CHECKing activity limitations in persons with early osteoarthritis of the knee or hip

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2014

Chapter 8

Decrease of muscle strength is associated with increase of activity limitations in early knee osteoarthritis: 3-year results from the Cohort Hip and Cohort Knee study

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Archives of Physical Medicine and Rehabilitation 2014

[Accepted for publication]

Abstract

Objective. Muscle weakness has been hypothesized as being an important factor in the development of activity limitations in patients with knee osteoarthritis (OA). Longitudinal evidence to support this hypothesis is scarce. The aims of the study were (1) to determine whether a decrease in muscle strength over three years is associated with an increase in activity limitations, and (2) to examine whether the longitudinal association between muscle strength and activity limitations is moderated by knee joint proprioception and laxity in early symptomatic knee OA.

Design. A longitudinal cohort study with three-year follow-up. Measurements were performed at the second (T_0) and fifth (T_1) year of the Cohort Hip and Cohort Knee (CHECK) study. Statistical analyses included paired *t*-tests, chi-square tests, and regression analyses. In regression analyses, the association between muscle strength and activity limitations was adjusted for confounders.

Setting. Reade, Centre for Rehabilitation and Rheumatology, Amsterdam, the Netherlands.

Participants. Subjects ($n = 146$) with early symptomatic knee OA from the CHECK study.

Main outcome measures. Muscle strength, proprioception, and laxity were assessed using specifically designed measurement devices. Self-reported and performance-based activity limitations were measured with the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), the get-up-and-go test, 100m walk test, and stair-climb test.

Results. A total of 116 (79.5%) women and 30 (20.5%) men, with a mean (SD) age of 58.4 (4.9) and a mean (SD) BMI of 25.5 (3.6), were included in the study. Overall, small three-year changes in muscle strength and activity limitations were observed. At the group level the average muscle strength increased by 10% (1.0 (0.3) to 1.1 (0.3)) Nm/kg over the three years. The three-year decrease in muscle strength was independently associated with an increase in performance-based activity limitations on all three measures ($B = -1.12$, $B = -5.83$, and $B = -1.25$, respectively). Proprioception and laxity did not moderate this association.

Conclusions. In patients with early knee OA, decreased muscle strength is associated with an increase in activity limitations. Our results are a step towards understanding the role of muscle weakness in the development of activity limitations in knee OA. Further, well-designed experimental studies are indicated to establish causality between muscle weakness and activity limitations.

Introduction

Activity limitations (e.g., walking, stair-climbing) are common among individuals with knee osteoarthritis (OA).[1,2] Muscle weakness has been hypothesized as being a causal factor in the development of activity limitations.[3-9] However, the evidence for muscle strength being a causal factor is limited. The association between muscle strength and activity limitations has been found in cross-sectional studies.[10-12] Moreover, baseline muscle strength has been found to be a predictor of activity limitations.[13-19] A causal association, however, requires that a decrease in muscle strength be shown to be associated with an increase in activity limitations. This longitudinal association has been studied in two observational studies, which showed conflicting results,[17,20] and in a clinical trial.[21] The latter study, however, failed to control for confounding variables. We, therefore, decided to study the association between change in muscle strength and change in activity limitations in a longitudinal, well controlled observational study. If muscle weakness is indeed a causal factor in the increase in activity limitations, one would hypothesize a decrease in muscle strength to be associated with an increase in activity limitations.

Activity limitations might be affected by several neuromuscular factors.[22] In addition to muscle weakness, it is hypothesized that poor knee joint proprioception and high knee joint laxity contribute to the increase in activity limitations.[10,11] In these cross-sectional studies, it has been demonstrated that the association between muscle strength and activity limitations was stronger in patients with knee OA with poor proprioception than in patients with accurate proprioception, while the results for laxity were conflicting.[9-11] Longitudinal studies are not available. It has been hypothesized that the impact of muscle weakness on activity limitations is even greater in the presence of poor proprioception and laxity: Poor proprioception and laxity are hypothesized to lead to instability of the knee, thereby aggravating the impact of muscle weakness on activity limitations.[22] However, evidence to support this hypothesis is based on cross-sectional studies only. Whether the longitudinal association between change in muscle strength and change in activity limitations is moderated by poor proprioception and high laxity in individuals with knee OA is unknown.

