ORIGINAL ARTICLE

Persistent pain following total knee arthroplasty: The role of underlying diseases

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Background: With increasing age and joint-destructive diseases, the need for novel surgeries such as total knee arthroplasty (TKA) has increased. Complications such as pain exacerbation and persistent pain after surgery may occur which increases rehabilitation programs. Factors such as body mass index (BMI), psychiatric disorders, spine diseases, and comorbidities diseases can affect outcomes. Our study was conducted to evaluate the effect of BMI, psychiatric disorders, spine diseases, and underlying diseases on persistent and annoying pain after TKA. **Materials and Methods:** This is a case–control study that was conducted on patients who underwent TKA in Kashani Hospital in Isfahan City in 2020–2022. Demographic data of patients including age and BMI, diabetes mellitus (DM), history of psychiatric disorders, spine disorders such as spondylolisthesis or disc herniation, and other underlying diseases were obtained. Patients were assigned to case or control groups based on pain complaints after surgery. All patients were evaluated 6 months after the initial surgery. After collecting the study data, they were entered into SPSS software (version 25, IBM Corporation, Armonk, NY, USA) and analyzed. **Results:** We enrolled 35 patients in the case group and 39 patients in the control group between June 2020 and September 2022, based on the severity of pain measured using a Visual Analog Scale score. Our results show that BMI and DM had a meaningful relationship with pain after surgery ($P \leq 0.01$). Other factors did not show a significant difference between groups. **Conclusion:** Underlying diseases, psychiatric diseases, and spine disorders did not significantly affect the pain after TKA. Patients with DM and higher BMI experienced more persistent pain after TKA.

Key words: Arthroplasty, body mass index, diabetes mellitus, knee, persistent knee pain

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INTRODUCTION

The importance of arthroplasty cannot underestimate one of the most frequently performed procedures in the field of orthopedics.[1,2] Multiple institutions have estimated that by 2050, the rate of this operation will grow by 143%.[3-5] Total knee arthroplasty (TKA) involves removing the damaged joint surface and replacing it with various types of metal and polyethylene covers. Among the most common causes of TKA, we can mention diseases that destroy the joint surfaces, such as osteoarthritis and inflammatory arthritis, the prevalence of osteoarthritis.[6-8] Despite the advantages of TKA, this operation is an optional one and should be placed after sufficient conservative. The benefits and side effects of this operation for the patients should be carefully evaluated to ensure that the optimum benefit is provided. Various studies demonstrated that if patients are correctly selected for TKA, the outcome of the operation such as pain reduction, improvement of knee function, and improvement of quality of life.[8,9] Although pain reduction is one of the most important benefits of TKA, in 25% of cases, patients complain of persistent pain (with different qualities) after surgery that needs more rehabilitation. Rehabilitation is offered

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to patients undergo TKA to improve the quality of life after but its effect on surgery postoperative pain is unclear.[10] After TKA, the functional ability of the patients improves significantly.[9,11,12] Debilitating and severe postoperative complications, as well as mortality after TKA, are generally low and include about half to 1% per year, which is mostly related to the comorbidities of the patients, such as cardiovascular diseases, diabetes mellitus (DM), and higher body mass index (BMI). Higher BMI at the time of TKA negatively impacts the prognosis of the surgery.[13-15] Recent studies have emphasized the need to identify individual factors in patients that lead to poor outcomes after TKA so that by eliminating or adjusting them, the quality of surgical outcomes and satisfaction of patients could improve. It is important to consider the impact of obesity on surgical outcomes, as some studies have suggested that it may be harmful. However, it is worth noting that other research has raised doubts about this finding. The same holds true for the effects of depression, which should not be overlooked when making medical decisions.[16-20] Considering the widespread and growing prevalence of TKA and the importance of postoperative complications such as persistent pain, there is a need for detailed and comprehensive studies to determine the factors deteriorating postoperative outcomes. Therefore, the present study was conducted to survey the effect of individual patient factors such as depression, obesity, underlying diseases, and spine deformities on persistent pain after TKA.

