

## Determinants of outcome prior to and after total hip and knee arthroplasty

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# Chapter IV

No associations between self-reported knee joint instability and radiographic features in knee osteoarthritis patients prior to Total Knee Arthroplasty: a cross-sectional analysis of the Longitudinal Leiden Orthopaedics Outcomes of Osteo-Arthritis study (LOAS) data

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## Abstract

**Background:** To describe the prevalence of self-reported knee joint instability in patients with pre-surgery knee osteoarthritis (OA) and to explore the associations between self-reported knee joint instability and radiological features.

**Methods:** A cross-sectional study including patients scheduled for primary Total Knee Arthroplasty (TKA). Self-reported knee instability was examined by questionnaire. Radiological features consisted of osteophyte formation and joint space narrowing (JSN), both scored on a 0 to three scale. Scores >1 are defined as substantial JSN or osteophyte formation. Regression analyses were provided to identify associations of radiological features with self-reported knee joint instability.

**Results:** Two hundred and sixty-five patients (mean age 69 years and 170 females) were included. Knee instability was reported by 192 patients (72%). Substantial osteophyte formation was present in 78 patients (41%) reporting and 33 patients (46%) not reporting knee joint instability. Substantial JSN was present in 137 (71%) and 53 patients (73%), respectively. Self-reported knee instability was not associated with JSN (relative to score 0, odds ratios (95%CI) of score 1, 2 and 3 were 0.87 (0.30-2.54), 0.98 (0.38-2.52), 0.68 (0.25-1.86), respectively) or osteophyte formation (relative to score 0, odds ratios (95%CI) of score 1, 2 and 3 were 0.77 (0.36-1.64), 0.69 (0.23-1.45), 0.89 (0.16-4.93), respectively). Stratified analysis for pain, age and BMI showed no associations between self-reported knee joint instability and radiological features.

**Conclusion:** Self-reported knee joint instability is not associated with JSN or osteophyte formation.

## Introduction

Self-reported knee instability has been defined as a sensation of buckling, shifting, or giving way of the knee [1]. Knee joint stability has been studied in patients with mild to moderate knee osteoarthritis (OA), of which 60-80% of the patients reported this sensation [1-4]. The sensation itself or fear of the sensation may lead to limitations in daily life [3]. Besides, self-reported knee joint instability is associated with pain and muscle strength [1-3]. So far, knowledge on joint stability in patients with knee OA prior to Total Knee Arthroplasty (TKA) is scarce with only one study reporting a prevalence of 72% [5]. A clear cause for this sense of instability in patients with knee OA has not been elucidated yet. A possible mechanism underlining the presence of self-reported knee instability in severe knee OA is structural damage of the knee joint. No studies have so far addressed the relationship between self-reported knee instability in knee OA prior to TKA and structural damage of the knee presented by radiological features.

With respect to radiological features, two opposing hypotheses on knee joint instability have been described in patients with knee OA: (i) knee joint instability is low due to osteophyte formation and (ii) knee joint instability is high due to joint space narrowing [6,7]. The first hypothesis is based on the premise that osteophytes, fibrosis of joint ligaments and capsular thickening are responsible for an increased tightness of the joint and restriction of movement, resulting in a stiff and stable knee joint. The second hypothesis is based on the premise that more pronounced joint space narrowing leads to reduced stress on the ligaments and capsule of the knee, resulting in a less stable knee joint. In severe knee OA, osteophytes and joint space narrowing are well-known features, however in mild knee OA these features are less pronounced [8]. In mild to moderate knee OA no associations were found between radiographic features and knee joint stability, which might be explained by a reduced emphasis of these features [3]. It is to be expected that in patients with knee OA prior to TKA, osteophyte formation is more distinct and will result in a more stable knee joint. Whereas, in patients with a more distinct joint space narrowing instability will be more reported.

The aims of the study were to determine the prevalence of selfreported knee joint instability and to determine the association between radiographic features (i.e. joint space narrowing and osteophyte formation) with self-reported knee joint stability in patients with knee OA prior to TKA.

