Neuropathic pain-like symptoms and pre-surgery radiographic severity contribute to patient satisfaction 4.8 years post-total joint replacement

Sophie C Warner, Helen Richardson, Wendy Jenkins, Thomas Kurien, Michael Doherty, Ana M Valdes

Sophie C Warner, Helen Richardson, Wendy Jenkins, Michael Doherty, Ana M Valdes, Academic Rheumatology, University of Nottingham, Clinical Sciences Building, Nottingham City Hospital, Nottingham NG5 1PB, United Kingdom

Sophie C Warner, Department of Cardiovascular Sciences, University of Leicester and National Institute for Health Research, Leicester Cardiovascular Biomedical Research Unit, Leicester LE3 9QP, United Kingdom

Thomas Kurien, Michael Doherty, Ana M Valdes, Arthritis Research UK Pain Centre, Nottingham NG5 1PB, United Kingdom

Thomas Kurien, Academic Division of Trauma and Orthopaedics, Queens Medical Centre, Nottingham NG7 2UH, United Kingdom

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Correspondence to: Sophie C Warner, PhD, Department of Cardiovascular Sciences, University of Leicester and National Institute for Health Research, Leicester Cardiovascular Biomedical Research Unit, Glenfield Hospital Groby Road, Leicester LE3 9QP, United Kingdom. scw27@le.ac.uk

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Abstract

AIM
To investigate a comprehensive range of factors that contribute to long-term patient satisfaction post-total joint replacement (TJR) in people who had undergone knee or hip replacement for osteoarthritis.

METHODS
Participants (n = 1151) were recruited from Nottinghamshire post-total hip or knee replacement. Questionnaire assessment included medication use, the pain-DETECT questionnaire (PDQ) to assess neuropathic pain-like symptoms (NP) and TJR satisfaction measured on average 4.8 years post-TJR. Individual factors were tested for an association with post-TJR satisfaction, before incorporating all factors into a full model. Data reduction was carried out using LASSO and receiver

Case Control Study

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operator characteristic (ROC) curve analysis was used to quantify the contribution of variables to post-TJR satisfaction.

**RESULTS**

After data reduction, the best fitting model for post-TJR satisfaction included various measures of pain, history of revision surgery, smoking, pre-surgical X-ray severity, WOMAC function scores and various comorbidities. ROC analysis of this model gave AUC = 0.83 (95%CI: 0.80-0.85). PDQ scores were found to capture much of the variation in post-TJR satisfaction outcomes: AUC = 0.79 (0.75-0.82). Pre-surgical radiographic severity was associated with higher post-TJR satisfaction: ORsatisfied = 2.06 (95%CI: 1.15-3.69), P = 0.015.

**CONCLUSION**

These results highlight the importance of pre-surgical radiographic severity, post-TJR function, analgesic medication use and NP in terms of post-TJR satisfaction. The PDQ appears to be a useful tool in capturing factors that contribute to post-TJR satisfaction.

**Key words:** Osteoarthritis; Patient satisfaction; Total joint arthroplasty; Neuropathic pain; Surgery outcomes

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Core tip: The growing number of total joint replacement (TJR) surgeries performed worldwide every year means that research in this area has the potential to impact millions of people. These results highlight the importance of a number of factors with regards to post-TJR satisfaction. The PDQ appears to be a useful tool in capturing factors that contribute to post-TJR satisfaction. Individuals with NP prior or post-TJR could be indicated using this short questionnaire and referred for further testing and treatment to improve outcomes at every stage of their osteoarthritic treatment process.

**INTRODUCTION**

A total joint replacement (TJR) is the only treatment for clinically severe osteoarthritis (OA). A TJR should be considered in individuals with marked symptoms of OA which significantly limit activity and participation and reduce quality of life if conservative treatments (e.g., exercise, weight loss if overweight, analgesic medication) are insufficient[1]. In the United Kingdom alone 160000 TJR are performed every year[2]. Generally very good outcomes are reported post-TJR[3] but pain can remain a concern for some individuals. According to one study, 27% of people who had undergone total hip replacement (THR) and 44% of people who had undergone a total knee replacement (TKR) had joint pain 3-4 years after surgery[4]. This pain can be inflammatory, nociceptive or neuropathic in nature[5].

