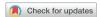


Original Article Musculoskeletal Disorders, Rehabilitation & Sports Medicine



Presence of Night Pain, Neuropathic Pain, or Depressive Disorder Does Not Adversely Affect Outcomes After Total Knee Arthroplasty: A Prospective Cohort Study

Na-Kyoung Lee , Samuel Jaeyoon Won , Jun-Young Lee , Seung-Baik Kang , So Young Yoo , And Chong Bum Chang , So Young Yoo

¹Department of Orthopaedic Surgery, Seoul National University Bundang Hospital, Seongnam, Korea ²Department of Psychiatry, Seoul Metropolitan Government-Seoul National University Boramae Medical Center, Seoul, Korea

³Department of Psychiatry and Neuroscience Research Institute, Seoul National University College of Medicine, Seoul, Korea

⁴Department of Orthopaedic Surgery, Seoul Metropolitan Government-Seoul National University Boramae Medical Center, Seoul, Korea

⁵Department of Orthopaedic Surgery, Seoul National University College of Medicine, Seoul, Korea



Received: Aug 1, 2022 Accepted: Sep 5, 2022 Published online: Oct 11, 2022

Address for Correspondence: So Young Yoo, MD, PhD

Department of Psychiatry, Seoul Metropolitan Government-Seoul National University Boramae Medical Center, 20 Boramae-ro 5-gil, Dongjak-gu, Seoul 07061, Republic of Korea. Email: soyoung.yoo29@gmail.com

Chong Bum Chang, MD, PhD

Department of Orthopaedic Surgery, Seoul National University College of Medicine, Seoul National University Bundang Hospital, 82 Gumi-ro 173-beon-gil, Bundang-gu, Seongnam 13620, Republic of Korea. Email: ccbknee@gmail.com

-mail: сськпее@gmail.com ccb1013@snu.ac.kr

© 2022 The Korean Academy of Medical Sciences.

This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (https://creativecommons.org/licenses/by-nc/4.0/) which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

ABSTRACT

Background: A considerable proportion of patients warranting total knee arthroplasty (TKA) have night pain, neuropathic pain, and/or depressive disorder, which may not be resolved by TKA. This prospective, longitudinal cohort study aimed to document the prevalence of night pain, neuropathic pain, and depressive disorder in patients with advanced knee osteoarthritis undergoing TKA and to determine whether the specific coexisting pain and/or disorder at the time of TKA adversely affected postoperative outcomes.

Methods: In this study, 148 patients undergoing TKA were longitudinally evaluated. The presence of night pain, neuropathic pain (determined using Douleur Neuropathique 4 [DN4]) and depressive disorder (determined using the Patient Health Questionnaire-9 [PHQ-9]) was determined before and 6 weeks, 3 months and 1 year after TKA. In addition, Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) and EuroQol-5 Dimension (EQ-5D) scores were assessed before and 1 year after TKA. Potential associations of night pain, neuropathic pain, and/or depressive disorder with pre- and postoperative WOMAC and EQ-5D scores were examined in subgroup analyses.

Results: Preoperatively, 72% (n = 106) of patients reported night pain, and the prevalences of neuropathic pain and depressive disorder were 15% and 17%, respectively. Preoperatively, compared with patients without night pain, those with night pain had significantly poorer preoperative WOMAC scores, but no significant difference was seen between groups 1 year after TKA. Preoperatively, the WOMAC, EQ-5D, and EQ-5D health scores of patients with neuropathic pain were not significantly different from those of patients without neuropathic pain, and there was no difference in clinical outcome scores 1 year after TKA between these groups. Preoperatively, the patients with depressive disorder showed significantly poorer preoperative WOMAC, EQ-5D, and EQ-5D health scores than those without depressive disorder, but no significant differences in scores were observed 1 year after TKA between these groups.



ORCID iDs

Na-Kyoung Lee 📵

https://orcid.org/0000-0001-7545-9797 Samuel Jaeyoon Won

https://orcid.org/0000-0002-7907-7283

Jun-Young Lee 🝺

https://orcid.org/0000-0002-5893-3124

Seung-Baik Kang 📵

https://orcid.org/0000-0002-1184-4482

So Young Yoo 🕞

https://orcid.org/0000-0001-9964-126X

Chong Bum Chang

https://orcid.org/0000-0002-8597-1054

Disclosure

The authors have no potential conflicts of interests to disclose.

Author Contributions

Conceptualization: Lee JY, Kang SB, Yoo SY, Chang CB. Data curation: Lee NK. Formal analysis: Lee NK. Investigation: Lee NK, Won SJ, Kang SB, Chang CB. Methodology: Lee JY, Kang SB, Yoo SY, Chang CB. Resources: Kang SB, Chang CB. Supervision: Yoo SY, Chang CB. Visualization: Lee NK. Writing - original draft: Lee NK. Writing - review & editing: Lee JY, Yoo SY, Chang CB.

Conclusion: This study revealed a considerable prevalence of night pain, neuropathic pain, and depressive disorder in patients undergoing TKA and that patients with these specific conditions reported poorer functional and quality of life scores preoperatively. However, such adverse effects disappeared after TKA. Our study findings suggest that TKA can provide satisfactory outcomes for patients with these specific conditions.

