Chapter 2

Self-reported knee instability and activity limitations in patients with knee osteoarthritis: results from the Amsterdam Osteoarthritis cohort

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Clinical Rheumatology 2012;31(10):1505-10

Abstract

The objective of this study was to evaluate whether self-reported knee instability is associated with activity limitations in patients with knee osteoarthritis (OA), in addition to knee pain and muscle strength. A cohort of 248 patients diagnosed with knee OA was examined. Self-reported knee instability was defined as the perception of any episode of buckling, shifting or giving way of the knee in the past 3 months. Knee pain was assessed using a numeric rating scale, and knee extensor and flexor strength were measured using an isokinetic dynamometer. Activity limitations were measured by using the Western Ontario and McMasters Universities Osteoarthritis Index questionnaire (subscale physical function), the timed Get Up and Go test and the timed stair climbing test, and 3 questionnaires evaluating walking, climbing stairs, and rising from a chair. Other potential determinants of activity limitations were also collected, including joint proprioception, joint laxity, age, sex, body mass index (BMI), disease duration, and radiographic disease severity. Regression analyses evaluated the effect of adding self-reported knee instability to knee pain and muscle strength, when examining associations with the activity limitations measures. Self-reported knee instability was common (65%) in this cohort of patients with knee OA. Analyses revealed that self-reported knee instability is significantly associated with activity limitations, even after controlling for knee pain and muscle strength. Joint proprioception, joint laxity, age, sex, BMI, duration of complaints, and radiographic severity did not confound the associations. In conclusion, self-reported knee instability is associated with activity limitations in patients with knee OA, in addition to knee pain and muscle strength. Clinically, self-reported knee instability should be assessed in addition to knee pain and muscle strength.

Introduction

In patients with knee osteoarthritis (OA), knee pain and lower limb muscle weakness are established risk factors for limitations in daily activities, such as walking, stair-climbing and rising up from or sitting down on a chair (1,2). It has been demonstrated that a majority of knee OA patients reports knee instability (3-5). Self-reported knee instability has been defined as a sensation of buckling, shifting or giving way of the knee (3). The sensation itself or fear of the sensation might lead to an avoidance of daily activities. The relationship between self-reported knee instability and activity limitations (3,4,7) and the relationship between self-reported knee instability and knee pain and muscle strength (5,6) has been shown in a number of studies. However, although studies focused on these relationships it is unknown whether self-reported knee instability further contributes to activity limitations in addition to knee pain and muscle strength. It is possible that the relationship between self-reported knee and activity limitations is due to confounding by pain or muscle strength. In assessing the relationship between self-reported knee instability, knee pain, muscle strength and activity limitations, there is a need to control for other potential confounders found in previous studies: poor joint proprioception, high joint varus-valgus laxity, age, and body mass index (BMI) (1,8,9).

The objective of the present study was to evaluate whether self-reported knee instability is associated with activity limitations in patients with knee OA, in addition to knee pain and muscle strength.

Methods

Patients

Data from the present study are from the Amsterdam Osteoarthritis (AMS-OA) cohort (5). Patients are included in the AMS-OA cohort if knee OA is diagnosed, according to the American College of Rheumatology (ACR) clinical criteria (10). Total knee replacement, rheumatoid arthritis or any other form of arthritis (crystal arthropathy, septic arthritis, reactive arthritis, spondylo-arthropathy) and neurological deficits are exclusion criteria. The Medical Ethics Institutional Review Board of Reade approved the study. All patients provided written, informed consent.

Measures

Knee instability. Self-reported knee instability was defined as the sensation of an episode of buckling, shifting or giving way of the knee in the previous 3 months (3,11). Persons reporting knee instability were additionally asked for the number of episodes of instability,

whether these episodes concerned the left, right or both knees, if any episodes had resulted in a fall, and the particular activity that induced an episode of instability (3).

Knee pain. Knee pain over the past week was assessed by an 11 point numeric rating scale (0 -10), with higher scores representing more pain. Patients were asked: What was your pain rating on average over the past week?

Muscle strength. Muscle strength of the left and right leg was measured isokinetically (EnKnee, Enraf-Nonius, Rotterdam, Netherlands) at 60^{o}/second (8,9). The mean muscle strength (i.e. extension and flexion) per leg was calculated to obtain a measure of overall leg muscle strength (Nm). For the analysis, individual mean muscle strength was divided by the patient's body weight for a normalized measure (Nm/kg).