Patient satisfaction post-TJR has been the subject of some studies[6-10] which have focused on only pain and function post-TJR[11]. Pre-operative radiographic severity, co-occurrence of painful conditions, a history of revision surgery, other comorbidities, and pain catastrophizing have also been linked to post-TJR outcomes in the literature but not all in the same cohort[8,12-15].

Neuropathic pain-like symptoms (NP) are caused by changes or damage to the nervous system, which can result from chronic nociceptive input (as seen in chronic pain states) and nerve damage during surgery[15,16,17]. NP has been reported in people with OA and post-TJR[4,18]. However, to our knowledge, currently no studies have investigated the role of NP on patient satisfaction post-TJR.

As TJR is currently the only long-term treatment for OA, if its effectiveness can be improved with better understanding of the individual differences in post-operative outcomes, this must be addressed. Due to the high number of TJR carried out in the United Kingdom and worldwide, research in this area has the potential to impact many individuals.

The aim of the present study was to investigate a comprehensive range of factors that contribute to long-term patient satisfaction post-TJR in people who had undergone knee or hip replacement for OA.

**MATERIALS AND METHODS**

**Participants**

The North Nottinghamshire Research Ethics Committee approved the study protocol (REC number: 07/Q2501/22). Participants who had undergone a TJR for OA were recruited from secondary care in Nottinghamshire (n = 1151) and gave written, informed consent. All participants had symptomatic and radiographic OA prior to TJR surgery. Between 2008 and 2011, nurse-administered questionnaires were completed by participants (n = 1219) on average 18 mo after surgery. These questionnaires included information on demographic variables, pain scores, TJR satisfaction and medication use. A subsequent follow-up postal questionnaire was sent to those who consented to further involvement in the study. This questionnaire was very similar in design to the baseline questionnaire. There was an average of 3.3 years between the first and second questionnaires. When the baseline and follow-up responses of participants who completed both questionnaires were compared there were no significant differences in age (P < 0.38), sex (P < 0.89), BMI (P < 0.07) or WOMAC pain scores (P < 0.51). There was not a significant difference in satisfaction levels (P =
The PDQ is a validated index. It was examined using the “PredictABEL” package for R above models. The discrimination ability of the models derived were used.

A logistic link function and the fitted LASSO coefficients were employed a LASSO-regularised regression model as case post-TJR satisfaction), fits a linear model to measure associations between TJR satisfaction and potential risk factors.

To select the risk factors contributing to post-TJR satisfaction, the least absolute shrinkage and selection operator method (LASSO) was used. LASSO is a feature selection method which, given a set of input measurements and an outcome measurement (in this case post-TJR satisfaction), fits a linear model. We employed a LASSO-regularised regression model as implemented by the R package “glmnet” (http://cran.r-project.org/web/packages/glmnet/index.html) using a logistic link function and the fitted LASSO coefficients derived were used.

Receiver operating characteristic (ROC) analysis was used to quantify the contribution of variables in the above models. The discrimination ability of the models was examined using the “PredictABEL” package for R (http://cran.r-project.org/web/packages/PredictABEL/index.html).

Statistical analysis
Statistical review of this study was performed by a biomedical statistician. The statistics package R (version 3.0.2) was used to run logistic regression analyses to measure associations between TJR satisfaction and potential risk factors.

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0.22). Individuals had not been not phenotyped for pain pre-surgery but pre-operative radiographic severity grade has been linked previously to TJR outcomes. The study design is presented in Figure 1.

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Pain severity: A visual analogue scale (VAS) was used to categorise individuals with high or low pain intensity at the operated joint (knee or hip). Scores range from 0-10, with ≥ 6 used to categorise high pain intensity.

TJR satisfaction: Individuals were asked to state how satisfied they felt with their TJR using an ordinal scale of “very satisfied”, “not very satisfied” and “dissatisfied”. For logistic regression analysis, individuals were dichotomised between: (1) “very satisfied”; and (2) “not very satisfied” and “dissatisfied”.