Keywords: Night Pain; Neuropathic Pain; Depressive Disorder; Total Knee Arthroplasty; Clinical Outcome

INTRODUCTION

Total knee arthroplasty (TKA) is an established modality to improve pain and functioning in patients with severe knee osteoarthritis (OA).^{1,2} Despite advances in surgical techniques, postoperative management strategies, and prostheses, a considerable number of patients still complain of discomfort after TKA; several studies found that up to 20% of patients report disappointing results after TKA although no major problems are present from the surgeon's perspective.²⁻⁸

It is our anecdotal experience that a considerable proportion of patients have night pain and sleep disturbances after TKA. Several studies have shown an association between sleep deprivation and increased pain sensitivity. 9·13 In one report, approximately 81% of patients with knee and hip OA experienced night pain. 14 Gong et al. 15 demonstrated that a good sleep quality group showed faster recovery than a control group in the early period after TKA. However, to the best of our knowledge, there are no studies on the prevalence of night pain and sleep disorders after TKA or on whether the presence of night pain affects outcomes even a year after TKA.

The nature of neuropathic pain in OA patients warranting TKA is another concern. The contribution of neuropathic natural pain in OA has been reported in previous studies. ¹⁶⁻¹⁹ More than 20% of patients with knee or hip OA showed pain scores in the neuropathic range before total joint arthroplasty. ^{20,21} Whether the presence of neuropathic pain before surgery adversely affects the outcome after TKA surgery is controversial. A recent study reported that patients with high preoperative neuropathic pain scores had higher pain visual analogue scale (VAS) scores at 6 months postoperatively than those with low preoperative neuropathic pain scores. ²² On the other hand, there are reports that preoperative neuropathic pain scores had no significant effect on postoperative pain VAS scores. ^{23,24}

In addition, surgeons are concerned and anticipate poor postoperative outcomes for patients with depressive disorder or other psychiatric disorders. Whether depression adversely affects clinical outcomes after TKA is controversial. Some studies show that depression is one of the factors significantly related to negative outcomes.8,25,26 Pérez-Prieto et al.27 revealed that patients with depression had poorer pain scores and clinical results before and after TKA than patients without depression. However, they showed that the net changes in clinical outcome scores were not significantly different and that patient satisfaction was similar.27 Rice et al.28 showed that depression was not a statistically significant variable of persistent postoperative pain predictors.



This prospective, longitudinal cohort study aimed to 1) document the prevalence of night pain, neuropathic pain, and depressive disorder in patients with advanced knee OA undergoing TKA and 2) determine whether the specific coexisting pain and/or disorder at the time of TKA adversely affected postoperative outcomes.

METHODS

Study patients

Among the patients with Kellgren-Lawrence grade 3 or 4 advanced knee OA who complained of persistent moderate to severe knee pain and dysfunction after at least 3 months of conservative treatment, 174 patients undergoing TKA from January 2017 to January 2019 were prospectively recruited and longitudinally evaluated for this study. The exclusion criteria were as follows: 1) patients who had been diagnosed with knee arthritis other than primary OA; 2) patients who did not agree to participate in the study; 3) patients who were unable to complete questionnaires due to an inability to communicate; and 4) patients with serious neurological or medical impairment.

Of the 174 patients enrolled in the study, 2 cancelled their surgeries and 24 patients were lost during the follow-up periods of 6 weeks, 3 months and 1 year after surgery. Therefore, data for a total of 148 patients were analysed. The demographic data of the patients, including age, sex, height, weight, body mass index, and medical history, were collected.

Among the 148 patients, 16 (10.8%) were men, and 132 (89.2%) were women. The mean age of the patients was 70.7 ± 5.3 years. In addition, only 2 patients reported that they had been diagnosed with depressive disorder and were receiving psychiatric treatment.

Assessment of neuropathic pain

Neuropathic pain in patients was evaluated using Douleur Neuropathique 4 (DN4) before TKA.²⁹ DN4 consists of 4 questions containing 10 items. The total score is calculated as the sum of the scores on the 10 items, and the cut-off value for neuropathic pain is a total score of 4/10.³⁰ However, only 8 out of 148 patients had preoperative DN4 scores of 4 or more; in this study, the cut-off value for neuropathic pain was set at 3 points. In addition, patients' neuropathic pain was evaluated at 6 weeks, 3 months, and 1 year after TKA.

Assessment of depressive disorder

Depressive disorder in patients was assessed by the Patient Health Questionnaire-9 (PHQ-9). The questionnaire consists of 9 items to assess whether there have been any such problems in the past two weeks. The total score is calculated as the sum of the scores on the 9 items; less than 4 points indicates no depression, 5 to 9 points indicates mild depression, 10 to 14 points indicates moderate depression, 15 to 19 points indicates moderate depression that needs management, and 20 to 27 points indicates severe depression that requires active treatment. Therefore, in this study, patients with PHQ-9 scores of 5 or more were determined to have a depressive disorder. PHQ-9 scores were measured in the patients before the operation and at 6 weeks, 3 months and 1 year after TKA.

Assessment of night pain

The presence of night pain in patients was evaluated before and 6 weeks, 3 months, and 1 year after TKA. Night pain was defined as pain around the knee experienced at night that could



disturb the patient's sleep. In patients with night pain, the severity of the pain was evaluated using a 0 to 10 VAS.