## **Materials and methods**

#### Study design

The study participants were selected from the Longitudinal Leiden Orthopeadics Outcomes of Osteo-Arthritis study (LOAS), which is an ongoing multi-centre, longitudinal prospective cohort study designed to determine long-term outcomes of Total Hip Arthroplasty (THA) and TKA. The LOAS study (Trial ID NTR3348) started in June 2012 and included 2556 participants until December 2014, of which 1234 underwent TKA.

#### Study population

The present cross-sectional sub-study included all patients scheduled for primary TKA in the Alrijne (former Rijnland) Hospital Leiderdorp, the Netherlands. Patients who were able to complete questionnaires in Dutch and who were 18 years or older were included. Excluded were patients who did not provide informed consent, possessed insufficient Dutch language skills, had a physical or mental status not allowing participation, already underwent TKA or received a Unicompartmental Knee Arthroplasty (UKA) instead of a TKA after surgery. Eligible patients were informed about the study through written and oral information by their treating medical specialist at the outpatient clinic. Only patients who approved to be approached by the researcher received additional written information about the study by regular mail, as well as a questionnaire, a stamped return envelope and a consent form. Patients who did not return their preoperative questionnaire within one week were contacted by telephone. Patients were included once written informed consent was obtained according to the Declaration of Helsinki. For the purpose of the present analysis only data from patients who provided information about the presence of self-reported knee joint instability were included. Ethical

approval was obtained by the Medial Ethics Committee of the Leiden University Medical Center (registration number P12.047) and funding was received from the Dutch Arthritis Foundation (LLP13).

The inclusion of patients is shown in Figure 1. During the first months of recruitment (June 2012 – December 2014) a sample of 349 participants with knee OA, scheduled for TKA was included at baseline in the Alrijne Hospital, Leiden, the Netherlands. Of these, 73 patients already possessed a TKA in the contralateral knee, three patients did not provide information on knee joint instability and eight patients received a UKA instead of TKA, resulting in 265 patients (76%) eligible for the present analysis.

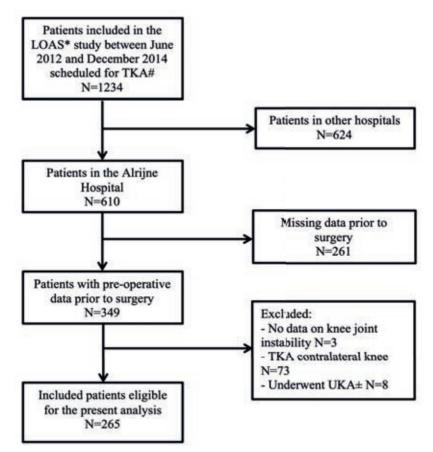


Figure 1. Flow-chart'

- \* LOAS = Longitudinal Leiden Orthopaedics and Outcomes of Osteo-Arthritis Study
- # TKA = Total Knee Arthroplasty
- ± UKA = Unicompartmental Knee Arthroplasty

#### Assessments

#### Sociodemographic characteristics

Patient characteristics included: age, sex, weight (kg), height (m), Body Mass Index (BMI) and the duration of knee complaints (less than 1 year; between 1 - 5 years; between 5 - 10 years; more than 10 years).

#### Self-reported knee instability

Self-reported knee instability was assessed by means of a knee joint instability questionnaire, according to the questionnaire of Felson et al. [1]. The item on the presence of knee joint instability was formulated as follows: 'the sensation of buckling, shifting or giving way of the knee in the previous 3 months' with the following answering options: 1 never (0 episodes); 2 seldom (one or two episodes); 3 regular (three to five episodes); 4 very often (more than five episodes). These options were dichotomized into no episodes of knee joint instability (answering option 1) or one or more episodes of knee instability (answering options 2 to 4) [3].

Patients reporting knee instability were additionally asked if the sensation of buckling, shifting or giving way of the knee concerned the left, right or both knees and to what activities the sensation was perceived (walking; rising from chair; ascending stairs; twisting or turning; descending stairs; sitting down in chair).