Radiographic severity: The extent of joint damage evident by X-rays was categorised by assessment of pre-surgery knee and hip radiographs by a single observer. For knees, the Kellgren-Lawrence (K/L) grading system was used. Scores range from 0-4, with ≥ 3 classified as severe and 2 classified as not severe (K/L < 2 no OA). An association with minimum joint space width (JSW) pre-surgery and pain post-surgery has been reported in a separate cohort. The minimum JSW was therefore used to classify hip OA, with minimum JSW ≤ 2.5 mm (which is a standard cut-off) being classified as radiographically severe. For bilateral surgery the joint with the most severe radiographic score was used.

Pain catastrophizing: The 13-item Pain Catastrophizing Scale (PCS) is a measure of the tendency to exaggerate the threat of a perceived harmful stimulus. Scores range from 0-52 and the highest tertile was used as a cut-off point to classify individuals as high catastrophizers, as previously described.

WOMAC pain, stiffness and function: The OA-specific Western Ontario and McMaster Universities Arthritis Index (WOMAC) questionnaire includes questions about pain (scored from 0-20), stiffness (scored from 0-8) and function (scored from 0-76). WOMAC function scores were categorised according to an OMERACT-defined PASS score of “acceptable function” (a score of ≤ 22) to allow a clinical guideline to be used in this study to put the importance of post-TJR satisfaction into a clinical context.

Medication use
Questionnaire responses were used to classify participants as taking over-the-counter analgesics (OTC), opioids, non-steroidal anti-inflammatory drugs (NSAIDs) or other prescription medications which can be used to treat pain, as previously described.

Trait definitions for statistical analysis
Neuropathic pain-like symptoms at the operated joints (knees or hips): The PDQ is a validated instrument for assessing NP. Scores range from 0-35, with > 12 indicating possible NP and ≥ 19 indicating likely NP.

Pain severity: A visual analogue scale (VAS) was used to categorise individuals with high or low pain intensity at the operated joint (knee or hip). Scores range from 0-10, with ≥ 6 used to categorise high pain intensity.

TJR satisfaction: Individuals were asked to state how satisfied they felt with their TJR using an ordinal scale of “very satisfied”, “not very satisfied” and “dissatisfied”. For logistic regression analysis, individuals were dichotomised between: (1) “very satisfied”; and (2) “not very satisfied” and “dissatisfied”.

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Table 1  Descriptive statistics categorised by total joint replacement satisfaction status and their contribution to the risk of dissatisfaction post-total joint replacement