Clinical outcome measurement

Clinical outcome was assessed using the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), EuroQol-5 Dimension (EQ-5D), and EQ-5D health scores before and 1 year after TKA.

Outcome assessment

The prevalence of night pain, neuropathic pain, and depressive disorder was analysed in 148 patients before surgery and 6 weeks, 3 months, and 1 year after TKA.

Subgroup analysis was performed to compare the clinical outcome scores before and after TKA. Patients were divided into two subgroups for each of the three categories: 1) a preoperative night pain group and non-night pain group; 2) a preoperative neuropathic pain group and nonneuropathic pain group; and 3) a preoperative depressive disorder group and nondepressive disorder group.

Surgical technique and perioperative management protocol

Surgeries were performed by two experienced surgeons using the same surgical protocol. All surgeries were performed using the medial parapatellar approach and mechanically aligned TKA. All prostheses were posterior-stabilized implants with a fixed bearing system and were fixed with cement.

In patients identified as having neuropathic pain and/or depressive disorder before surgery, medications such as gabapentinoids or serotonin-norepinephrine reuptake inhibitors (SNRIs) were administered after TKA. In addition, pregabalin was prescribed for night pain after surgery, and sleeping pills were prescribed for patients complaining of severe sleep disorders through consultation with psychiatrists.

Statistical analysis

Descriptive statistical analysis was performed, and data normality was evaluated using the Kolmogorov-Smirnov test. To compare the differences in categorical variables between subgroups, the chi-square and Fisher exact tests were employed. The differences in continuous variables between the subgroups were analysed using independent t tests or the Mann-Whitney U test when normality was not satisfied. All statistical analyses were performed using SPSS software (version 25.0; IBM Corp., Armonk, NY, USA). P values < 0.05 were considered statistically significant.

Sample size calculation was performed using G-power (version 3.1). To estimate the sample size, a pilot study was conducted with 50 initially recruited patients. In the pilot study, patients with preoperative night pain had a significantly poorer preoperative WOMAC score by 10.6 points compared to patients without night pain. In addition, patients with preoperative depressive disorder showed a significantly poorer preoperative WOMAC score by 9.0 points than that of the nondepressive disorder group. Therefore, it was assumed that the WOMAC score 1 year after TKA in the preoperative night pain group and preoperative depressive disorder group would be poorer than each control group by a similar score difference. The sample size for the two-independent sample *t*-test was calculated with a two-tailed test, an alpha error of 0.05, and a power of 0.8. The calculated total sample size was 90



patients and 108 patients for night pain and depressive disorder, respectively. Considering the prevalence of neuropathic pain and depressive disorder in TKA patients reported in previous studies and a dropout rate (including loss of follow-up) of approximately 20%, about 170 patients were recruited.

Ethics statement

This prospective longitudinal cohort study was approved by the local ethical committee in Seoul Metropolitan Government-Seoul National University Boramae Medical Center (approval No. 26-2016-175), and all patients provided written informed consent before enrolment.

RESULTS

Prevalence of night pain, neuropathic pain, and depressive disorder

The proportion of patients who reported night pain before TKA was 71.6% (106 patients). The prevalence of night pain was 46.6% until 3 months after surgery, but it decreased significantly to 7.4% in the first year after TKA (**Fig. 1A**). When only patients with night pain were analysed, the average night pain VAS score was 4.75 (range 1 to 10) before TKA but gradually decreased after surgery, and the average night pain VAS score at 1 year after TKA was 3.0 (range 1 to 5) (**Fig. 1B**).

The proportion of patients with neuropathic pain was 14.9% (22 patients) before TKA. The prevalence of neuropathic pain increased to 53.3% at 6 weeks after TKA and then gradually decreased to 14.2% at 1 year after TKA, slightly lower than before surgery (Fig. 2).

The prevalence of depressive disorder before TKA was 16.9% (25 patients). The percentage of patients with depressive disorder increased to 23.0% at 6 weeks and decreased to 9.5% at 1 year after TKA (Fig. 2).

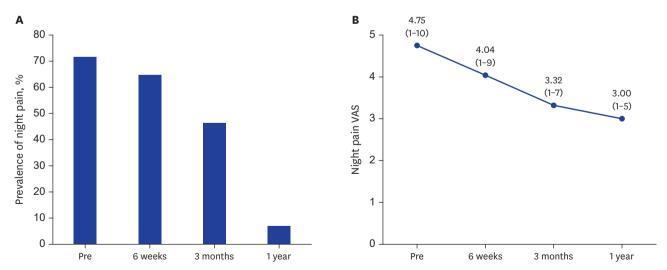


Fig. 1. Prevalence of night pain and the night pain VAS score in patients with night pain. (A) A significant number of patients showed night pain before TKA, and approximately half of patients complained of night pain by 3 months after TKA. However, in most patients, night pain improved 1 year after surgery. (B) Even in patients with night pain after TKA, the mean pain VAS score was lower than that before surgery.

VAS = visual analogue scale, TKA = total knee arthroplasty.