#### Radiological damage

All radiographs were standardised according to the local protocol. This protocol included (1) standing, weight-bearing anteroposterior radiographs and (2) standing, weight-bearing lateral radiographs of the knee joint. All radiographs were assessed by an experienced musculoskeletal radiologist (HMK), who was blinded from patient characteristics. Ten percent of the radiographs were scored twice to establish inter-reader reliability (Intra-Class Correlation: 98% (95% CI 97-98%)). Discrepancies between the first and second readings were solved by consensus. The used scoring system [9,10] consisted of three items which were independently scored for the lateral and medial sides of the joint and separately for the left as well as the right knee. The scored items were (a) joint space narrowing (JSN) (b) osteophyte formation on the joint margins or tibial spines and (c) the Kellgren and Lawrence (K&L)

score. JSN and osteophyte formation were scored on a 0-3 scale ranging from 0 no JSN/osteophytes, 1 minute JSN/osteophytes, 2 definite JSN/ osteophytes and 3 ankylosis JSN/large osteophytes. Substantial JSN or osteophyte formation is defined as a score greater than one. The K&L score was scored on a 0-4 scale (grade 0: indicating no OA; grade 1: doubtful OA; grade 2: minimal OA; grade 3: moderate OA and grade 4: indicating severe OA) [8].

For the present analysis the highest scores of osteophyte formation and joint space narrowing from the lateral or medial tibiofemoral compartment from the knee scheduled for surgery (the index knee) were used.

#### Comorbidity

Information on comorbidities was gathered to measure musculoskeletal and non-musculoskeletal comorbidities that potentially could influence to the sensation of instability. A comorbidity questionnaire developed by the Dutch Central Bureau of Statistics (CBS) [11] was used in which the presence or absence of comorbidities in the previous year was asked. These comorbidities were classified in two domains: musculoskeletal comorbidities (severe elbow, wrist or hand pain; back pain; other rheumatic diseases) and non-musculoskeletal comorbidities (chronic lung diseases; cardiac disorder or coronary disease; arteriosclerosis; hypertension; (consequences of) stroke; severe bowel disorder; diabetes mellitus; migraine; psoriasis; chronic eczema; cancer; incontinence of urine; hearing or vision impairments; dizziness in combination with falling) [12].

#### Pain and function in daily living

Pain and function in daily living were assessed using two of the subscales from the self-reported Dutch version of the Knee Injury and Osteoarthritis Outcome Score (KOOS) [13]. The KOOS is a knee-specific instrument, developed to assess the opinion of patients about their knee and associated problems. The KOOS holds 42 items divided over five separately scored subscales: Pain (nine items); Activities of daily living (ADL) (17 items); Symptoms (seven items); Sport and Recreation Function (Sport) (five items); and Knee Related Quality of Life (QoL) (four items). Standardised answer options are given on a five-point Likert scale resulting in a score from 0 to four. A normalized score (100 representing

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the best outcome and 0 indicating the worst outcome) is calculated for each subscale. In 2007 Groot et al. translated and validated the KOOS into a Dutch version [14].

#### Statistical analyses

Firstly, descriptive statistics for patient characteristics were calculated in the total group, as well as for persons reporting knee instability and persons reporting no knee instability. Chi-square tests and independent T-tests were used to identify significant differences in demographic variables between patients reporting knee joint instability and patients reporting no knee joint instability. Secondly, logistic regression analyses were provided to identify associations of JSN and osteophyte formation (independent variables) with self-reported knee joint instability (dependent). In addition, stratified logistic regression analyses were performed for sex, comorbidities and, based on the median, for BMI, pain and limitations in daily activities. Statistical significance was accepted at p values less than 0.05. All data were analysed using the SPSS statistical package (version 20.0, SPSS, Chicago, Illinois).

## Results

#### Characteristics of all patients

The characteristics of the participants are described in Table 1. Two hundred and sixty-five patients with a mean age of 68.9 years (standard deviation (SD) 8.4) and a mean BMI of 28.6 (SD 4.3) were included. A total of 244 patients (93%) reported knee complaints for more than a year; 126 patients (48%) even for more than five years. Furthermore, comorbidities were observed in 188 patients (72%) of which 89 patients reported a musculoskeletal comorbidity. In addition, 55 patients (29%) reported comorbidities in more than one category and six patients (three percent) reported comorbidities in all the three categories.