Activity limitations. Four self-report questionnaires and two performance based tests were used to measure activity limitations. The Dutch version of the Western Ontario and McMasters Universities (WOMAC) Osteoarthritis Index physical function subscale was used to assess general lower-extremity related limitations in daily activities (12,13). The timed Get Up and Go (GUG) test was conducted over a distance of 15 meters, comparable to Hurley et al (14,15). A timed stair-climb test was used to assess the time (in seconds) patients needed to ascend and descend a stair (12 steps, 16 cm high, as fast as possible). The correlation between ascending and descending stair-climb times was r (95% CI)=0.90 (0.85, 0.97). Therefore, in analyses, the ascending stair-climb time was used. The Walking Questionnaire (WQ35), the Climbing Stairs Questionnaire (CStQ15), and the Questionnaire Rising and Sitting down (QR&S39) were used to assess specific lower-extremity related limitations in daily activities and have been validated in OA patients (16-19).

Radiology. Weightbearing, anteroposterior radiographs of the knee joints were obtained following the Buckland-Wright protocol (20) and graded according to Kellgren & Lawrence (K/L) (21). The ICC of the interrater reliability for the K/L grade was 0.89.

Other variables. Joint proprioception was measured as the threshold of detection of passive joint movement (9). Joint varus-valgus laxity was measured as the total movement in the frontal plane during varus-valgus load in a non-weight bearing position (8). For both joint proprioception and joint laxity, the mean of 3 measurements (in degrees) was calculated for each knee. A series of demographic variables were obtained including age, sex, height, weight, and duration of complaints.

Statistical analysis

Descriptive statistics (mean±SD) were calculated for measures of knee pain, muscle strength, activity limitations (WOMAC physical function [WOMAC-pf], GUG, timed stair-climb, WQ35, CStQ15 and QR&S39), joint proprioception, joint laxity, age, BMI, and duration of

complaints. For categorical or nominal level variables (self-reported knee instability, sex and radiographic severity of OA), frequencies and percentages were calculated.

Linear regression analyses were performed to analyze the association of self-reported knee instability as independent variable with activity limitations, controlling for knee pain and muscle strength. Self-reported knee instability was dichotomized as in a previous study (5). To differentiate between self-reported in stability in 1 knee and self-reported instability in 2 knees, compared to no instability, we made 2 dummy variables of self-reported knee instability (no instability versus unilateral instability and no instability versus bilateral instability). For muscle strength, the sum of both knee measurements and the absolute difference between both knee measurements were added to the regression analyses. This procedure controls for the independent contribution to the regression model of the left and right knee data of muscle strength. First, univariable regression analyses were performed to assess the marginal association of knee pain, muscle strength, and self-reported knee instability with 3 generally accepted outcomes of activity limitations (WOMAC-pf, timed GUG and timed stair-climb) and 3 new outcomes of specific activity limitations (walking, stair-climbing and rising and sitting questionnaires). Second, multivariable regression analyses were performed to assess the impact of self-reported knee instability on activity limitations in addition to knee pain and muscle strength. Third, background knowledge identified joint proprioception, joint varus-valgus laxity, age, sex, BMI, duration of complaints, and radiographic severity as potentional confounders, according to the confounder selection by Greenland (22). The regression analyses were repeated with these potential confounders entered one at a time (enter method). The impact of the potential confounders on the primary model (self-reported knee instability, knee pain, and muscle strength) was determined from the unstandardized regression coefficient (i.e., *B*). When a potential confounder changed the regression coefficient of self-reported knee instability, knee pain or muscle strength by more than 10%, this variable was considered to be a confounder (23). For joint proprioception, joint varus-valgus laxity, and radiographic severity, the independent contribution to the regression model of the left and right knee data was assessed in the same way as for muscles strength.

The significance level for exclusion from the regression analysis was set at *P* values less than 0.05. All analyses were performed using SPSS software, version 18.0 (Chicago, IL).

Results

Table 1 shows the characteristics of patients with knee OA. In univariable analyses (Table 2), unilateral self-reported knee instability (either left or right) was significantly associated with WOMAC-pf, timed GUG, and timed stair-climb. Bilateral self-reported knee instability was only associated with the WOMAC-pf. The difference between the left and right data of the variable muscle strength was not significantly associated with activity limitations.

