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Influence of Self-Reported Knee Instability on Outcomes Following Education and Exercise: A Cohort Study of 2,466 Patients With Knee Osteoarthritis

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Objective. To study the influence of self-reported knee instability on changes in knee pain and gait speed following patient education and supervised exercise therapy in patients with knee osteoarthritis (OA).

Methods. We included patients enrolled in the Good Life With Osteoarthritis in Denmark (GLA:D) program, an 8-week education and supervised neuromuscular exercise program. Patients were classified into 4 groups according to their level of self-reported knee instability (never; rarely; sometimes; most of the time or all the time). Knee pain intensity was evaluated on a 0–100 mm scale and gait speed from the 4 × 10 meters fast-paced walk test at baseline and after the program. Using linear regression, we examined the association between knee instability and the change in pain and gait speed, respectively. Sex, age, body mass index, physical activity level, and previous knee surgery were covariates in adjusted models.

Results. Among 2,466 patients with knee OA, mean baseline pain and gait speed varied between 38–59 mm and 1.39–1.56 meters/second in patients experiencing no instability and patients experiencing instability most or all the time, respectively. All instability groups improved in pain and gait speed. Compared to the no instability group, patients reporting instability most or all the time experienced larger improvements in pain (4.3 mm [95% confidence interval 1.2, 7.5]), while no difference between instability groups was found for gait speed.

Conclusion. Knee OA patients with self-reported instability seem to benefit even more from a patient education and supervised exercise therapy program than OA patients without instability.

INTRODUCTION

Knee instability is a common symptom in patients with knee osteoarthritis (OA) (1), representing a distinct knee OA subgroup (2) with worse activity-related pain (3), worse function (4), lower activity level (5), lower muscle strength (6), altered somatosensation (7), poorer balance, and higher risk of falls (8).

Only 2 previous studies on the role of exercise therapy in patients with knee OA and instability exist (9,10). A study by Assar et al compared land-based and aquatic exercise programs and showed that both programs were beneficial, with land-based resistance exercises being slightly more effective in patients with instability (9). Knoop et al reported the benefit from an aerobic, strengthening, and functional exercise program in patients with knee instability, with no additional benefit from adding exercises focusing on knee stability (10). However, neither of the studies indicated the severity of knee instability or examined the potential influence of the level of knee instability on the benefit from treatment.

Neuromuscular exercise has been shown to be effective in patients with knee OA (11), and promoting neuromuscular control and using exercises focusing on functional tasks for knee OA patients with self-reported instability is recommended (12–14). However, little is known about whether the effect of neuromuscular exercise is different among patients with knee OA and different levels of knee instability as compared to those without perceived instability.

The aim of this study was to investigate the influence of self-reported knee instability on changes in pain and gait speed immediately after an 8-week patient education and neuromuscular

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SIGNIFICANCE & INNOVATIONS

- Three of 4 patients with knee osteoarthritis (OA) had self-reported knee instability.
- In patients with knee OA, those with high level of self-reported knee instability had lower age and higher body mass index, and more had previous knee surgery (other than total knee joint replacement) and were physically inactive.
- Patients with knee OA and higher level of self-reported knee instability had higher pain intensity and lower gait speed at baseline and experienced larger improvements in pain intensity following patient education and supervised exercise.
- Knee OA patients with self-reported instability seem to benefit even more from a patient education and supervised exercise therapy program than OA patients without instability.

exercise program in patients with knee OA. Our hypothesis was that improvements in pain and gait speed after an 8-week patient education and neuromuscular exercise program were larger among patients with knee instability compared to patients without knee instability.

PATIENTS AND METHODS

Design. This was a registry-based retrospective cohort study based on prospectively collected data from the Good Life With Osteoarthritis in Denmark (GLA:D) registry. The study was reported according to recommendations of the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement for reporting observational studies (15). According to the local ethics committee of the North Denmark Region, ethics approval of GLA:D was not required. GLA:D has previously been approved by the Danish Data Protection Agency (SDU; 10.084), and according to the Danish Data Protection Act, patient consent was not required, as personal data were processed exclusively for research and statistical purposes.