METHODS

This retrospective study was conducted on patients who underwent primary TKA in Kashani Hospital in Isfahan City in 2020–2022. From June 2020 to September 2022, 346 patients underwent TKA at applying the exclusion criteria. The study protocol was approved by the Research Committee of Isfahan University of Medical Sciences and the Ethics Committee also approved it (IR.MUI.MED.REC.1400.815). The inclusion criteria for patients included in the study were ages between 40 and 74, patients who underwent primary TKA, consent to perform surgery, and giving informed and written consent. Exclusion criteria were insufficient demographic information, TKA for a reason other than osteoarthritis or inflammatory arthritis, unwillingness to participate in the study, and nonreferral for follow-up treatment. All patients whom met the inclusion criteria entered the study using the census method.

Demographic data including age, gender and BMI, reason for TKA (osteoarthritis vs. inflammatory arthritis), length of hospital stay, history of psychiatric disorders, spine disorders such as spondylolisthesis or disc herniation, and other underlying diseases were obtained. The severity of pain was measured using a Visual Analog Scale (VAS) score. This score is a visual scale in that the lowest pain of the patient is (0) and the highest level of pain is 10 and is asked from patients to score their pain. All the patients were interviewed after surgery, and patients with VAS scores 0–3 were assigned to the no pain group, patients with VAS scores between 4 and 6 were assigned to the moderate pain group, and patients with VAS scores higher than 6 were assigned to the severe pain group. In the current study, patients were divided into two groups, including without pain (VAS score ≤3) and with persistent pain (VAS score ≥4).[21]

Statistical analysis

After collecting data, they were entered into SPSS software (version 25, IBM Corporation, Armonk, NY, USA) and analyzed. Descriptive statistics for quantitative data were done using mean ± standard deviation and compared with the independent samples *t*-test. Qualitative data were represented as numbers (percentages) and were compared with the Chi-square test. Finally, logistic regression was used to explain the relationship between the underlying disease and the binary pain variable. In all tests, values of $P < 0.05$ were considered a significant level.

RESULTS

Analyzing the data of the study was demonstrated. Among them, 74 patients (21%) reported their pain intensity as 4 or higher during the interview, and finally, 35 patients (47.3%) were classified as a group with pain due to meeting the including and excluding criteria. Furthermore, 39 patients (52.7%) were included in the study as patients without pain (VAS score between 1 and 3). Demographic information, including BMI ($P = 0.05$) and age ($P = 0.41$), and the BMI were significant, so the study demonstrated the increase in BMI, the VAS score [Table 1].

About the underlying diseases consist of grade two spondylolisthesis, lumbar disc herniation, spinal canal stenosis, depression, bipolar disease, and dyslipidemia were not significant between the two groups ($P > 0.05$). It is worth noting that the group without pain experienced higher rates of anxiety, high blood pressure, and ischemic heart disease. These health issues were not significantly

Table 1: Demographic data of participants

Variables	Mean±SD		*P*
	Without pain (VAS ≤3) (*n*=39)	With pain (VAS ≥4) (*n*=35)	
Age (year)	69.28±6.41	70.54±6.7	0.41*
BMI	25.30±3.60	27.52±3.59	0.005*

*Independent-samples *t*-test. SD=Standard deviation; VAS=Visual Analog Scale; BMI=Body mass index

different between the two groups. However, it is important to consider the potential negative impact of living with pain on overall health and well-being. However, DM was reported to be significantly higher in the group with pain [$P = 0.01$, Table 2 and Figure 1].

The logistic regression analysis found no evidence to suggest that underlying disease factors have any impact on pain. This means that regardless of age, gender, or health conditions, we can take comfort in the fact that these factors are unlikely to affect patient's experience of pain [Table 3].

DISCUSSION

Our study was a case–control study and was conducted to investigate the effect of factors such as psychiatric disorders, BMI, underlying diseases, and the simultaneous presence of spine diseases on persistent pain after TKA. According to our results, underlying diseases, psychiatric diseases, and spine disorders did not significantly affect the pain after TKA. However, patients with DM and higher BMI had greater pain after TKA.

