

Predictors and Prevalence of Persistent Pain after Total Knee Arthroplasty in One-Year Follow-up

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Abstract

Background: Total knee arthroplasty (TKA) is one of the most common surgeries performed to reduce pain and disability in knee arthritis. Comprehension of the etiology and prevalence of persistent postoperative knee pain can help reduce this pain and identify the predictive factors leading to it. This study aimed to investigate the predictive factors and the prevalence of persistent pain after total knee arthroplasty in one-year follow-up.

Materials and Methods: This was a prospective cohort study. Demographic data including age, sex, body mass index (BMI), hospital anxiety and depression scale (HADS), and comorbidities were collected. In 242 patients, preoperative and postoperative Western Ontario and McMaster Universities Arthritis Index (WOMAC) scores were measured before and immediately after surgery and in 3-, 6-, and 12-month intervals during follow-up. Loosening of the prosthesis was also investigated by radiographic imaging in every postoperative visit.

Result: WOMAC pain decreased from a mean (standard deviation) of 49 before surgery to 18 at 6 months and 13 at 12 months. Despite this, the prevalence of moderate-to-severe persistent postoperative pain (PPP) was 13.22% ($n = 32$) and 9.09% ($n = 22$) at 6 and 12 months lower preoperative WOMAC (odd's ratio:2.8), loosening of the prosthesis (odd's ratio:1.9), higher HADS (odd's ratio:2.1) were main predictors for PPP in TKA patients as in rheumatoid arthritis (odd's ratio:1.2).

Conclusion: Loosening of the prosthesis and higher preoperative WOMAC scores are key factors in persistent post-TKA pain. Depression and anxiety are more popular among patients with more pain after TKA. RA is more prevalent in patients with PPP after TKA.

Keywords: Persistent pain, postoperative pain, primary osteoarthritis, total knee arthroplasty

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INTRODUCTION

Chronic pain is defined as pain that remains on average for 3 to 6 months after surgery, and its intensity and level sometimes increase. A study in England showed 22.5% of persistent and chronic pain after surgery. Despite many measures to reduce pain, chronic pain is known as one of the complications of surgeries.^[1,2]

One of the surgeries that cause chronic pain is total knee arthroplasty and studies show that the incidence of TKA is

expected to increase about 70% by the year 2030.^[3] This pain can last up to 3 to 6 and even a year or more. TKA is one of the commonest surgeries that are performed to reduce pain and disability in knees that are in the last stage of their arthritis, and nonsurgical treatments are not the answer to the patient's pain and disability; however, many studies revealed that TKA improves the quality of life and knee functions.^[4] As severe pain is the main indication for total knee arthroplasty, persistent

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postoperative pain (PPP) can lead to the dissatisfaction of the patients.^[5,6]

Unexplained persistent pain after TKA is a common and difficult problem for surgeons to solve. Approximately 10–34% of TKA patients have moderate-to-severe pain long after the operation. The causes of these pains are multifocal and are divided into etiologies related to the person and etiologies related to the treatment. From the person-oriented causes of postoperative pain, we can mention genetics, underlying diseases, and psychological aspects.^[7,8]

As the prevalence and etiologies for this persistent pain are not well recognized and are the field of debating, studying the etiologies and prevalence of persistent pain can help manage it and identify the factors leading to it. The current study aimed to investigate the predictive factors and the prevalence of persistent pain after primary TKA for one year.

MATERIAL AND METHOD

Patients and study design

This prospective cohort study was approved by the Isfahan University of Medical Sciences Ethics Committee (and registered IR.MUI.MED.REC.1399.755). After obtaining informed consent, inclusion criteria were planned for primary unilateral TKA. Exclusion criteria were <18 year old, diagnosed learning disability, Raynaud's syndrome, unsuitable for neuraxial anesthesia, previous periarticular fractures, and a diagnosed neurological condition that hurts pain sensation or revision surgery within the follow-up period with progressive radiolucency around prosthesis. Patients were recruited between October 2018 and November 2021 [Figure 1].