The GLA:D program. GLA:D is an ongoing nationwide program in Denmark initiated in 2013 with the aim of implementing national and international knee and hip OA guidelines into clinical practice. Patients could enter the GLA:D program by referral from a general practitioner and orthopedic surgeon or by themselves. All patients in the study were enrolled in the GLA:D program, which consists of 2 patient education sessions and 12 supervised neuromuscular exercise sessions. Each exercise session was led by a certified physical therapist and included 60 minutes of neuromuscular exercise. Treating physical therapists evaluated all patients for eligibility according to clinical criteria for knee OA. Eighty-one percent of patients self-reported to have radiographically confirmed OA. Details of the GLA:D program and outcomes can be found elsewhere (11).

Patients. Patients with knee joint problems enrolled in the GLA:D program between the January 1, 2019 (introduction of the question about knee instability) and November 10, 2019 (enabling program completion prior to the COVID-19 pandemic lockdown in Denmark) were included in the study. Patients were excluded if they had another reason than OA for the problems (e.g., tumor, inflammatory joint disease, or sequelae after hip fracture), other symptoms that were more pronounced than the OA problems (e.g., chronic, generalized pain, or fibromyalgia), or had undergone total knee joint replacement (TJR) surgery in the most affected knee prior to the intervention. Patients who did not answer the knee instability question at baseline, those who did not have data on any of the outcome measures at baseline or follow-up, and those with a follow-up measure later than March 10, 2020 were also excluded.

Exposure. Exposure was the level of self-reported knee instability at baseline before initiating the intervention. Patients answered the question "Have you felt your knee give way or let you down within the last week?" on a 5-point Likert scale (0 = never to 4 = all the time). Patients were classified into 4 groups based on their answers to the question related to instability: no instability (0 = never); low instability (1 = rarely); moderate instability (2 = sometimes); high instability (3 = most of the time, or 4 = all the time). Due to the low number of cases in the "4 = all the time" response group, "3 = most of the time" and "4 = all the time" were categorized together as high instability.

Outcomes. The change in knee pain intensity and gait speed from baseline to immediately after the 8-week supervised patient education and exercise therapy program (~3 months) were the outcomes of interest. Since we wanted to study whether a potential association was present in both a self-reported and performance-based measure, pain intensity was evaluated as mean pain during the past month on a visual analog scale (VAS; range 0–100 mm), and gait speed (meters/second) was calculated from a 4 × 10 meters fast-paced walk test (16). A difference of a minimum 15-mm change in pain intensity (17) and a 0.095-meters/second change in gait speed (18) were considered as minimum clinically important differences (MCIDs).

Covariates. Age, sex, body mass index (BMI), physical activity level, and previous surgery in the most affected knee (other than TJR) (yes/no) were included as potential confounders for changes in knee pain and gait speed. BMI was evaluated from weight divided by the square of the body height and expressed as kg/m^2 (therapist reported). Self-reported physical activity level was assessed with the University of California, Los Angeles (UCLA) scale on 10 levels ranging from inactive (level 1) to regular

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participation in impact sports (level 10). The UCLA activity scores were categorized into low (≤4), moderate (5–6), and high (≥7) activity level (19).

Statistical analyses. Baseline characteristics among the knee instability groups were reported as mean ± SD or using a table of frequencies (no. [%]) where appropriate. If the variables were normally distributed and Levene's test showed homogeneity of variance, a one-way analysis of variance was used to compare baseline variables (pain intensity, gait speed, age, and BMI) among the knee instability groups. For categorical variables (sex, physical activity level, previous knee surgery, and the proportion of patients achieving the MCID for pain and for gait speed), the Kruskal-Wallis test was used to compare the variables among the knee instability groups. The Mann-Whitney U test was performed to test the significance of pairwise differences for the proportion of patients achieving the MCID for pain and for gait speed.

Unadjusted and adjusted linear regression analyses were performed to examine the association between knee instability groups (exposure) and the change in pain intensity and gait speed from baseline to follow-up (outcome variables). Two crude regression models were constructed that consisted of the exposure and the 2 outcome variables. The 2 adjusted analyses were performed by multiple linear regression models in which each model included the covariates in addition to the exposure. We did not adjust for baseline pain/gait speed in our regression analyses of change, as baseline scores of the outcome would be correlated with the error term, and as such adjustment is associated with bias (20). Assumptions of the regression models were assessed by inspecting the normal distribution residuals through histograms for all regression models, and assumptions were met. P values less than or equal to 0.05 were considered significant, and all analyses were carried out in SPSS, version 22.0.