The aims of the study were: 1) to determine whether a decrease in muscle strength over three years is associated with an increase in activity limitations; and 2) to examine whether the longitudinal association between muscle strength and activity limitations is moderated by knee joint proprioception and laxity, in early symptomatic knee OA.

Methods

Study design

Out of 1002 participants in the Cohort Hip and Cohort Knee (CHECK) cohort, the participants (*n* = 151) in our hospital who reported knee symptoms at the second year were assessed on muscle strength, proprioception, laxity, and performance-based activity limitations and were included in the present three-year follow-up study.[9] Measurements performed at the second (T0) and fifth (T1) year of the CHECK study were used in the present study (in the CHECK study, biomechanical factors were not assessed at baseline).

Parent study

The CHECK cohort was formed between October 2002 and September 2005, and consists of 1002 participants with early symptomatic knee and/or hip OA.[23] Ten general and academic hospitals in the Netherlands participated. General practitioners (GPs) in the vicinity of the participating centres were invited to refer eligible persons. Participants were also recruited through announcements in local newspapers and on the Dutch Arthritis Foundation website. The physicians in the participating centres checked whether participants fulfilled the inclusion criteria. Inclusion criteria were knee or hip pain or morning stiffness < 30 minutes, in participants aged 45 – 65 years, who had not yet consulted their physician for these symptoms (or where the first consultation had been within the six months immediately preceding inclusion). Participants 1) with any other pathological condition that could explain their symptoms, 2) with comorbidity that would not allow physical evaluation and/or follow-up for at least 10 years, 3) with malignancy in the last five years, and 4) unable to understand Dutch, were excluded.[23] The medical ethics committees of all participating centres approved the CHECK study. The medical ethical committee of the Slotervaart Hospital and Reade approved the additional measurements necessary for the present study. All participants gave their written informed consent before entering the study.

Study population

All participants with knee symptoms recruited at Reade, Centre for Rehabilitation and Rheumatology, Amsterdam, the Netherlands, underwent additional measurements (muscle strength, joint proprioception, varus-valgus laxity, and performance-based measures of activity limitations). These measurements were performed in the existing measurement schedule for CHECK. These participants constituted the study population of the present study.

Measurements

Assessment procedure

A single physical therapist assessed all participants at T0 and T1 according to a standardized protocol.

Activity limitations

Self-reported activity limitations were measured with the physical function subscale of the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC-pf).[24,25] Each item is scored on a 5-point Likert scale. Scores range from 0 to 68, with higher scores indicating greater activity limitations. The reliability and the validity of the WOMAC-pf have been established.[27] The intraclass correlation (ICC) coefficient for the Dutch WOMAC-pf is 0.92.[25]

Performance-based activity limitations were measured using a get-up-and-go (GUG) test, a 100m walk test, and a stair-climb test,[22] all timed with a stopwatch. The GUG test was conducted over a distance of 15 m, comparable to Hurley et al.[26,27] Participants sat on a standard-height chair with armrests. On the command "go", participants stood up without use of their arms and walked along a level, unobstructed corridor as fast as possible.

The next performance-based test was a timed 100 m walk test. In this test participants walked 20 m five times along a level and unobstructed corridor as fast as possible.[28]

The last performance-based test was a timed stair-climb. Participants stood at the foot of a stairway of 12 steps (16 cm high) and on the command "go", ascended the stairs as fast as possible. Participants were encouraged not to use the handrail, but were not prohibited from doing so for safety. Excellent test-retest reliability was reported for a comparable stair-climb task in participants with knee OA.[29]

Muscle strength

Muscle strength was assessed for flexion and extension of the knee using an isokinetic dynamometer (EnKnee; Enraf-Nonius, Rotterdam, the Netherlands). Concentric quadriceps and hamstring strength were measured isokinetically at 60°/s. All participants were assessed according to a previously described device and protocol.[10,11] The maximum contraction of three measurements of the quadriceps and three measurements of the hamstrings were averaged to obtain a measure of total muscle strength around the knee. In the analyses the maximum strength in Newton meter per kilogram body weight (Nm/kg) of the index knee (i.e. most affected knee) was used.[10] Excellent intrarater reliability (intraclass correlation coefficient [ICC] 0.93) has been reported.[30]

Proprioception

Proprioception was assessed in a knee joint motion detection task, expressed as the joint motion detection threshold.[10] A device was used that provided knee angular displacement in extension and precise measurement of the angular displacement with accuracy to 0.1°. The measurement of proprioception has been described in a previous study.[10] The mean of three measurements was calculated for each knee. The mean of the index knee was used in the analyses. This method has been shown to yield reproducible and valid results.[31]