In a similar study, Yang *et al*.[22] reported the prevalence of chronic pain after TKA to be 30% of all patients, while the prevalence of pain in the present study was calculated to be 21%. This difference can be caused by the difference in implementation methods between the previous studies and the current study (such as the patient population, the number of centers under study, and the duration of the study). Mathis *et al*.[19] suggest that factors such as high BMI and depression can cause more severe knee pain after TKA. However, as mentioned above, the mentioned factors have been reported only with a possible and nonspecific effect on pain after TKA, and no study has been conducted to find their definitive effect. In a retrospective study conducted by Singh and Lewallen[20] in two phases, the authors concluded that patients with underlying diseases such as heart disease, as well as psychiatric diseases such as anxiety, have a significantly higher chance of experiencing moderate-to-severe knee pain 5 years after TKA. However, no significant relationship has been found between patients suffering from DM, peripheral vascular diseases, kidney diseases, chronic obstructive pulmonary disease, and pain. Furthermore, in a recent meta-analysis study, Jump *et al*.[23] concluded that there is no direct relationship between patients suffering from DM and pain after TKA. The abovementioned studies contrast with our study. However, in another study conducted by Rajamäki *et al*.,[24] they found that having DM and metabolic syndrome affected the persistence of pain after surgery in patients who underwent a TKA. In the present study, the patients suffering from DM were significantly more prevalent in the group with pain, and it can be considered an effective factor in the continuation of pain. However, as explained in the previous studies, there is a need to conduct a study on a wider population. Furthermore, there is a possibility that things such as the number of years of DM, race, gender, the skill of the surgeon, and the quality of the surgery, which are different in various centers, are effective in explaining the difference between the results of this and previous studies. On the other hand, the results of this

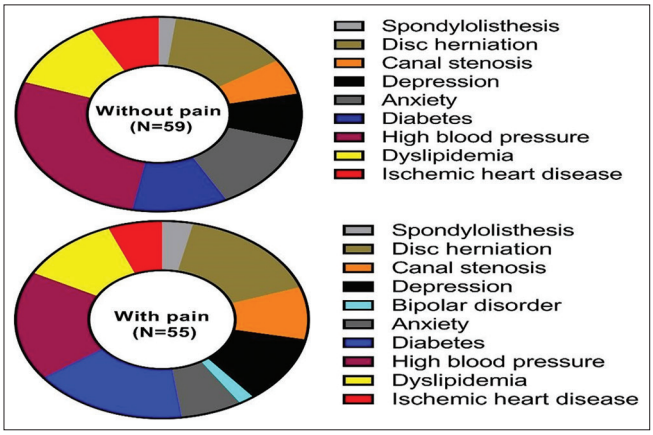

Figure 1: Schematic of statistical analysis of the data of both groups under study

Table 2: Number (percentage) of underlying disease factors in by pain groups

Variables	Without pain (*n*=39), *n* (%)	With pain (*n*=35), *n* (%)	*P**
Spondylolisthesis	2 (5.1)	4 (11.4)	0.28
Disc herniation	14 (35.9)	19 (54.3)	0.16
Canal stenosis	6 (15.4)	10 (28.6)	0.17
Depression	8 (20.5)	13 (37.1)	0.13
Bipolar disorder	0	2 (5.7)	0.22
Anxiety	13 (33.3)	8 (22.9)	0.31
DM	11 (28.2)	20 (57.1)	0.01
High blood pressure	28 (71.8)	21 (60)	0.24
Dyslipidemia	12 (30.8)	13 (37.1)	0.62
Ischemic heart disease	8 (20.5)	7 (20)	0.95