RESULTS

Table 1 provides a summary of the baseline characteristics of the 2,466 patients included in the analysis, of which 78% reported some degree of instability. There were statistically significant differences between instability groups at baseline for all characteristics except for sex. In patients with knee OA, those with a high level of self-reported knee instability had lower age and higher BMI, and more had previous knee surgery (other than TJR) and were physically inactive.

Table 2 shows both unadjusted and adjusted associations between knee instability groups and changes in pain and gait speed. The high knee instability group had the highest mean baseline pain intensity, and the no knee instability group had the lowest mean baseline pain intensity. For gait speed, the high knee instability group had the lowest, and the no knee instability group had the highest mean baseline gait speed. The absolute improvements ranged from 13.5 to 15.3 mm for pain and 0.12 to 0.13 meters/second for gait speed.

In the adjusted model, compared to the no instability group, no differences in improvement were observed for the low knee instability group (β = −1.2 mm [95% confidence interval (95% CI) −3.9, 1.5]) and moderate knee instability group (β = 0.2 mm [95% CI −2.4, 2.8]) in pain intensity, while the group with high knee instability experienced a larger improvement in pain intensity (β = 4.7 mm [95% CI 1.6, 7.9]). In the adjusted model, compared to the no instability group, no differences in improvement were observed for any of the other instability groups (Table 2).

Figures 1 and 2 show the proportion of patients achieving the MCID for pain and gait speed, respectively, with the greatest proportion in the high knee instability group (56% and 59%, respectively). There was a statistically significant difference in the proportion of patients achieving the MCID between groups for pain ($P = 0.001$), but no statistically significant difference observed for gait speed ($P = 0.194$). The pairwise comparisons showed that the high instability group had statistically significantly higher

Table 1. Baseline characteristics of patients, stratified by knee instability groups*

Knee instability groups	All participants (n = 2,466)	No instability (n = 540)	Low instability (n = 620)	Moderate instability (n = 957)	High instability (n = 349)	P
Age, mean ± SD years	66.6 ± 8.9	67.1 ± 8.5	66.4 ± 8.5	66.9 ± 9.2	65.4 ± 9.6	0.036†
Sex						0.107‡
Male	785 (31.8)	193 (35.7)	187 (30.2)	289 (30.2)	116 (33.2)	
Female	1,681 (68.2)	347 (64.3)	433 (69.8)	668 (69.8)	233 (66.8)	
BMI, mean ± SD kg/m^2	28.7 ± 5.3	27.8 ± 4.8	28.5 ± 5.1	29.0 ± 5.4	29.7 ± 5.7	<0.001†
Previous surgery						<0.001§
Yes	630 (25.5)	105 (19.4)	142 (22.9)	269 (28.1)	114 (32.7)	
No	1,836 (74.5)	435 (80.6)	478 (77.1)	688 (71.9)	235 (67.3)	
UCLA activity level						<0.001§
Low	649 (26.3)	120 (22.2)	146 (23.5)	254 (26.5)	129 (37.0)	
Moderate	1,199 (48.6)	267 (49.4)	295 (47.6)	483 (50.5)	154 (44.0)	
High	618 (25.1)	153 (28.3)	179 (28.9)	220 (23.0)	66 (19.0)	

* Values are the number (%) unless indicated otherwise. BMI = body mass index; UCLA = University of California, Los Angeles (scale).
† Significant; one-way analysis of variance.
‡ Kruskal-Wallis test.
§ Significant; Kruskal-Wallis test.

Table 2. Association of knee instability level with change in pain and gait speed*