Table 1. Characteristics of patients with knee osteoarthritis (*n*=248)

	Number (%)	**Mean ± SD**
Age, years		61.0 ± 7.9
Female	161 (65%)	
Body mass index, kg/m^2		28.9 ± 5.3
Duration of complaints, years		8.8 ± 8.9
Knee instability in past 3 months		
No	86 (35%)	
Unilateral, right	73 (29%)	
Unilateral, left	52 (21%)	
Bilateral	37 (15%)	
Knee instability during activities		
Walking	96 (59%)	
Stair-climbing ascend	46 (28%)	
Stair-climbing descend	30 (19%)	
Twisting/turning	48 (30%)	
Chair rising up	52 (32%)	
Chair sitting down	4 (2%)	
Knee instability resulting in fall incident	16 (10%)	
Pain (NRS 0-10)		5.0 ± 2.2
Isokinetic upper leg muscle strength, Nm/kg		
Right knee		1.81 ± 0.83
Left knee		1.87 ± 0.84
WOMAC-pf (0-68)		26.1 ± 12.6
Timed GUG, seconds		10.9 ± 3.2
Timed Stair-climb, ascent, seconds		7.4 ± 4.6
Timed Stair-climb, descent, seconds		8.1 ± 5.7
WQ35 (0-100)		28.4 ± 22.2
CStQ15 (0-100)		39.1 ± 20.8
QR&S39 (0-100)		38.5 ± 25.1
Joint proprioception, degrees		
Right knee		2.98 ± 2.16
Left knee		3.02 ± 2.66
Joint laxity, degrees		
Right knee		7.46 ± 3.92
Left knee		7.36 ± 3.98
K&L score, no of knees		
Right (*n*=248)		
Grade 0	10 (4%)	
Grade 1	87 (35%)	
Grade 2	72 (29%)	
Grade 3	49 (20%)	
Grade 4	30 (12%)	
Left (*n*=247*)		
Grade 0	9 (4%)	
Grade 1	86 (35%)	
Grade 2	82 (33%)	
Grade 3	47 (19%)	
Grade 4	23 (9%)	

WOMAC-pf=Western Ontario and McMasters Universities Osteoarthritis Index-physical function; Timed GUG=Timed Get Up and Go test; WQ35=Walking Questionnaire; CStQ15=Climbing Stairs Questionnaire; QR&S39=Questionnaire Rising and Sitting down; K&L=Kellgren and Lawrence; * *n*=1 missing.

After adding self-reported knee instability to the multivariable model with knee pain and muscle strength, unilateral self-reported knee instability (either left or right) was still significantly associated with all 3 outcomes measures, but bilateral self-reported knee instability with none.

Decreased joint proprioception, joint varus-valgus laxity, age, sex, BMI, disease duration, and radiographic severity did not confound the association of self-reported knee instability, knee pain, and muscle strength with activity limitations.

The univariable regression analysis of self-reported knee instability on specific limitations in daily activities (walking, stair-climbing and rising up or sitting down) demonstrated that both unilateral and bilateral self-reported knee instability were significantly associated with each of these activities (Table 3). The associations of self-reported knee instability, knee pain and muscle strength with specific daily activities were not confounded.

Discussion

Our results showed that self-reported knee instability was significantly associated with activity limitations (self-reported and performance-based), in addition to knee pain and muscle strength. These associations were not confounded by joint proprioception, joint laxity, age, sex, BMI, duration of complaints, or radiographic severity of OA. The results demonstrate that self-reported knee instability is a relevant independent variable related to activity limitations. It implies that self-reported knee instability should be addressed in clinical assessment and could be a target for therapeutic interventions.

Two previous studies have focussed on the relationship between self-reported knee instability and activity limitations (3,4). The results of our study are in line with both studies. First, the population-based Framingham Offspring Study from Felson et al (3) demonstrated a significant difference in WOMAC-pf between participants who had more than one episode of knee buckling in the previous 3 months compared to participants without instability, with adjustment for knee pain, age, muscle weakness, and BMI. Second, self-reported instability, although measured in a different manner than we did, was found to be associated with activity limitations in a knee OA sample as well (4). In this second study, self-reported knee instability was assessed by the question whether the perception of instability affects specific daily activities (4,7). Such a methodology examines the consequences of perceived instability on activity limitations. However, we believe that the relationship between the response to such a question and measured daily activities is self-evident and may result in spuriously high correlations. Hence, our study is the first to adequately examine the relationship between self-reported knee instability and activity limitations in patients with clinical knee OA, by using an appropriate measure of self-reported knee instability. In addition, the

Table 2. Unadjusted and adjusted regression analyses with WOMAC, timed GUG, and timed stair climbing as dependent variables and self-reported knee instability as an independent variable (*n*=248)