Laxity

Joint varus-valgus laxity was measured as the total movement in the frontal plane during varus-valgus load in a non-weight bearing position.[11] The mean of three measurements (degrees) was calculated for each knee. The measurement of laxity has been described in a previous study.[11] The mean of the index knee was used in the analyses. The intra- and interrater reliability (ICC) for the measurement of laxity was 0.80 and 0.88, respectively.[32]

Other measures

Characteristics of the participants, including age, gender, and body-mass index (BMI), were collected at T0 and T1. Pain was assessed by a numeric rating scale (NRS).[33] Radiological assessment of the severity of knee OA was scored according to Kellgren and Lawrence (KL), ranging from 0 to 4[34-36] and performed according to a protocol.[37,38] In the analyses, dichotomized scores were used (KL-grade <2 vs. KL-grade ≥2).

Statistical analyses

An index knee was identified in the clinical interview ($n = 47$) at T0. For participants with bilateral symptoms ($n = 85$), we defined an index knee based on the following decision tree using data at T0: 1) highest KL-grade, 2) lowest degree of active knee flexion, 3) highest pain during active knee flexion, and 4) crepitus during knee flexion. In participants for whom we could not define an index knee on this basis, an index knee was randomly assigned ($n = 19$).

Descriptive statistics were performed for demographic variables, biomechanical factors of the index knee (muscle strength, proprioception and laxity), the WOMAC, the GUG, the walk test, and the stair-climb test at T0 and T1. Differences in change scores of these variables between T0 and T1 were analysed using paired-samples *t*-tests. Differences in gender and the KL-grades were analysed using chi-square tests.

Regression analyses were performed to assess the associations between muscle strength, proprioception, laxity, and activity limitations. Separate analyses were performed for the self-report (WOMAC-pf) and performance-based (GUG, walk test, and stair-climb test) outcome measures. Independent variables were included in all four models in the same stepwise manner. Prior to the regression analyses, it was checked whether the assumptions for linear regression (e.g., no strong multi-collinearity between independent variables [Pearson's correlation coefficient (r) < 0.80], homoscedasticity, linearity) were met. To determine the change score in activity limitations, scores at T0 of the outcome measure were entered as the first variable in all analyses.[39] First, the association between change in muscle strength and change in activity limitations was assessed (model 1). Subsequently, proprioception at T0 and the interaction between proprioception and change in muscle strength were added to the model (model 2). In model 3, laxity at T0 and the interaction between laxity and change in muscle strength was examined. Finally, the association between change in muscle strength and change in activity limitations was adjusted for age at T0, gender, change in pain (difference between T1 and T0), and KL-grade (difference between T1 and T0) (model 4). When one of these variables changed the regression coefficient of change in muscle strength by more than 10%, this variable was considered to be a confounder.[40] Results were considered statistically significant at $p < 0.05$.

The independent variables change in muscle strength, proprioception T0, and laxity T0 were centred around the mean.[41] Multicollinearity reduces when variables are centered.[36] In addition, centred variables allow for a more meaningful interpretation of lower order effects.[41] All analyses were performed using SPSS software, version 19.0 (SPSS, Chicago, IL, USA).

Results

Study population

Of 151 participants, five underwent total knee or total hip replacement during the three-year follow-up. These five participants were excluded, leaving 146 participants for analysis. The 146 participants did not differ in age, gender, BMI, KL-grade, pain, and WOMAC-pf compared to the total CHECK population. To be included in analysis, participants had to have complete data at T0 and T1.

Missing data

For the WOMAC-pf, the number of participants with missing data at T1 (fifth year) was 9. These nine participants had significantly ($p < 0.001$) higher scores compared with the rest of the study population at T0. Participants with missing data at T1 also differed significantly at T0 on the timed walk test ($p = 0.030$), stair-climb test ($p = 0.006$), and pain ($p < 0.001$), showing higher scores. No differences were found for the GUG ($p = 0.118$), muscle strength, proprioception, and laxity ($p = 0.216$, $p = 0.391$, and $p = 0.578$, respectively).