			Unadjusted model		Adjusted model§	
	Baseline pain/ gait speed†	Follow-up pain/ gait speed†	Mean change, β (95% CI)	Difference in change, β (95% CI)‡	Mean change, β (95% CI)	Difference in change, β (95% CI)‡
Pain						
No instability (ref.)	38.1 ± 21.1	24.2 ± 18.7	13.9 (12.0, 15.9)	13.9 (12.0, 15.9)	14.0 (11.2, 16.7)	14.0 (11.2, 16.7)
Low instability	41.6 ± 20.5	28.8 ± 20.4	12.8 (11.0, 14.6)	−1.1 (−3.8, 1.6)	12.8 (10.1, 15.6)	−1.2 (−3.9, 1.5)
Moderate instability	50.2 ± 20.5	36.0 ± 21.4	14.1 (12.6, 15.7)	0.2 (−2.2, 2.7)	14.2 (11.7, 16.6)	0.2 (−2.4, 2.8)
High instability	59.1 ± 20.2	40.4 ± 23.0	18.6 (16.1, 21.2)	4.7 (1.6, 7.9)	18.7 (15.4, 21.8)	4.7 (1.6, 7.9)
Gait speed						
No instability (ref.)	1.56 ± 0.33	1.70 ± 0.35	0.13 (0.12, 0.15)	0.13 (0.12, 0.15)	0.14 (0.12, 0.16)	0.14 (0.12, 0.16)
Low instability	1.52 ± 0.30	1.64 ± 0.32	0.11 (0.10, 0.12)	−0.02 (−0.05, 0.00)	0.12 (0.10, 0.14)	−0.02 (−0.05, 0.00)
Moderate instability	1.44 ± 0.30	1.56 ± 0.34	0.12 (0.11, 0.13)	−0.01 (−0.03, 0.01)	0.13 (0.11, 0.15)	−0.01 (−0.03, 0.01)
High instability	1.39 ± 0.30	1.54 ± 0.35	0.14 (0.12, 0.16)	0.01 (−0.02, 0.04)	0.15 (0.13, 0.17)	0.01 (−0.02, 0.03)

* Values are the mean ± SD unless indicated otherwise. 95% CI = 95% confidence interval; ref. = reference (group).
† Visual analog scale (mm) / gait speed (meters/second).
‡ For the "No instability" group, beta is equal to the change from baseline to follow-up; for the remaining groups, beta is equivalent to the difference in change compared with the "No instability" group (ref.).
§ Adjusted for age, sex, body mass index, physical activity level, and previous knee surgery at baseline.

proportion of patients who achieved the MCID compared to the no, low, and moderate instability groups ($P < 0.05$); no other between-group difference was observed ($P > 0.05$).

DISCUSSION

We investigated changes in pain and gait speed after an 8-week patient education and supervised exercise program in patients with knee OA according to baseline level of self-reported instability. We found that 78% had varying degrees of self-reported knee instability at baseline and that baseline pain and gait speed varied with worse outcomes among those with high instability. Patients with high instability at baseline had greater improvements in pain intensity, while no difference between instability groups was found for gait speed.

We are only aware of 2 previous studies focusing on treatment outcomes in knee OA patients with self-reported instability (9,10). Knoop et al (10) found clinically relevant improvements in pain similar to those in our study (on average, improvement of 1.5–1.7 cm compared to 1.3–1.5 cm in our study) and physical function (5–7% improvement in the get-up-and-go test compared to 7–11% improvement in gait speed in our study) when investigating the added effects of knee joint stabilization exercises in addition to patient education, aerobic, strengthening, and functional exercises. The functional exercises were based on daily activities like walking, stairclimbing, and rising from a chair, highlighting the similarities with the content of the GLA:D program (10). Comparing the percentages achieving the MCID for pain improvement (i.e., 15 mm on a VAS of 0–100 mm), we found that the percentage varied between 60% and 66%, while Knoop et al reported that 70% of participants in the experimental group and 72% in control group achieved the MCID for pain. The small variation in effect between studies could be due to different methods for measuring pain intensity, difference in program duration, and number of exercise sessions (10). Another study, limited by a small sample size and retrospective clinical trial registration,

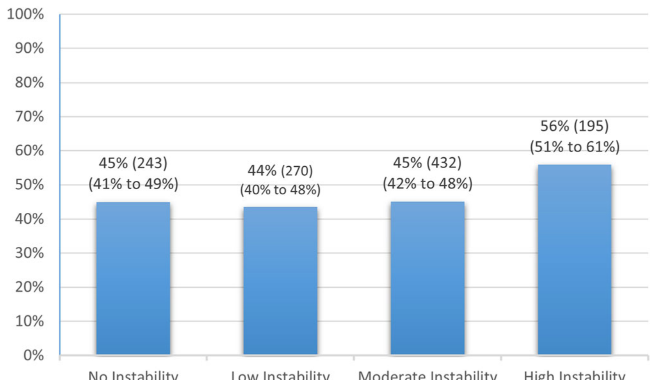

Figure 1. Proportion (numbers) and 95% confidence intervals of patients achieving the minimum clinically important difference for pain (≥15 mm improvement in pain intensity) in each of the knee instability groups.