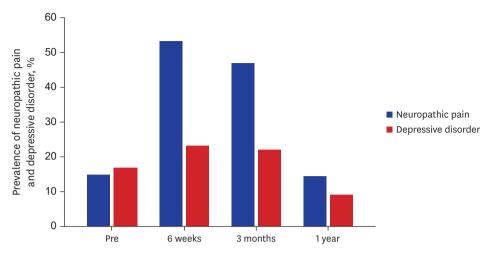


Fig. 2. Prevalence of neuropathic pain and depressive disorder. Approximately 14.9% patients showed neuropathic pain before TKA. The prevalence of neuropathic pain increased to 53.3% at 6 weeks after TKA and then gradually decreased to the previous level at 1 year after TKA. The prevalence of depressive disorder before TKA was 16.9% and decreased to 9.5% at 1 year after TKA.

TKA = total knee arthroplasty.

Subgroup analysis 1: Preoperative night pain group vs. non-night pain group

Among the 148 patients, 106 (71.6%) and 42 (28.4%) patients were classified into the preoperative night pain group and preoperative non-night pain group, respectively. Compared with the patients without night pain preoperatively, the patients with preoperative night pain had significantly poorer preoperative WOMAC scores. However, there was no significant difference between the two groups in WOMAC scores at 1 year after TKA. In addition, there was no statistically significant difference in EQ-5D and EQ-5D health scores between the two groups before and 1 year after TKA (Table 1).

Subgroup analysis 2: Preoperative neuropathic pain group vs. nonneuropathic pain group

Of the 148 patients, 22 (14.9%) were classified into the neuropathic pain group, and 126 (85.1%) were classified into the nonneuropathic pain group. The preoperative WOMAC score in the neuropathic pain group was poorer than that in the nonneuropathic pain group, but the difference was not statistically significant. There was no difference between the two groups in any other clinical scores before and 1 year after surgery (**Table 2**).

Table 1. Comparison between the preoperative non-night pain group and the night pain group

Variables	Non-night pain group (n = 42)	Night pain group (n = 106)	P value
Patient demographic characteristics			
Age	72.40 ± 4.84	70.06 ± 5.39	0.015^{*}
Sex (female)	32 (76.2)	100 (94.3)	0.003**
BMI	26.98 ± 2.96	27.31 ± 3.94	0.573
Preoperative clinical scores			
WOMAC	28.50 ± 12.20	37.79 ± 10.55	< 0.001***
EQ-5D	8.60 ± 1.06	8.74 ± 1.06	0.469
EQ-5D health	76.31 ± 15.02	74.48 ± 12.82	0.458
1-year postoperative clinical scores			
WOMAC	10.55 ± 11.44	11.60 ± 10.92	0.601
EQ-5D	6.07 ± 1.42	6.44 ± 1.59	0.188
EQ-5D health	75.36 ± 13.90	74.95 ± 13.28	0.869

Values are presented as mean \pm standard deviation or number (%).

BMI = body mass index, WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index, EQ-5D = EuroQol-5 Dimension.

^{*}P < 0.05, **P < 0.01, ***P < 0.001.



Table 2. Comparison between the preoperative nonneuropathic pain group and the neuropathic pain group

Variables	Nonneuropathic pain group (n = 126)	Neuropathic pain group (n = 22)	P value
Patient demographic characteristics			
Age	71.26 ± 4.92	67.64 ± 6.56	0.003**
Sex (female)	110 (87.3)	22 (100.0)	0.130
BMI	27.24 ± 3.50	27.09 ± 4.66	0.693
Preoperative clinical scores			
WOMAC	34.13 ± 11.91	39.05 ± 9.69	0.061
EQ-5D	8.71 ± 1.01	8.64 ± 1.33	0.984
EQ-5D health	74.76 ± 13.61	76.36 ± 12.74	0.813
1-year postoperative clinical scores			
WOMAC	11.82 ± 11.28	8.36 ± 9.24	0.208
EQ-5D	6.37 ± 1.60	6.18 ± 1.18	0.901
EQ-5D health	75.12 ± 13.86	74.77 ± 10.74	0.606

Values are presented as mean ± standard deviation or number (%).

BMI = body mass index, WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index, EQ-5D = EuroQol-5 Dimension.

Subgroup analysis 3: Preoperative depressive disorder group vs. nondepressive disorder group

Of the 148 patients, 25 (16.9%) and 123 (83.1%) were classified into the preoperative depressive disorder group and the nondepressive disorder group, respectively. The patients in the depressive disorder group showed significantly poorer preoperative WOMAC, EQ-5D, and EQ-5D health scores than the patients in the nondepressive disorder group, but there were no significant differences in these scores between these groups at 1 year after TKA (**Table 3**).

DISCUSSION

This study revealed a considerable prevalence of night pain, neuropathic pain, and depressive disorder in patients undergoing TKA and found that patients with these specific conditions reported poorer functional outcome scores and health-related quality of life (HRQOL) scores preoperatively. However, there was no difference in functional outcome scores and HRQOL scores after TKA between the groups with and without the preoperative coexisting conditions.