Table 1. Descriptive statistics for demographics, activity limitations, and biomechanical variables

Characteristics	T0	n	T1	n	Change	p-value
Demographics						
Age, years	58.4 (4.9)	146	61.1 (4.9)	137		
Female, n (%)	116 (79.5)	146	110 (73.0)	137		
Body-mass index, kg/m²	25.5 (3.6)	141	26.2 (5.2)	134	0.7 (4.3)	0.068
Knee pain last week (NRS), range: 0-10	3.5 (2.4)	146	3.8 (2.4)	137	0.4 (2.4)	0.038
KL-grade ≥ 2, n (%)	25 (17.1)	134	30 (20.6)	131		<0.001
Activity limitations						
WOMAC-PF, range: 0-68	14.9 (12.1)	146	16.6 (13.2)	137	2.6 (10.2)	0.003
GUG test, sec	9.6 (1.7)	144	9.4 (1.8)	119	-0.1 (1.2)	0.271
Timed walk test, sec	70.4 (10.1)	145	69.8 (10.1)	126	-0.03 (6.5)	0.962
Timed stair climb test, sec	5.1 (1.7)	145	5.5 (1.7)	125	0.5 (1.4)	<0.001
Biomechanical variables of index knee						
Muscle strength, Nm/kg	1.0 (0.3)	146	1.1 (0.3)	125	0.1 (0.2)	0.004
Proprioception, degrees	3.3 (3.1)	146	2.4 (1.5)	125	-0.9 (2.5)	<0.001
Varus-valgus laxity, degrees	12.3 (5.2)	146	8.4 (3.9)	125	-4.0 (4.2)	<0.001

Values are presented as mean (standard deviation) unless otherwise indicated.
KL-grade = Kellgren and Lawrence grade; NRS = numeric rating scale;
WOMAC-PF = physical function subscale of the Western Ontario and McMasters Universities Osteoarthritis Index;
GUG test = get-up-and-go test.

Table 2. Results of the regression analyses of activity limitations (WOMAC-PF, GUG test, walk test and stair-climb test) at T1 (3-year follow-up) on activity limitations at T0, change in muscle strength, proprioception at T0, laxity at T0, gender, age, change in knee pain and KL-grade

Variables	WOMAC-PF B	WOMAC-PF 95% CI	WOMAC-PF P	GUG test B	GUG test 95% CI	GUG test P	Walk test B	Walk test 95% CI	Walk test P	Stair-climb test B	Stair-climb test 95% CI	Stair-climb test P
Model 1		n = 124			n = 117			n = 123			n = 123	
Activity limitations To*	0.79	0.63, 0.95	< 0.001	0.84	0.71, 0.97	<0.001	0.79	0.68, 0.90	<0.001	0.74	0.56, 0.92	<.001
Δ Muscle strength	-7.06	-14.50, 0.38	0.063	-1.12	-1.97, -0.25	0.012	-5.83	-10.35, -1.31	0.012	-1.25	-2.28, -0.23	0.017
		R² = 0.45, p < 0.001			R² = 0.60, p < 0.001			R² = 0.64, p < 0.001			R² = 0.38, p < 0.001	
Model 2		n = 124			n = 117			n = 123			n = 123	
Activity limitations To*	0.77	0.60, 0.93	<0.001	0.83	0.69, 0.97	<0.001	0.80	0.68, 0.92	<0.001	0.69	0.50, 0.88	<0.001
Δ Muscle strength	-5.94	-14.07, 2.20	0.151	-1.05	-1.99, -0.10	0.030	-5.28	-10.27, -0.29	0.038	-1.02	-2.13, 0.10	0.074
Proprioception To	0.38	-0.22, 0.98	0.212	0.01	-0.06, 0.08	0.788	-0.01	-0.40, 0.38	0.969	0.06	-0.02, 0.15	0.154
Δ Muscle strength X proprioception To	1.81	-2.35, 5.97	0.390	0.09	-0.38, 0.56	0.705	0.67	-1.86, 3.20	0.600	0.37	-0.20, 0.93	0.200
		R² = 0.46, p < 0.001			R² = 0.60, p < 0.001			R² = 0.64, p < 0.001			R² = 0.40, p < 0.001	
Model 3		n = 124			n = 117			n = 123			n = 123	
Activity limitations To*	0.80	0.63, 0.96	<0.001	0.85	0.72, 0.98	<0.001	0.81	0.70, 0.92	<0.001	0.75	0.57, 0.93	<0.001
Δ Muscle strength	-7.11	-14.76, 0.54	0.068	-0.99	-1.87, -0.12	0.027	-4.64	-9.17, -0.12	0.044	-1.04	-2.08, -0.01	0.049
Laxity To	0.05	-0.31, 0.40	0.800	0.01	-0.04, 0.05	0.803	-0.07	-0.28, 0.13	0.484	-0.03	-0.08, 0.02	0.238
Δ Muscle strength X laxity To	0.04	-1.74, 1.83	0.962	0.15	-0.05, 0.35	0.137	1.37	0.32, 2.43	0.011	0.21	-0.03, 0.45	0.092
		R² = 0.45, p < 0.001			R² = 0.61, p < 0.001			R² = 0.66, p < 0.001			R² = 0.40, p < 0.001	
Model 4		n = 121			n = 114			n = 119			n = 119	
Activity limitations To*	0.87	0.73, 1.01	<0.001	0.85	0.71, 0.99	<0.001	0.81	0.69, 0.93	<0.001	0.75	0.56, 0.95	<0.001
Δ Muscle strength	-6.11	-12.44, 0.21	0.058	-1.12	-2.00, -0.24	0.013	-5.42	-9.97, -0.86	0.020	-1.19	-2.24, -0.14	0.027
Female	0.89	-2.90, 4.68	0.640	-0.07	-0.65, 0.50	0.897	-0.78	-3.76, 2.11	0.593	0.11	-0.55, 0.77	0.742
Age	-0.01	-0.32, 0.31	0.979	-0.01	-0.05, 0.04	0.720	0.13	-0.10, 0.35	0.275	0.01	-0.04, 0.06	0.696
Δ Knee pain	2.26	1.64, 2.89	<0.001	0.07	-0.02, 0.15	0.151	0.56	0.11, 1.01	0.015	0.11	0.01, 0.21	0.040
KL-grade	-0.04	-1.85, 1.78	0.970	0.09	-0.16, 0.35	0.452	0.49	-0.83, 1.81	0.466	0.09	-0.21, 0.39	0.536
		R² = 0.63, p < 0.001			R² = 0.62, p < 0.001			R² = 0.66, p < 0.001			R² = 0.41, p < 0.001	