| Trait | Very satisfied (n = 861) | Not very satisfied (n = 227) | Dissatisfied (n = 63) | OR not very satisfied/ dissatisfied (95%CI) |
|-------|--------------------------|----------------------------|----------------------|----------------------------------------|
| Demographic and morphometric | | | | |
| Age ± SD (yr) | 73.2 ± 8.6 | 73.0 ± 8.8 | 72.2 ± 9.1 | 1.00 (0.98-1.01) |
| % female | 57.4 | 56.8 | 47.6 | 0.85 (0.65-1.12) |
| BMI ± SD (kg/m²) | 29 ± 5.2 | 29.4 ± 5.1 | 30.7 ± 5.9 | 1.03 (1.00-1.06) |
| Type of surgery | THR (n = 494) | 407 (82.4%) | 74 (15.0%) | 13 (2.6%) | 0.58 (0.44-0.77) |
| | TKR (n = 591) | 410 (69.4%) | 136 (23.0%) | 45 (7.6%) | 2.02 (1.50-2.71) |
| | THR + TKR (n = 66) | 44 (66.7%) | 17 (25.8%) | 5 (7.6%) | 1.63 (0.95-2.75) |
| | | | | | 0.99 (0.96-1.03) |
| Pre-operative X-ray | Radiographically severe OA | 92.10% | 93.40% | 96.50% | 0.49 (0.27-0.87) |
| History of surgery | Previous arthroscopic knee surgery | 20.00% | 26.40% | 34.90% | 1.65 (1.21-2.25) |
| Psychological | % depression | 15.9 | 22.0 | 28.6 | 1.64 (1.17-2.30) |
| | PCS score (0-52) | 8.2 | 12.8 | 19.7 | 1.06 (1.05-1.08) |
| | Top tertile of PCS | 20.80% | 37.80% | 55.60% | 3.40 (2.54-4.59) |
| Use of medication | % opioid | 21.7 | 39.5 | 41.3 | 2.37 (1.77-3.18) |
| | % OTC | 49.0 | 64.5 | 61.9 | 1.33 (0.84-2.12) |
| | % NSAIDs | 7.8 | 12.3 | 3.2 | 1.83 (1.38-2.42) |
| | % other prescription analgesics | 12.2 | 20.0 | 23.8 | 1.85 (1.29-2.66) |
| Measures of pain | PDQ score (0-35) | 4.8 | 10.1 | 14.3 | 1.15 (1.31-1.18) |
| | Possible Neuropathic Pain (PDQ > 12) | 10.00% | 35.90% | 57.10% | 5.91 (4.22-8.29) |
| | Likely Neuropathic Pain (PDQ ≥ 19) | 6.50% | 18.10% | 34.90% | 7.66 (4.80-12.22) |
| | VAS (0-10) | 3.1 | 7.0 | 7.0 | 1.35 (1.29-1.41) |
| | HighVAS (> 3) | 30.80% | 61.20% | 76.20% | 6.47 (4.80-8.73) |
| | WOMAC pain (0-20) | 5.2 | 8.5 | 10.9 | 1.28 (1.23-1.33) |
| | WOMAC stiffness (0-8) | 2.9 | 4.1 | 4.4 | 1.62 (1.49-1.76) |
| | WOMAC function (0-76) | 25.7 | 38.0 | 47.8 | 1.07 (1.06-1.08) |
| Comorbidities | % heart disease/angina | 16.7 | 19.4 | 27.0 | 1.34 (0.95-1.89) |
| | % stroke | 5.1 | 9.3 | 12.7 | 2.09 (1.26-3.44) |
| | % hypertension | 52.3 | 50.2 | 57.1 | 0.95 (0.72-1.25) |
| | % asthma/COPD | 13.8 | 15.4 | 14.3 | 1.07 (0.73-1.57) |
| | % irritable bowel syndrome | 10.2 | 14.5 | 11.1 | 1.44 (0.96-2.17) |
| | % diabetes | 11.8 | 15.0 | 19.0 | 1.28 (0.86-1.90) |
| | % gout | 7.5 | 11.9 | 11.1 | 1.50 (0.95-2.37) |
| | % osteoporosis | 11.0 | 10.1 | 19.0 | 1.23 (0.80-1.88) |
| | % cancer | 15.9 | 19.8 | 17.5 | 1.29 (0.91-1.83) |
| | % current smoker | 6.5 | 11.0 | 14.3 | 1.93 (1.23-3.07) |

1All ORs are adjusted for age, sex and BMI; 2This classification includes any previous arthroscopic knee surgery. 3PDQ score and high pain intensity, PDQ scores and pain catastrophizing Scale; BMI: Body mass index.

Comorbidities

Comorbid conditions are commonly seen in people with OA, and people with OA are more likely to develop comorbid conditions such as cardiovascular disease and diabetes[20]. A list of comorbidities was included in the questionnaire. Participants were asked to indicate which of these conditions they had been previously diagnosed with by a doctor.

RESULTS

The descriptive characteristics, stratified by TJR satisfaction status, are shown in Table 1. One fourth of study participants (290) were dissatisfied or not very satisfied with the outcome of their surgery. The study was thus powered (80%, P < 0.05) to detect associations with odds ratios of 1.75 or higher for binary traits with a prevalence of 10% or higher in the satisfied group, such as neuropathic pain (Table 1).

On univariate analysis, the majority of the variables tested were found to be significantly associated with satisfaction post-TJR. This includes a higher BMI, various measures of pain (such as PDQ scores, high pain intensity and WOMAC pain scores), WOMAC function scores and pain catastrophizing (Table 1). Additionally, THR participants reported higher levels of being very satisfied (82.4%) than TKR patients (69.4%) (Table 1). Some factors were highly correlated with each other, such as PDQ scores and high pain intensity, PDQ scores and WOMAC pain scores and WOMAC pain scores and high pain intensity (P < 0.001 for all).