Table 3. Comparison between the preoperative nondepressive disorder group and the depressive disorder group

Variables	Nondepressive disorder group (n = 123)	Depressive disorder group (n = 25)	P value
Patient demographic characteristics			
Age	70.89 ± 5.41	69.88 ± 4.94	0.388
Sex (female)	107 (87.0)	25 (100.0)	0.075
ВМІ	27.35 ± 3.52	26.56 ± 4.37	0.207
Preoperative clinical scores			
WOMAC	33.59 ± 11.19	41.12 ± 12.41	0.003**
EQ-5D	8.59 ± 1.05	9.20 ± 1.00	0.009**
EQ-5D health	75.81 ± 13.68	71.00 ± 11.73	0.043*
1-year postoperative clinical scores			
WOMAC	11.73 ± 11.35	9.20 ± 9.31	0.385
EQ-5D	6.37 ± 1.56	6.16 ± 1.52	0.515
EQ-5D health	74.96 ± 13.75	75.60 ± 11.84	0.846

Values are presented as mean \pm standard deviation or number (%).

BMI = body mass index, WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index, EQ-5D = EuroQol-5 Dimension.

^{**}P < 0.01.

^{*}P < 0.05, **P < 0.01.



Night pain is the most common problem that patients complain of before and after TKA, and this problem has yet to be resolved. When night pain and the accompanying sleep disturbances improve after TKA is still unknown and controversial. In our study cohort, 71.6% of patients complained of night pain before TKA, which is well matched with the study of Sasaki et al., 31 in which 75% of patients with Kellgren-Lawrence grade 4 OA complained of night pain. Although sleep disturbances were not evaluated in our study, nearly half of the patients complained of night pain up to 3 months after surgery, and the results showed that most of these disturbances improved at 1 year after surgery. In addition, the severity of pain was reduced in patients who still had night pain after TKA. Previous studies did not directly assess night pain, but they reported that sleep disturbances were worse or not significantly different in the early postoperative period (4.7 \pm 2.0 weeks or 6 weeks) but significantly improved in the late postoperative period (3, 6 or 10 months) compared with before surgery, $^{32-34}$ These results seem to be consistent with our results.

In a subgroup analysis, the preoperative functional outcome score was poorer in the night pain group than in the non-night pain group, but at 1 year after surgery, both the clinical outcome and quality of life score were not significantly different from those of the preoperative non-night pain group. These results are consistent with the report that TKA improves both pain and sleep quality.^{34,35} Although there was also a paper that showed that poor sleep quality before surgery affects postoperative pain and functioning, it was shown that poor preoperative sleep quality had no significant correlation with the clinical outcome at 2 weeks or more after TKA surgery. 36 Based on our results, we can inform patients who complain of night pain before and after surgery that night pain will decrease after 3 months and that such preoperative night pain will not worsen the long-term outcome. However, how to alleviate night pain after TKA has not vet been established. Gong et al. 15 reported that postoperative administration of zolpidem reduced postoperative night pain and increased postoperative satisfaction; however, this study showed results only up to 2 weeks after surgery, so further studies are needed. Other studies have reported that gabapentin was effective in the treatment of insomnia in various medical conditions, 37,38 but further studies are needed to determine whether gabapentin is effective in relieving pain after orthopaedic surgery.

Neuropathic pain was seen in approximately 15% of patients before surgery, appeared in almost half of patients at 6 weeks and 3 months after surgery, and decreased to a level similar to that before surgery at 1 year after surgery. In our study cohort, all patients with preoperative neuropathic pain were female. A higher rate of neuropathic pain in women than in men has already been reported.²⁰ In addition, it is thought that this result in our cohort was due to the proportion of men being significantly small. However, the percentage of patients with neuropathic pain is lower than that reported in a systematic review (by approximately 23%) that evaluated the prevalence of neuropathic pain in patients with knee and hip OA. 21,22,24 The cause of these results is the difference in the questionnaire used to evaluate neuropathic pain, and there may be demographic differences in the study group. In particular, our cohort was composed of patients who decided on TKA, and patients with severe pain of neuropathic nature may have been excluded from the decision-making process to undergo TKA. From 6 weeks to 3 months after surgery, it is thought that the number of patients with high DN4 scores increased due to symptoms such as tingling, pins and needles, surgical wound itching, and the numbness of the lateral side of the knee. When surgical wound recovery was complete, DN4 scores seemed to return to the previous level.



In one study, patients with neuropathic pain were reported to have worse postoperative results,²² but our study adds strength to the evidence that patients with preoperative neuropathic pain do not show poorer results after TKA.^{23,24} Many studies have reported that preoperative central sensitization or widespread pain sensitization is associated with chronic pain or dissatisfaction after TKA.^{22,39,40} However, it is thought that it is difficult to conclude that a person has sensitization to pain simply by showing pain of a neuropathic nature, especially when using DN4, which does not evaluate the severity of neuropathic nature pain.

The prevalence of depressive disorder before TKA was 16.9% and decreased to 9.5% at 1 year after TKA. The prevalence of depression before TKA surgery differs from study to study, ranging from 10% to 27.9%. 26,27,41-44 This difference is thought to be due to differences in the demographic characteristics of the study groups and in the tools used to evaluate depression. However, in several studies, similar to the results of our study, depression tended to improve after TKA surgery, although not completely. 26,41,44,45 Therefore, it is thought that the pain and dysfunction caused by knee OA act as causes of depression. Therefore, in some patients with depression before surgery, knee pain and dysfunction as well as depression may be improved through TKA.