The mean (SD) KOOS subscale scores were 39.3 (17.8) for pain, 46.1 (18.3) for ADL, 44.3 (13.4) for symptoms, 10.5 (14.4) for sport and 26.5 (15.6) for QoL in the total group.

	Total group (n=265)	Knee-instability (n=192)	Knee- stability (n=73)	p-value
Age, mean (SD)	68.9 (8.4)	68.1 (8.0)	70.7 (9.0)	0.028
Sex, Female; n (%)	170 (64%)	121 (63%)	49 (67%)	0.567
Body Mass Index, mean (SD)	28.6 (4.3)	28.4 (4.4)	29.1 (3.9)	0.203
<b>Comorbidity</b> , n (%) Musculoskeletal Non-musculoskeletal	(n=172) 89 (52%) (n=259) 157 (61%)	72 (61%) 113 (61%)	17 (32%) 44 (60%)	0.001* 0.943
Duration of knee complaints, years <1 1-5 5-10 >10	17 (7%) 118 (45%) 47 (18%) 79 (30%)	13 (7%) 79 (42%) 34 (18%) 64 (34%)	4 (6%) 39 (55%) 13 (18%) 15 (21%)	0.184
Knee joint instability Activities performed when instability was experienced Walking Ascending stairs Descending stairs Twisting or turning Sitting down in chair Rising from chair		(n=162) 140 (86%) (n=135) 63 (47%) (n=125) 59 (47%) (n=146) 92 (63%) (n=124) 17 (14%) (n=145) 65 (45%)		
Radiology indexknee K&L indexknee				
0-1 2 3-4	43 (16%) 49 (19%) 173 (65%)	31 (16%) 34 (18%) 127 (66%)	12 (16%) 15 (21%) 46 (63%)	0.141
Osteophyte formation No Minute Definite Large	57 (21%) 97 (37%) 103 (39%) 8 (3%)	44 (23%) 70 (36%) 72 (38%) 6 (3%)	13 (17%) 27 (37%) 31 (43%) 2 (3%)	0.814
<b>Joint Space Narrowing</b> No Minute Definite Ankylosis	28 (11%) 47 (18%) 126 (47%) 64 (24%)	21 (11%) 34 (18%) 94 (49%) 43 (22%)	7 (10%) 13 (17%) 32 (44%) 21 (29%)	0.744
Health-related Quality of Life				
ADL Symptoms Sport Quality of Life	39.3 (17.8) 46.1 (18.3) 44.3 (13.4) 10.5 (14.4) 26.5 (15.6)	36.7 (16.2) 43.6 (17.8) 41.5 (12.3) 8.6 (11.8) 24.6 (14.8)	45.7 (20.0) 52.1 (18.3) 51.3 (13.7) 15.4 (18.8) 31.4 (16.7)	0.001* 0.000*

Table 1. Patient characteristics, self-reported knee instability and radiological features of the study population

SD = standard deviation

n = number of patients

K&L = Kellgren & Lawrence score

KOOS = Knee injury and Osteoarthritis Outcome Score

ADL = Activity limitations Daily Living

\*Comparison of patients with knee stability and patients with knee instability by means of Chi Square or Independent tests where appropriate. Significance level < 0.05

#### Self-reported knee joint instability

Self-reported knee instability in the previous three months was present in 192 patients (72%), of which 170 patients (89%) also reported knee joint instability in the previous six weeks. Most patients (91%) reported instability in one of the knees, whereas nine percent of the patients in both knees. In addition, in 98% of the patients, the knee scheduled for surgery was reported as (one of the) instable. Furthermore, an episode of knee joint instability occurred most in the majority (86%) of patients during walking, followed by twisting or turning movements (reported by 63% of the patients).

Moreover, the proportions of patients with a younger age (p = 0.028), reporting more often musculoskeletal comorbidities (p = 0.001) as well as the proportions of patients with worse KOOS Pain (p = 0.001), ADL (p = 0.001), Symptoms (p = 0.000), Sport (p = 0.001) and Quality of Life (p = 0.001) subscale scores were somewhat higher in patients reporting knee joint instability compared to patients reporting no knee joint instability.