All patients with inclusion criteria underwent a unilateral, TKA with or without patella resurfacing in some cases according to clinical indication. All patients underwent combined spinal epidural (CSE) with sedation and if it was necessary general anesthesia was done. All patients received multimodal analgesia after surgery including acetaminophen (paracetamol),

NSAIDs, and oral opioids (oxycodone) as required. In some cases, gabapentin was the only available medication. The formula for calculating sample size for a prospective cohort study is as follows:

$$N = (Z\alpha/2 + Z\beta)^2 * (p(1-p))/(p1-p2)^2$$

$$Z\alpha/2 = 1.96, Z\beta = 0.86, p = 0.09, p1 = 0.05, p2 = 0.015$$

Measurement of effective factors

Variables of this study were age (year), gender (male and female), and body mass index (BMI) (kg/m²) as the demographic factors that were collected from patients' documents. Postoperative pain severity (measured by WOMAC (The Western Ontario McMaster Universities Osteoarthritis Index) scale), preoperative anxiety and depression (measured by HADS (hospital anxiety and depression scale that is a fourteen-item scale with seven items each for anxiety and depression subscale, scoring for each item varies from zero to three)) and prosthesis loosening (identified as radiolucency around the prosthesis, which was progressive in the patients' follow-ups, but did not require revision, measuring in every visit and comparing it to the previous image for detecting any periprosthetic lucency) were other documented factors. Total surgical time (in minutes) was a confounding variable of this study which was measured. Considering that all the surgeries performed were accompanied by tourniquet closing, the time of surgery is the indicator of tourniquet closing time. Since the duration of tourniquet closure is related to tissue ischemia, this issue can be involved in persistent postoperative pain. (This issue is mentioned in orthopedic references). Also, data like underlying diseases such as diabetes mellitus (DM) (patients' documents), rheumatoid arthritis (diagnosed by a rheumatologist), and thyroid malfunction (hypo and hyper) (diagnosed by an endocrinologist) were collected.

Moderate-to-severe PPP (WOMAC pain $\geq 30/100$) in the operated knee 3, 6, and 12 months after the operation was the primary outcome of the present study. A score of $\geq 30/100$ defines moderate-to-severe pain, and people with arthritis and after TKA typically find this pain intensity unacceptable. The HADS scale in follow-ups of more than 8 denotes anxiety and depression.

Statistical analysis

Categorical variables were analyzed by Chi-square tests or Fisher's exact tests. Mann-Whitney U tests were done to examine differences in pain between patients with and without moderate-to-severe PPP. Multivariate logistic regression models were then developed to examine moderate-to-severe PPP predictors 6 and 12 months after surgery. Models were developed using a stepwise approach, accounting for interaction and collinearity. Model covariates were included if variance inflation factors were < 2 and their correlations with one another were < 0.4 . Sensitivity and specificity and receiver operating characteristic (ROC) analyses were calculated.

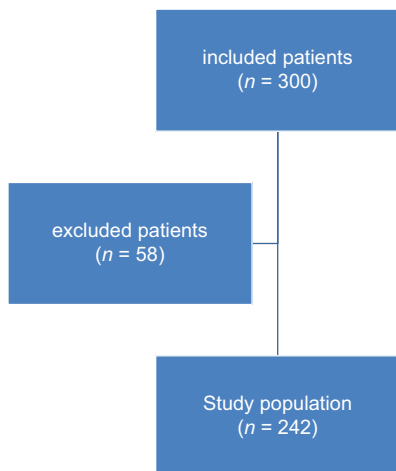


Figure 1: Schematic diagram of the study

A significance level of 5% ($P < 0.05$) and confidence intervals of 95% were used. Statistical analyses were carried out using SPSS v. 24 (IBM Corp., Armonk, USA).

RESULT

In this study, 300 patients enrolled in the study, and 58 patients were excluded because exclusion criteria patients were included in the study and were evaluated and follow-ups were done for them. Data, after analysis, are demonstrated in Table 1.

WOMAC pain decreased from a mean (standard deviation) of 49 before surgery to 18 at 6 months and 13 at 12 months. Despite this, the prevalence of moderate-to-severe PPP (WOMAC pain, $\geq 30/100$) was 13.22% ($n = 32$) and 9.09% ($n = 22$) at 6 and 12 months.

We evaluated 242 patients with 69.4-year mean age of them (69.3 in PPP and 69.5 in non-PPP) ($P > 0.39$). One hundred and eleven of these patients were male and 131 patients were female (55 male and 65 female in PPP and 56 male and 66 female in non-PPP) ($P > 0.55$). According to Table 1, the mean BMI was 31.15 which is 31.4 in the PPP group and 30.9 in the non-PPP group ($P > 0.8$). Total surgical time was 92.75 minutes and there was no significant difference between PPP and non-PPP ($P > 0.65$). Forty-nine patients had higher preoperative WOMAC that had a meaningful connection with post-operation pain ($P > 0.3$ and odd's ratio: 1.3).²⁴ and eight had DM and thyroid malfunction that had no meaningful connection with postoperative persistent pain ($P > 0.3$ and $P > 0.8$). RA was a risk factor of postoperative persistent pain that five patients had ($P < 0.05$ and Odd's ratio = 1.2). Loosening of the prosthesis happened in 49 patients after surgery which was more prevalent in the PPP group ($P < 0.05$ and odd's ratio = 1.9) [Table 2].