A number of papers have suggested that pre- and postoperative functional outcome scores and HRQOL scores are poorer in patients with preoperative depression than in those without depression. 25,27,42,46,47 However, some papers report that the net change in the outcome improvement itself is no different between the groups with and without depression^{27,41,48} and that there is no difference in satisfaction, ^{26,27,43} In addition, some studies have reported that depression is not included as a predictor of persistent postoperative pain or poor outcome. ^{28,49} Among the results of our study, the poor preoperative functional outcome scores and HRQOL scores in the group with preoperative depression were consistent with those in previous reports. However, there was no significant difference in functional outcome scores and HROOL scores in the groups with and without preoperative depression 1 year after TKA. This result differs from those of previous papers in that the net change in the outcome score was larger in the group with depression. These results may be due to drug administration, such as SNRIs, or active cooperative treatment with psychiatrists in patients with depression. However, in a recent study, there was no difference in postoperative outcomes between the treated group and the untreated group in patients with depression, 42 so further studies are thought to be needed.

This study has several limitations. First, although the total sample size of our study was not small, the numbers of patients with preoperative neuropathic pain or depressive disorder were relatively small. However, the sample size was sufficient to reject the hypothesis that differences in clinical outcome scores at 1 year after TKA were maintained between subgroups. Second, the patient group was recruited from only a single institution in one country, and the proportion of women was overwhelmingly high. Third, DN4 was used as a tool to evaluate neuropathic pain, and central sensitization was not directly evaluated. In addition, the cut-off value for neuropathic pain was set at 3 points because only 8 patients had preoperative DN4 scores of 4 or more. Since there were few patients with very high DN4 scores in our cohort, additional studies on patients with neuropathic pain of various severities are needed. Fourth, because this study was not a randomized controlled trial, there is a limitation that all drugs taken by patients were not controlled equally. Appropriate medications were additionally administered according to the patient's complaint. Because this is what happens in real practice, full control over the drug was not considered necessary.



In conclusion, this study revealed a considerable prevalence of night pain, neuropathic pain, and depressive disorder in patients undergoing TKA and found that patients with these specific conditions reported poorer functional and quality of life scores preoperatively. However, such adverse effects disappeared at 1 year after TKA. The findings of our study suggest that TKA can provide satisfactory outcomes for patients with preoperative night pain, neuropathic pain, or depressive disorder, equivalent to those for patients without these conditions.

REFERENCES

- Callahan CM, Drake BG, Heck DA, Dittus RS. Patient outcomes following tricompartmental total knee replacement. A meta-analysis. *JAMA* 1994;271(17):1349-57.
 PUBMED I CROSSREF
- Heck DA, Robinson RL, Partridge CM, Lubitz RM, Freund DA. Patient outcomes after knee replacement. Clin Orthop Relat Res 1998;356:93-110.

PUBMED | CROSSREF

- Wylde V, Learmonth I, Potter A, Bettinson K, Lingard E. Patient-reported outcomes after fixed- versus mobile-bearing total knee replacement: a multi-centre randomised controlled trial using the Kinemax total knee replacement. J Bone Joint Surg Br 2008;90(9):1172-9.

 PUBMED I CROSSREF
- 4. Noble PC, Conditt MA, Cook KF, Mathis KB. The John Insall Award: patient expectations affect satisfaction with total knee arthroplasty. *Clin Orthop Relat Res* 2006;452:35-43.
- 5. Bourne RB, Chesworth BM, Davis AM, Mahomed NN, Charron KD. Patient satisfaction after total knee arthroplasty: who is satisfied and who is not? *Clin Orthop Relat Res* 2010;468(1):57-63.
- 6. Ranawat CS, White PB, West S, Ranawat AS. Clinical and radiographic results of attune and PFC sigma knee designs at 2-year follow-up: a prospective matched-pair analysis. *J Arthroplasty* 2017;32(2):431-6.
- Parvizi J, Nunley RM, Berend KR, Lombardi AV Jr, Ruh EL, Clohisy JC, et al. High level of residual symptoms in young patients after total knee arthroplasty. Clin Orthop Relat Res 2014;472(1):133-7.
 PUBMED | CROSSREF
- 8. Choi YJ, Ra HJ. Patient satisfaction after total knee arthroplasty. *Knee Surg Relat Res* 2016;28(1):145.

 PUBMED I CROSSREF
- Roehrs TA, Harris E, Randall S, Roth T. Pain sensitivity and recovery from mild chronic sleep loss. Sleep (Basel) 2012;35(12):1667-72.
 PUBMED I CROSSREF
- Moldofsky H, Scarisbrick P. Induction of neurasthenic musculoskeletal pain syndrome by selective sleep stage deprivation. Psychosom Med 1976;38(1):35-44.

 PUBMED | CROSSREF
- Smith MT, Edwards RR, McCann UD, Haythornthwaite JA. The effects of sleep deprivation on pain inhibition and spontaneous pain in women. Sleep 2007;30(4):494-505.
- 12. Onen SH, Alloui A, Gross A, Eschallier A, Dubray C. The effects of total sleep deprivation, selective sleep interruption and sleep recovery on pain tolerance thresholds in healthy subjects. *J Sleep Res* 2001;10(1):35-42.
- 13. Roehrs T, Hyde M, Blaisdell B, Greenwald M, Roth T. Sleep loss and REM sleep loss are hyperalgesic. *Sleep* 2006;29(2):145-51.