#### Radiographic severity

Both patients reporting knee joint instability as well as patients reporting no knee joint instability 84% (158 and 61 patients, respectively) had a K&L score >1. In the 43 patients with K&L <2, the decision for surgery was based on symptomatology (pain and function) (17 patients), information from arthroscopy (three patients) or information from Magnetic Resonance Imaging (MRI)/Computed Tomography (CT) (22 patients). Osteophyte formation was substantial in 78 patients reporting knee joint instability (46%) along with 33 patients reporting no knee joint instability (46%). Besides, 137 patients reporting knee joint instability (71%) and 53 patients reporting no knee joint instability (71%) had substantial JSN. Osteophyte formation and JSN were not significantly different between patients reporting knee instability and patients reporting no knee instability (p = 0.814 and p = 0.744, respectively).

#### <u>Associations of self-reported knee joint instability and radiographic</u> <u>severity</u>

In univariate regression analyses no significant associations were found between self-reported knee instability and JSN (relative to score 0, the outcomes of score 1, 2 and 3 were odds ratio (OR) 0.87; 95% CI 0.30-2.54. OR 0.98; 95% CI 0.38-2.52, OR 0.68; 95% CI 0.25-1.86, respectively) or osteophyte formation (relative to score 0, the outcomes of score 1, 2 and 3 were OR 0.77; 95% CI 0.36-1.64, OR 0.69; 95% CI 0.23-1.45, OR 0.89: 95% CI 0.16-4.93, respectively) (shown in Table 2). Additional stratified analyses were provided for sex, BMI, limitations in daily living, pain and comorbidities. Analysis in men and females separately showed no association between OA and self-reported knee joint instability. Furthermore, separate analyses of patients with a BMI > 27.9 versus patients with a BMI < 27.9 or patients with severe limitations in daily activities versus patients with minor limitations in daily activities (ADL median subscale score of 44.1) showed no associations between selfreported knee instability and JSN or osteophyte formation. In addition. stratified analyses for patients with severe pain versus minor pain (pain median subscale score of 39.3) showed no associations. Finally, stratified analyses for the presence/absence of comorbidities were done in the two dichotomized groups separately; 1) musculoskeletal comorbidities present/absent; and 2) non-musculoskeletal comorbidities present/ absent. There were no significantly different associations between selfreported knee joint instability and radiographic features between patients with comorbidities or not in any of the groups.

	В	P-value	OR	95% CI
Osteophyte formation score, relative to score 0 (no				
osteophyte formation)	0.166	0.631	1.2	0.6-2.3
1 (minute osteophyte formation)	0.045	0.898	1.0	0.5-2.1
2 (definite osteophyte formation) 3 (large osteophyte formation)	0.171	0.832	1.2	0.2-5.8
JSN score, relative to score 0 (no JSN)				
1 (minute JSN)	-0.112	0.821	0.9	0.3-2.4
2 (definite JSN)	-0.123	0.778	1.2	0.4-2.1
3 (ankylosis)	0.187	0.702	1.3	0.5-3.1

\*B = regression coefficient; OR = odds ratio; 95% CI = 95% confidence interval

## Discussion

This cross-sectional cohort study focused on the presence of selfreported knee joint instability in 265 patients with knee OA awaiting TKA surgery. Furthermore, the associations between self-reported knee joint instability and radiological features were evaluated. The majority of patients (72%) with knee OA prior to TKA reported knee joint instability. Though we hypothesised that self-reported knee joint instability would be associated with radiographic features, no associations were found with either JSN or osteophyte formation. This suggests that structural damage of the knee joint prior to TKA might not be related to the sense of knee instability. The high prevalence of self-reported knee instability in patients awaiting knee surgery indicates that it is an important issue in patients with knee OA, warranting the need to identify factors responsible for the sense of instability in this patient group.