	WOMAC-pf		**Timed GUG**		**Timed Stair-climb**	
	B (SE)	*P*	B (SE)	*P*	B (SE)	*P*
Unadjusted						
Unilateral instability	6.44 (1.79)	< 0.001	1.39 (0.36)	< 0.001	1.47 (0.44)	< 0.001
Bilateral instability	5.47 (0.30)	0.03	070 (0.51)	0.17	1.14 (0.63)	0.07
	R^2=0.45; *P*<0.001		R^2=0.33; *P*<0.001		R^2=0.33; *P*<0.001	
Adjusted*						
Unilateral instability	2.92 (1.38)	0.04	0.74 (0.29)	0.01	0.73 (0.36)	0.04
Bilateral instability	3.09 (1.90)	0.11	0.35 (0.40)	0.39	0.79 (0.49)	0.11
	R^2=0.47; *P*<0.001		R^2=0.35; *P*<0.001		R^2=0.34; *P*<0.001	

Self-reported knee instability: unilateral instability and bilateral instability versus reference no instability.
B=unstandardized regression coefficient; SE=standard error; WOMAC-pf=Western Ontario and McMasters Universities Osteoarthritis Index-physical function; Timed GUG=Timed Get Up and Go test; * adjusted for knee pain and muscle strength.

Table 3. Unadjusted and adjusted linear regression analyses with WQ35, StCQ15, QR&S39 as dependent variables and self-reported knee instability as independent variable (*n*=248)

	WQ35		**StCQ15**		**QR&S39**	
	B (SE)	***P***	**B (SE)**	***P***	**B (SE)**	***P***
Unadjusted						
Unilateral instability	11.65 (3.14)	< 0.001	10.11 (2.93)	< 0.001	15.80 (3.50)	< 0.001
Bilateral instability	9.56 (4.42)	0.03	12.09 (4.09)	< 0.001	11.97 (4.89)	0.02
	R^2=0.22; *P*<0.001		R^2=0.17; *P*<0.001		R^2=0.20; *P*<0.001	
Adjusted*						
Unilateral instability	8.56 (2.86)	< 0.001	7.28 (2.77)	< 0.001	11.25 (3.25)	< 0.001
Bilateral instability	8.83 (3.97)	0.03	10.67 (3.79)	< 0.001	10.21 (4.45)	0.02
	R^2=0.26; *P*<0.001		R^2=0.21; *P*<0.001		R^2=0.24; *P*<0.001	

Self-reported knee instability: unilateral instability and bilateral instability versus reference no instability.
B=unstandardized regression coefficient; SE=standard error; WQ35=Walking Questionnaire; CStQ15=Climbing Stairs Questionnaire; QR&S39=Questionnaire Rising and Sitting down; * adjusted for knee pain and muscle strength.

strengths of our study are that we used multiple generally accepted outcome measures of activity limitations and new measures of specific activity limitations, a large cohort of knee OA patients, and took into account several potential confounders.

The contribution of self-reported knee instability to the variance in activity limitations over knee pain and muscle strength was small. The most important contributors to the variance in activity limitations are knee pain and muscle strength. However, self-reported

knee instability showed to be an independent variable in all analyses. Unilateral self-reported knee instability was associated with all outcome measures, but bilateral self-reported knee instability was only associated with the GUG and specific self-reported outcomes. An explanation for bilateral self-reported knee instability not being significantly associated with the WOMAC-pf and the stair-climb test might be the small number of patients reporting bilateral knee instability.

We included 3 new questionnaires for the assessment of specific limitations in daily activities required for mobility independence (walking, stair climbing, rising and sitting down) in our study to provide a stronger validation of the relationship between self-reported knee instability and activity limitations. Considering our results, we believe that these analyses validate the relationship between self-reported knee instability and activity limitations.

Two limitations of our study should be acknowledged. Firstly, we dichotomized self-reported knee instability to make interpretation easier, although no previous criteria for this decision were available. However, when we analyzed self-reported knee instability with different cutoff points, the impact of self-reported knee instability over knee pain and muscle strength on activity limitations remained significant (data not shown). Secondly, the cross-sectional design of our study limits any causal interferences. Despite these limitations, our results provide evidence regarding the clinical relevance of self-reported knee instability in patients with knee OA.

In conclusion, self-reported knee instability is associated with activity limitations in patients with knee OA, in addition to knee pain and muscle strength. Clinically, self-reported knee instability should be assessed in addition to knee pain and muscle strength.

Acknowledgements. We gratefully acknowledge M. Fransen and A. Harmer for their assistance in correcting the manuscript. We also thank A. Jonkman for collecting data. This study was funded by the Dutch Arthritis Foundation. The study sponsor had no involvement in the study.

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