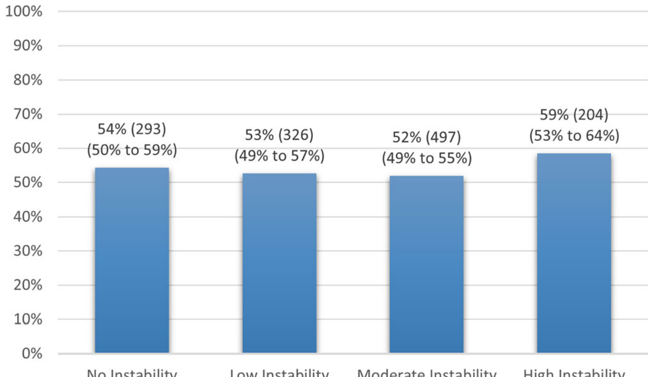

Figure 2. Proportion (numbers) and 95% confidence intervals of patients achieving the minimum clinically important difference for gait speed (≥0.095 meters/second improvement in gait speed) in each of the knee instability groups.

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observed surprisingly large statistically significant improvements in pain (4.0–4.2 cm) after 8 weeks of a land-based exercise program (focusing on the core, hip, and leg muscles in functional patterns by a resistance cord and weighted bar) or an aquatic exercise program (focusing on function, pain, and balance improvements) compared to a control group with no exercise intervention (9).

A recent systematic review by Kawabata et al underlines the urgent need for studies that focus on the impact of exercise therapy on knee joint instability in patients with OA with consideration of the severity of knee instability (21). Adding to the results from the previous treatment outcome studies (9,10), we investigated the influence of knee instability severity on benefit from an education and exercise program. The GLA:D program includes neuromuscular exercises performed in functional weight-bearing positions that are designed to improve functional joint stability, with a focus on sensorimotor deficiencies and postural control, and therefore has the potential to address self-reported instability (14). Supporting this, our results suggest that the group with worst instability is more likely to benefit more from an exercise program that focuses on knee joint stability.

The association between worse knee instability and higher pain intensity and lower gait speed at baseline is consistent with previous cross-sectional research (3,4). The greater improvement in pain after the GLA:D program in those with high knee instability could be explained by the higher baseline pain intensity, and therefore greater potential for improvement might be due to the impact of neuromuscular exercises on knee instability, as the program has been designed to improve functional joint stability.

The major strengths of the present study include the large sample size, the possibility of investigating the treatment responses of patients with different levels of knee instability, and the inclusion of both self-reported and objectively measured outcomes. The major limitation is the lack of a control group, prohibiting any conclusions on how much of the improvement can be attributed to the exercise program, the natural course of the disease, or regression to the mean. Second, we did not examine the role of fear, varus/valgus alignment, and bilateral/unilateral joint involvement on joint instability, and our results cannot necessarily be generalized to patients with objectively assessed knee instability because self-reported and objectively assessed knee instability are related but distinctly different concepts (22). Third, we did not include a self-reported physical function measure, and therefore our results only reflect objective data from a performance-based measure. Last, due to the lack of an MCID value for the fast-paced walk test that used in this study, the MCID values for the 4 × 10 meters self-paced walk test were used for gait speed because similar performance can be expected from older individuals with lower functionality during self-paced or fast-paced walk tests (23).

We suggest that future studies should investigate factors that might affect the benefit from exercise therapy in patients with knee OA and knee instability and elucidate the underlying causal relationships. Also, investigating the type of exercises that are especially effective in improving knee stability and the association between improvement in knee stability and improvements in muscle strength and structural changes in the knee joint would be valuable. In conclusion, knee OA patients with self-reported instability seem to benefit even more from a patient education and supervised exercise therapy program than OA patients without instability.

AUTHOR CONTRIBUTIONS

All authors were involved in drafting the article or revising it critically for important intellectual content, and all authors approved the final version to be submitted for publication. Dr. Skou had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study conception and design. Selçuk, Roos, Grønne, Thorlund, Sarı, Skou.

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