*Chi-square test. DM=Diabetes mellitus

Table 3: Logistic regression odds ratios of underlying disease factors

Parameter	OR (95% CI)	*P*
Age	1.01 (0.93–1.10)	0.792
BMI	1.16 (0.98–1.37)	0.081
Spondylolisthesis	0.55 (0.07–4.49)	0.579
Disc herniation	0.81 (0.24–2.72)	0.738
Canal stenosis	0.43 (0.11–1.68)	0.226
Depression	0.69 (0.18–2.63)	0.582
Anxiety	1.02 (0.30–3.48)	0.973
DM	0.51 (0.16–1.62)	0.254
High blood pressure	1.13 (0.33–3.90)	0.850
Dyslipidemia	0.54 (0.16–1.80)	0.315
Ischemic heart disease	1.30 (0.26–6.44)	0.745

DM=Diabetes mellitus; OR=Odds ratio; CI=Confidence interval; BMI=Body mass index

study indicate that if patients have DM and a higher BMI, the score given by the patients to the VAS score system was also higher. This issue is contrary to the results of previous studies and reminds us of the need to pay close attention to the demographic characteristics of the population under study. Another issue investigated in the present study was the effect of psychiatric diseases on the occurrence of persistent pain after TKA. Yang *et al*.[22] investigated the course of pain treatment in patients undergoing TKA. They listed the presence of severe and debilitating pain, psychiatric diseases, and the simultaneous use of support devices for movement as the causes of poor recovery from pain after surgery in these patients. In the meta-analysis study conducted by Lewis *et al*.,[25] they concluded that the presence of psychiatric diseases such as depression and anxiety, more severe pain in the knee or any other part of the body before TKA, and having pain in several parts of the body are predictive factors for persistent pain after surgery. They have also stated that despite adjusting these conditions before surgery, a negligible effect on the prevention of pain after surgery has been observed. However, in the current study, no significant relationship was observed between depression, bipolar disease, anxiety, and pain in patients. Among the causes for the difference in results is the length of time the patients were observed, the severity of the psychiatric condition, the quality of psychiatric care, and the number of patients in the study population. Another goal pursued in the current study was to survey the effect of patients suffering from spinal diseases on persistent pain after surgery. In 2021, Mathis *et al*.[19] investigated the typical characteristics of pain after TKA. In this study, knee pain with itching, knee pain with a piercing nature, knee pain with a crushing nature that leads to immobility, and knee pain with a feeling of heaviness were identified as the most common pain patterns after TKA had been introduced. Furthermore, out of the total number of 97 patients included in the study, 89.5% stated their pain was in the front of the knee, 48.1% stated that the pain worsened with activities such as going down the stairs, and 14% of the patients also reported shooting pain in other points. While suffering from spine diseases such as spinal canal stenosis can produce disruptions in the sense of pain and also affect the way a person moves, they exacerbate the complications of knee diseases such as pain, according to their idea. In another study, Petrin and Freedman[26] mentioned a case of chronic pain after TKA in a female patient with spondylolysis myelopathy, which was resolved after lumbar vertebrae fusion and spinal decompression surgery. The authors have pointed out that undiagnosed diseases related to the spinal cord and spine may be the reason for the continuation or exacerbation of pain after TKA. Sheppard *et al*. also found that by reducing the internal diameter of the spine, especially in lumbar levels 1–4, and creating pressure on the spinal cord, the range of motion of the lower limbs significantly decreased, and the pain and spasm of the lower limbs, including in the knees, were increased.[27] However, no significant relationship between spine diseases and pain was found in the patients of the present study. To explain the disparity between the results of the studies mentioned and those of the current study, it is possible to point to the type of previous studies, the lack of investigation into the age groups of patients and their gender in the current study, and the specific relationship between spinal disease (spondylolysis myelopathy) and pain in the previous studies. The scale systems used to measure the severity of pain can also influence the variation in outcomes.

CONCLUSION

Based on the study's findings, TKA in patients who suffer from depression, concomitant spine disorders, and other underlying diseases has no observable effect on the occurrence of pain. However, according to our research, patients with a higher BMI and DM reported more pain after TKA. Despite considering a variety of factors as methodological challenges, such as an inadequate sample size, conducting the study in one center, and the limitations of the study regardless, the authors suggested that studies with a larger sample size, in multiple centers, and for an extended time might be able to get a reassuring outcome.

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Conflicts of interest

There are no conflicts of interest.

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