It was our aim to identify an association between radiographic osteoarthritic features and self-reported knee joint instability. This aim was based on the assumption that osteophytes stabilise the knee joint as first described by Pottenger et al. [15] and widely accepted by physicians as well as cited in multiple articles and books [1,6,16,17]. It has been hypothesised that structural features compose the underlying mechanism for knee instability in patients with knee OA. Narrowing of the joint could contribute to a higher prevalence of knee joint instability in patients with knee OA [15], but results supporting this statement were lacking, as narrowing of the joint was not measured [15]. In addition, the authors suggested that osteophyte formation prevented progression of instability in OA knees [15]. Contradictory, our data do not support these suggestions. Two possible explanations for the differences in results were the used definition of stability and the different types of osteophytes. The difference in definition is based on previous studies where the varusvalgus laxity of the tibiofemoral joint was assessed, which is a different concept of knee stability as compared to self-reported knee stability [18]. The difference in definition of knee joint instability (self-reported versus laxity) could explain the difference in results. Knee joint instability measured with other techniques could still be associated with radiographic

features. The second possible explanation for the different results lies in the grouping of different types of osteophytes, which was beyond the scope of this study. A study of Nagaosa et al. [10] characterised the size and direction of osteophytes in knee OA and suggested that only small, predominantly outward extending osteophytes create stability. Thus, not only the size of osteophytes, but also the location in the tibiofemoral joint (e.g. central versus the edge of the joint) could be taken into account when performing the analysis. Future studies will be necessary to evaluate the effect of different types and locations of osteophytes on self-reported knee joint instability.

Muscle weakness was associated with self-reported knee joint instability in patients with knee OA [3]. It can be speculated that muscle weakness is associated with the perception of knee joint instability in situations when the joint is loaded, for example during walking. Muscles of the knee joint are delayed to respond to external forces, which can result in the perception of not controlling the knee. This is supported by our data. where a majority of the patients (86%) reported knee joint instability during walking. The perception of not controlling the knee during daily activities is closely related to the notion of confidence of the knee. In our study, uncertainty regarding knee control was highly prevalent and strongly associated with self-reported knee instability (data not shown). which is in agreement with previous studies [19,20]. In addition, effusion of the knee joint is common in patients with knee OA [21] and hypothesised to influence the perception of knee joint instability. Unfortunately, we had no data on knee effusion in our patients. Moreover, our study found age, pain and limitations in daily living to be associated with self-reported knee joint instability, which is in accordance with previous literature [1-3]. This illustrates that we used a representative approach to measure associations with self-reported knee joint instability. Besides, stratified analyses were performed, aiming to validate the results, showing no differences in associations between self-reported knee instability and radiological features. This supports the hypothesis that structural damage of the knee joint is not related to the perception of knee instability.

Several limitations of the study should be mentioned. First, this study was of a cross-sectional design, therefore, no causal conclusions are allowed. Second, since the assessment of the sensation of knee joint instability could be biased by subjective bias it is important to assess objectified knee instability. Future studies are needed to assess objectified knee ioint instability. Third, muscle strength was not assessed before surgery. This is a serious limitation since it is known that muscle strength is identified as one of the main factors associated with self-reported knee ioint instability [3]. Fourthly, other clinical characteristics of the knee were not assessed, such as local inflammation of the knee joint. It is to be expected that swelling of the joint by effusion and synovitis could increase the perception of knee instability. Hence, future studies would benefit from including inflammatory characteristics. Fifthly, self-reported knee instability has been included as outcome in an intervention study [22]. showing an improvement in self-reported knee instability by exercises. Reliability of this measure of instability is unknown. Sixthly, 43 patients with K&L score 0-1 were included. It has been reported that decisions for TKA should be based on symptomatology rather than radiographic features alone [23]. Therefore, the decision for surgery in these patients was based on symptomatology or information from arthroscopy or MRI. Moreover, several strengths of the study should be acknowledged. First, assessment of knee joint instability was done according to several previous studies and our prevalence rates are in accordance with previous literature. Secondly, we used unselected patients and thirdly. solely patients prior to TKA were included resulting in an appropriate population to test our hypothesis.

## Conclusion

In conclusion, self-reported knee joint instability is not associated with either JSN or osteophyte formation. If further studies aim to focus on the relationship between self-reported knee joint instability and radiographic features, the effect of different types, locations and directions of osteophytes should be taken into account.

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