PUBMED | CROSSREF

PUBMED | CROSSREF

- 14. Woolhead G, Gooberman-Hill R, Dieppe P, Hawker G. Night pain in hip and knee osteoarthritis: a focus group study. *Arthritis Care Res (Hoboken)* 2010;62(7):944-9.

 PUBMED | CROSSREF
- 15. Gong L, Wang Z, Fan D. Sleep quality effects recovery after total knee arthroplasty (TKA)--a randomized, double-blind, controlled study. *J Arthroplasty* 2015;30(11):1897-901.
- PUBMED | CROSSREF

 16. Thakur M, Dickenson AH, Baron R. Osteoarthritis pain: nociceptive or neuropathic? *Nat Rev Rheumatol*

2014;10(6):374-80.

PUBMED | CROSSREF



- Lluch E, Torres R, Nijs J, Van Oosterwijck J. Evidence for central sensitization in patients with osteoarthritis pain: a systematic literature review. Eur J Pain 2014;18(10):1367-75.

 PUBMED | CROSSREF
- Fingleton C, Smart K, Moloney N, Fullen BM, Doody C. Pain sensitization in people with knee osteoarthritis: a systematic review and meta-analysis. Osteoarthritis Cartilage 2015;23(7):1043-56.
 PUBMED | CROSSREF
- 19. Hochman JR, French MR, Bermingham SL, Hawker GA. The nerve of osteoarthritis pain. *Arthritis Care Res* (*Hoboken*) 2010;62(7):1019-23.
 - PUBMED | CROSSREF
- 20. Power JD, Perruccio AV, Gandhi R, Veillette C, Davey JR, Syed K, et al. Neuropathic pain in end-stage hip and knee osteoarthritis: differential associations with patient-reported pain at rest and pain on activity. *Osteoarthritis Cartilage* 2018;26(3):363-9.
 - PUBMED | CROSSREF
- 21. French HP, Smart KM, Doyle F. Prevalence of neuropathic pain in knee or hip osteoarthritis: a systematic review and meta-analysis. *Semin Arthritis Rheum* 2017;47(1):1-8.
 - PUBMED | CROSSREF
- 22. Kurien T, Arendt-Nielsen L, Petersen KK, Graven-Nielsen T, Scammell BE. Preoperative neuropathic painlike symptoms and central pain mechanisms in knee osteoarthritis predicts poor outcome 6 months after total knee replacement surgery. *J Pain* 2018;19(11):1329-41.
 - PUBMED | CROSSREF
- 23. Phillips JR, Hopwood B, Arthur C, Stroud R, Toms AD. The natural history of pain and neuropathic pain after knee replacement: a prospective cohort study of the point prevalence of pain and neuropathic pain to a minimum three-year follow-up. *Bone Joint J* 2014;96-B(9):1227-33.
 - PUBMED | CROSSREF
- 24. Fitzsimmons M, Carr E, Woodhouse L, Bostick GP. Development and persistence of suspected neuropathic pain after total knee arthroplasty in individuals with osteoarthritis. *PM R* 2018;10(9):903-9.
- Fisher DA, Dierckman B, Watts MR, Davis K. Looks good but feels bad: factors that contribute to poor results after total knee arthroplasty. *J Arthroplasty* 2007;22(6 Suppl 2):39-42.
 PUBMED | CROSSREF
- 26. Duivenvoorden T, Vissers MM, Verhaar JA, Busschbach JJ, Gosens T, Bloem RM, et al. Anxiety and depressive symptoms before and after total hip and knee arthroplasty: a prospective multicentre study. *Osteoarthritis Cartilage* 2013;21(12):1834-40.
 - PUBMED | CROSSREF
- 27. Pérez-Prieto D, Gil-González S, Pelfort X, Leal-Blanquet J, Puig-Verdié L, Hinarejos P. Influence of depression on total knee arthroplasty outcomes. *J Arthroplasty* 2014;29(1):44-7.

