast, only a few studies have reported the prevalence of CS in patients with hip

OA. A systematic review showed that the prevalence of neuropathic-like pain was 40% in knee OA patients and 29% in hip OA patients.³⁵⁾

Furthermore, in both the TKA and THA groups, some patients with preoperative CS also had CS 3 months after surgery. Residual CS after TKA is known to reduce patients' postoperative QOL.³⁶⁾ Severe and long-lasting postoperative pain results in chronic postsurgical pain (CPSP) and should ideally be avoided.³⁷⁾ We observed differences in postoperative improvements in symptoms and QOL with respect to preoperative CS between TKA and THA, despite a high prevalence of preoperative and postoperative CS for both surgeries. Among previous reports, some showed equal improvements or greater improvements following TKA than THA in disease-specific variables and in general health-related quality of life,^{38,39)} whereas some reports showed less improvement after TKA than after THA.^{40,41)} Preoperative anxiety and psychological distress among patients were

reportedly higher before TKA than THA.³⁹⁾ Our study could not identify why THA led to improved postoperative symptoms regardless of preoperative CS status. However, a systematic review reported that psychological factors influence outcomes after TKA and THA; patients with more pain catastrophizing preoperatively experienced more pain after TKA surgery.⁴²⁾

Our results suggest that preoperative CS and its persistence following surgery significantly influenced postoperative outcomes and satisfaction in TKA patients. Appropriate intervention for preoperative CS may help improve patient satisfaction. OA patients with CS reportedly experience depressive conditions or pain catastrophizing.²⁰⁾ In contrast, it is reported that the descending pain inhibitory pathway was a potential cause for chronic pain in end-stage OA.⁴³⁾ To prevent CPSP, early administration of duloxetine to patients before TKA could improve clinical outcomes.³³⁾ Furthermore, cognitive-behavioral therapy may help diminish the negative impact of preoperative kinesiophobia and CS in TKA patients.⁴⁴⁾ We inferred that evaluating the preoperative CS status and carrying out early intervention could help improve postoperative QOL, especially in TKA patients.

There were several limitations to this study in addition to the small sample size. First, CS was evaluated using only self-reported questionnaires. It is known that the diagnostic capability of CSI-9 is inferior to that of physical examinations with pain stimulation.^{45–47)} Moreover, the CSI-9 cutoff value for CS was set at 10 points, based on the literature²¹⁾; this point should be investigated precisely in patients with knee osteoarthritis in a future study. Second, EQ-5D-5l was used as a uniform scoring system for both surgeries because common patient-reported outcome scores for both TKA and THA were not available. Third, a postoperative examination should have been considered for statistical analysis to evaluate the influence of invasiveness and surgical techniques on postoperative satisfaction or symptoms, even though the same surgeon performed the surgeries. Fourth, the postoperative evaluation was performed only at 3 months after surgery. The WOMAC score of THA patients reportedly improves earlier than that of TKA patients.³⁸⁾ We believe that long-term observation might reveal an association between CS and residual symptoms. Despite these limitations, we observed apparent differences in postoperative responses in patients with preoperative CS who underwent TKA or THA. We found that preoperative intervention would likely benefit patients suffering from terminal OA and CS.

CONCLUSIONS

We investigated the prevalence of preoperative CS and postoperative residual CS after TKA and THA and evaluated the influence of residual CS on the improvement of general QOL after surgery. Postoperative improvement was observed 3 months after THA regardless of high residual CS. In contrast, preoperative CS was negatively associated with improvement after TKA.

CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

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