Given the large number of factors associated, many of them correlated with each other, we performed data reduction, using LASSO to identify which factors remain important contributors to post-TJR, post-THR and post-TKR satisfaction. After data reduction, the factors that remained in all three groups were: BMI, WOMAC function scores, PDQ scores, high pain intensity, severe pre-surgery radiographic OA and a past stroke. The full results of these analyses are shown in Table 2. Some
differences were observed in the factors that contribute to satisfaction post-THR and post-TKR, most notably a history of a revision surgery for THR and the WOMAC stiffness score for TKR. In both cases PDQ and VAS scores contribute significantly after adjustment for all other factors.

Higher pre-operative radiographic severity was also significantly associated with increased odds of TJR satisfaction: $\text{OR}_{\text{satisfied}} = 2.06$ (1.15-3.69), $P = 0.015$.

It was investigated whether patient satisfaction was related to measures of healthcare usage, specifically the use of analgesic medication. Strong associations were found between dissatisfaction and an increased likelihood of the use of some prescription analgesics (opioids and other prescription medications which can be used to treat pain) and OTC analgesics, but not prescription NSAIDs (Table 1). After adjustment for possible NP, high pain catastrophizing and high pain intensity (VAS) these associations become non-significant except in the case of opioids and OTC analgesics, [OR$_{\text{dissatisfied}}$ = 1.68 (1.21-2.34), $P = 0.002$; OR$_{\text{satisfied}}$ = 1.44 (1.06-1.97), $P = 0.020$, respectively].

Post-TJR satisfaction is strongly associated with a measure of acceptable function post-TJR, according to WOMAC-defined PASS scores in the literature.$^{[27,28]}$

This definition of acceptable function, according to a clinical guideline, was a very strong contributor to post-TJR satisfaction in this study after adjusting for age, sex and BMI: OR$_{\text{satisfied}}$ = 9.88 (95%CI: 6.58-14.85), $P < 0.001$. This association remained significant after further adjustment for possible NP, high pain catastrophizing and high pain intensity: OR$_{\text{satisfied}}$ = 4.82 (95%CI: 3.08-7.55), $P < 0.001$.

With regards to comorbidities, a history of stroke was associated with an increased risk of dissatisfaction post-TJR, as was being a current smoker (vs ex-smokers and people who have never smoked); $P < 0.01$ for both, see Table 1.

It was quantified how much these models contribute to satisfaction. The results of ROC analysis of the best-fitting model for each surgery group are shown in Table 2 and Figure 2. The results show that the list of identified factors explains an AUC of 0.83 of patient satisfaction for post-TJR, 0.84 for post-THR and 0.83 for post-TKR. This, however, includes a large number of factors and it was investigated whether one of the factors may capture the effects of most of the other factors.

Possible NP, classified using PDQ scores, was seen in 17.3% of participants in this study. However, in the dissatisfied group the prevalence of possible NP was 3.8 times higher than in the very satisfied group OR$_{\text{dissatisfied}}$ = 5.91 (4.22-8.29), $P < 0.001$ and the prevalence of likely NP was 5.4 times higher: OR$_{\text{likelyNP}}$ = 7.66 (4.80-12.22), $P < 0.001$ (see Table 1). Possible NP was less common in THR than TKR participants (11.9% and 22.3%, respectively) (Table 1). Likely NP has been reported previously to be present only in a small proportion of individuals post-TJR$^{[4]}$ using as a definition a PDQ > 19. However strong differences exist in satisfaction at various lower cut-offs which explains why pain-DETECT scores capture such a large proportion of patient satisfaction in these data (Figure 3).

Given this strong effect we hypothesised that PDQ scores, being strongly correlated with pre-surgery X-ray scores (Spearman’s rho = -0.13, $P < 0.001$) and associated with post-TJR pain intensity OR$_{\text{painintensity}}$ = 1.35 (1.30-1.40), $P < 0.001$, may capture much of the variation in post-TJR satisfaction outcomes, and indeed we find that this is the case. According to ROC analysis of PDQ scores (adjusted for age, sex and BMI), there is a significant contribution to post-TJR, post-THR and post-TKR satisfaction when this model is used (Table 2 and Figure 2). AUC values of 0.75 and over were reached in all three groups, even without the inclusion of any of the other available measures.

**DISCUSSION**

This study incorporated a comprehensive range of factors and shows that a number of factors including pain, comorbidities, smoking, history of revision surgery...
and pre-surgical radiographic severity contribute to post-TJR satisfaction 4.8 years after surgery. Scores measuring the presence of NP appear to capture a large proportion of the variation seen.