 PUBMED | CROSSREF
- 28. Rice DA, Kluger MT, McNair PJ, Lewis GN, Somogyi AA, Borotkanics R, et al. Persistent postoperative pain after total knee arthroplasty: a prospective cohort study of potential risk factors. *Br J Anaesth* 2018;121(4):804-12.
 - PUBMED | CROSSREF
- Kim HJ, Park JH, Bouhassira D, Shin JH, Chang BS, Lee CK, et al. Validation of the Korean version of the DN4 diagnostic questionnaire for neuropathic pain in patients with lumbar or lumbar-radicular pain. Yonsei Med J 2016;57(2):449-54.
 - PUBMED | CROSSREF
- 30. Bouhassira D, Attal N, Alchaar H, Boureau F, Brochet B, Bruxelle J, et al. Comparison of pain syndromes associated with nervous or somatic lesions and development of a new neuropathic pain diagnostic questionnaire (DN4). *Pain* 2005;114(1-2):29-36.
 - PUBMED | CROSSREF
- 31. Sasaki E, Tsuda E, Yamamoto Y, Maeda S, Inoue R, Chiba D, et al. Nocturnal knee pain increases with the severity of knee osteoarthritis, disturbing patient sleep quality. *Arthritis Care Res (Hoboken)* 2014;66(7):1027-32. PUBMED | CROSSREF
- Manning BT, Kearns SM, Bohl DD, Edmiston T, Sporer SM, Levine BR. Prospective assessment of sleep
 quality before and after primary total joint replacement. *Orthopedics* 2017;40(4):e636-40.
 PUBMED | CROSSREF
- 33. Koken M, Guclu B. The effects of total knee arthroplasty on sleep quality. *Malays Orthop J* 2019;13(2):11-4. PUBMED | CROSSREF
- Chen AF, Orozco FR, Austin LS, Post ZD, Deirmengian CA, Ong AC. Prospective evaluation of sleep disturbances after total knee arthroplasty. *J Arthroplasty* 2016;31(1):330-2.
 PUBMED | CROSSREF



- 35. Er MS, Altinel EC, Altinel L, Erten RA, Eroğlu M. An assessment of sleep quality in patients undergoing total knee arthroplasty before and after surgery. *Acta Orthop Traumatol Turc* 2014;48(1):50-4.

 PUBMED | CROSSREF
- 36. Luo ZY, Li LL, Wang D, Wang HY, Pei FX, Zhou ZK. Preoperative sleep quality affects postoperative pain and function after total joint arthroplasty: a prospective cohort study. *J Orthop Surg* 2019;14(1):378.

 PUBMED | CROSSREF
- 37. Lo HS, Yang CM, Lo HG, Lee CY, Ting H, Tzang BS. Treatment effects of gabapentin for primary insomnia. *Clin Neuropharmacol* 2010;33(2):84-90.

PUBMED | CROSSREF

38. Liu GJ, Karim MR, Xu LL, Wang SL, Yang C, Ding L, et al. Efficacy and tolerability of gabapentin in adults with sleep disturbance in medical illness: a systematic review and meta-analysis. *Front Neurol* 2017;8(316):316.

PUBMED | CROSSREF

- 39. Wylde V, Palmer S, Learmonth ID, Dieppe P. The association between pre-operative pain sensitisation and chronic pain after knee replacement: an exploratory study. *Osteoarthritis Cartilage* 2013;21(9):1253-6.

 PUBMED | CROSSREF
- Koh IJ, Kang BM, Kim MS, Choi KY, Sohn S, In Y. How does preoperative central sensitization affect quality of life following total knee arthroplasty? *J Arthroplasty* 2020;35(8):2044-9.
 PUBMED | CROSSREF
- 41. Tarakji BA, Wynkoop AT, Srivastava AK, O'Connor EG, Atkinson TS. Improvement in depression and physical health following total joint arthroplasty. *J Arthroplasty* 2018;33(8):2423-7.
- 42. Halawi MJ, Gronbeck C, Savoy L, Cote MP, Lieberman JR. Depression treatment is not associated with improved patient-reported outcomes following total joint arthroplasty. *J Arthroplasty* 2020;35(1):28-31.
- 43. Bian T, Shao H, Zhou Y, Huang Y, Song Y. Does psychological distress influence postoperative satisfaction and outcomes in patients undergoing total knee arthroplasty? A prospective cohort study. *BMC Musculoskelet Disord* 2021;22(1):647.

PUBMED | CROSSREF

44. Mahdi A, Hälleberg-Nyman M, Wretenberg P. Reduction in anxiety and depression symptoms one year after knee replacement: a register-based cohort study of 403 patients. *Eur J Orthop Surg Traumatol* 2021;31(6):1215-24.

PUBMED | CROSSREF

45. Blackburn J, Qureshi A, Amirfeyz R, Bannister G. Does preoperative anxiety and depression predict satisfaction after total knee replacement? *Knee* 2012;19(5):522-4.

PUBMED | CROSSREF

Moghtadaei M, Yeganeh A, Hosseinzadeh N, Khazanchin A, Moaiedfar M, Jolfaei AG, et al. The impact
of depression, personality, and mental health on outcomes of total knee arthroplasty. Clin Orthop Surg
2020;12(4):456-63.

PUBMED | CROSSREF

47. Hirschmann MT, Testa E, Amsler F, Friederich NF. The unhappy total knee arthroplasty (TKA) patient: higher WOMAC and lower KSS in depressed patients prior and after TKA. *Knee Surg Sports Traumatol Arthrosc* 2013;21(10):2405-11.

PUBMED | CROSSREF

48. Halawi MJ, Cote MP, Singh H, O'Sullivan MB, Savoy L, Lieberman JR, et al. The effect of depression on patient-reported outcomes after total joint arthroplasty is modulated by baseline mental health: a registry study. *J Bone Joint Surg Am* 2018;100(20):1735-41.

PUBMED | CROSSREF

49. Riddle DL, Wade JB, Jiranek WA, Kong X. Preoperative pain catastrophizing predicts pain outcome after knee arthroplasty. *Clin Orthop Relat Res* 2010;468(3):798-806.

PUBMED | CROSSREF