RA, higher preoperative WOMAC, depression/anxiety, and loosening of the prosthesis were variables that had an odd's ratio of more than 1 and were related to persistent pain after primary TKA.

DISCUSSION

In this study, we evaluated predictors and prevalence of post-TKA pain and concluded that BMI and demographic data like age and gender have no effect on pain which is compatible with a study conducted by Rice and colleagues (with BMI 31 kg/m²).^[9]

In our study, underlying diseases like diabetes mellitus and thyroid malfunction had no effect on pain. However, rheumatoid arthritis was a medical condition that affected pain, and patients with RA had more post-TKA persistent pain. In Lee's study in 2014, RA patients who underwent TKA were more susceptible to dislocation, infection, and other morbidities. These complications will cause more pain after TKA, but persistent pain was not measured in that study.

Patients who had more preoperative pain were those patients that had more pain after surgery and preoperative higher WOMAC score is a key factor that can be assessed for predicting persistent pain after surgery. Blackburn *et al.* in 2015 also did a systematic review and revealed the fact that preoperative pain can affect postoperative pain and preoperative depression can be a predictive factor for postoperative persistent pain. Depression and anxiety, which were measured by the HADS questionnaire in our study, are two important and effective predictive factors for persistent pain perception after primary TKA. Depression/anxiety exists in some of the patients undergoing TKA and can affect the prescription of pain. This preoperative factor should be checked before the surgery. Therefore, surgeons are trying to identify people with a high risk for depression/anxiety. Preoperative level of pain can affect postoperative pain suffered by the patients.^[10,11] Duivenvoorden *et al.* did a study about depression after TKA and concluded that patients' depression decreased after TKA in 12 months. Also, people who had more pain and depression before surgery had more pain after TKA.^[11] This is compatible with our study.

Loosening of the prosthesis was more common in patients with pain. Pain can be the result of the process that causes the loosening of the prosthesis. Causes of failure may be

Table 1: Different variables assumed to affect persistent postoperative pain

Variable	Total value $n=242$	Value in PPP $n=22$	Value in non-PPP $n=220$	P
Age (year)	69.4	69.3	69.5	>0.39
Gender				
Male	111	55	56	>0.55
Female	131	65	66	
BMI (kg/m ²)	31.15	31.4	30.9	>0.2
Surgical time	92.75	92.4	93.1	>0.8
DM (number)	24 (9.91%)	13 (5.37%)	11 (4.54%)	>0.3
RA (number)	5 (2.06%)	4 (1.65%)	1 (0.41%)	<0.05
Thyroid malfunction (number)	8 (3.30%)	4 (1.65%)	4 (1.65%)	>0.8
Loosening of prosthesis (number)	9 (3.71%)	8 (3.30%)	1 (1.65%)	<0.05
HADS (number)	6 (2.47%)	5 (2.06%)	1 (1.65%)	<0.05
Preoperative WOMAC	49 (20.24%)	54 (22.31%)	44 (18.18%)	<0.05

Table 2: Regression model of the variables contributing to persistent postoperative pain

Components of regression model	P	Odds ratio per unit change [95% CI]
RA	<0.05	1.2678 [1.1265, 1.7856]
Loosening of prosthesis	<0.05	1.9368 [0.3249, 6.9633]
HADS	<0.05	2.1873 [1.1534, 5.1464]
Preoperative WOMAC	<0.05	2.8694 [1.2342, 6.6513]

considered as being classified by clinical examinations and standard radiography, which includes loosening, wear of the polyethylene, instability, and others. Many causes of failure have been examined, but there are few reports investigating possible causes for persistent postsurgical pain.^[11,12]

Among the limitations of the present study, it can be pointed out that it was difficult to access patients undergoing surgery in follow-ups due to pain and their dissatisfaction and less cooperation due to painful knees. We advise further studies with larger sample sizes as recognizing the etiologies and risk factors for persistent pain after primary TKA is extremely helpful in patients' selection for preoperative pain consulting.

CONCLUSION

We concluded that RA is an underlying disease that can cause persistent pain after primary TKA. Also loosening of prosthesis and preoperative higher scores of pain (WOMAC) are key factors in predicting post-TKA pain. Depression and anxiety are more prevalent among patients with persistent pain after primary TKA.

Ethics approval and consent to participate

This research has been approved by the ethics committee of Isfahan University of Medical Sciences (Ethics code: IR.MUI.MED.REC.1399.755). Written informed consent was obtained from the patients.

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Conflicts of interest

There are no conflicts of interest.

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