Patient satisfaction is an outcome measure which is simple to use and accounts for the complex aspects of TJR\(^{[30]}\). It has been recommended that patient satisfaction should be incorporated into assessments of post-TJR outcomes\(^{[30]}\). Our results suggest that although post-TJR satisfaction is influenced by a large number of factors, it is well summarised by one single instrument, namely PDQ scores.

The proportion of possible NP identified in this study falls within the range reported by previous studies on NP post-TJR (reviewed in\(^{[31]}\)) particularly when differences in methodology and sample composition are taken into consideration\(^{[4,15,32-37]}\). At first sight the importance of NP post-TJR detailed here appears to contrast with the report by Wylde et al\(^{[4]}\) who suggested that NP is a minor component of post-TJR pain.

The current data indicate that people who undergo TJR with only modest radiographic structural damage are more likely to report NP post-surgery. Although this might suggest that the NP was also present pre-surgery, we lack the pre-operative pain assessments necessary to confirm if that is the case. In addition, pain may derive from other sources, such as bone marrow lesions, that are not evident on radiographs and may still be present post-surgery\(^{[38]}\). Central nervous system involvement in OA, such as seen in NP, seems likely when the inconsistent correlation between pain and radiographic severity and the non-linear relationship between nociception and pain experienced are considered\(^{[17]}\) supporting the findings in this study.

In this study we fitted prediction models for patient dissatisfaction using all the contributing risk factors selected by LASSO. These models are fairly complicated in terms of the number of variables and therefore may not be applicable in clinical practice. However, we also show that PDQ scores have almost as much predictive value as the best fitting models. Therefore, in terms of clinical application our data suggest that assessing NP symptoms using the PDQ will help identify patients at highest risk of surgery dissatisfaction.

One key limitation to this study is the lack of pre-surgical pain data. However, Phillips et al\(^{[39]}\) found

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Figure 2  Receiver operator characteristic curves adjusted for age, sex and body mass index to show the amount of post-surgery satisfaction predicted by preoperative radiographic severity, pain-DETECT questionnaire scores and the best fit model. A: Post-TJR (THR and TKR combined); B: Post-TKR; C: Post-THR. TJR: Total joint replacement; THR: Total hip replacement; TKR: Total knee replacement.
that it was not possible to reliably predict post-TKR outcomes from pre-operative pain intensity and PDQ scores[39], whereas Dualé et al.[46] have reported a higher risk of NP post-surgery if peripheral NP is present pre-surgery. Although the self-administered PDQ allows data collection from a large number of individuals it does not provide definitive evidence of NP[40]. Nonetheless, one study showed a correlation between PDQ scores and periaqueductal grey matter activation (which is involved in central sensitisation) in people with OA in areas of referred pain in response to punctate stimuli[41].

Although in this study we did not use the widely accepted National Joint Registry agreed Patient Reported Outcomes (PROMS) data[42], 92% of the questions in the Oxford hip and knee score (OXHS and OXKS, respectively) questionnaires are accounted for by the questionnaire used in this study, as was 83% of the content in the EQ-5D questionnaire. The questionnaire measured used in this study therefore reflects a large majority of the material covered in the PROMS. On the other hand we have examined other factors that are not usually included as part of post TJR PROMS, such as comorbidities, use of analgesic medication and pre-surgery X-ray severity all of which contribute to patient self-reported satisfaction in our data. To our knowledge this is one of the few studies to date which has looked at pain assessment integrated with comorbidities and use of medication.

Some of the factors identified as contributing to satisfaction could be addressed pre-surgery or considered when assessing outcomes post-surgery. The presence of comorbid conditions appears also to have a considerable effect on patient satisfaction, and this information may be used to manage patient expectations pre-surgery.

In conclusion, the PDQ appears to be particularly useful in capturing factors that contribute to post-TJR outcomes and may be considered as an important postsurgical assessment. These results also highlight the importance of understanding the mechanisms behind NP symptoms post-TJR, as it is a significant factor contributing to post-TJR satisfaction and, importantly, affects a considerable proportion of individuals post-TJR.

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P-Reviewer: Fisher DA, Fenichel I, Tangtrakulwanich B
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