B = unstandardized regression coefficient; CI = confidence interval; WOMAC-PF = physical function subscale of the Western Ontario and McMasters Universities Osteoarthritis Index; GUG test = get-up-and-go test; Δ Muscle strength = change in muscle strength from To to T1 (3-year follow-up); Δ Knee pain = change in NRS knee pain from To to T1 (3-year follow-up); KL-grade = Kellgren and Lawrence grade.
*Activity limitations To = scores on the outcome measure (WOMAC-pf, GUG test, walk test and stair-climb test) at To.

Course of activity limitations and biomechanical factors

The characteristics of the study population at T0 and T1 and mean changes in activity limitations (WOMAC-pf, GUG, timed walk test, timed stair-climb test), muscle strength, proprioception, laxity, pain, body-mass index, and radiographic OA over three years are presented in **Table 1**.

Self-reported (WOMAC-pf) and performance-based (stair-climb) activity limitations deteriorated significantly over three years ($p = 0.003$, 11% change and $p < 0.001$, 7% change, respectively). On average, no change in activity limitations was found for the GUG and walk test ($p = 0.271$ and $p = 0.962$, respectively), although the variability in change scores was large (-3.40 to 4.84 and -24.90 to 27.98, respectively). On average (mean ± SD), muscle strength showed a statistically significant increase (0.1 ± 0.2 Nm/kg; $p = 0.004$, 10% change). Proprioception showed an increase in accuracy over time (-0.9 ± 2.5 degrees; $p < 0.001$, 27% change) and joint laxity decreased over time (-4.0 ± 4.2 degrees; $p < 0.001$, 32% change).

In univariable analyses it was shown that change in muscle strength and change in performance-based activity limitations were associated: A decrease in muscle strength was associated with an increase in the time required to complete the three performance tests (GUG: $B = -1.12$, $p = 0.012$; timed walk test: $B = -5.83$, $p = 0.012$; timed stair-climb test: $B = -1.25$, $p = 0.017$). The association between change in muscle strength and change in self-reported activity limitations was not significant (WOMAC-pf: $B = -7.06$, $p = 0.063$) (**Table 2**, model 1). This indicates that patients with knee OA will show an increase in their activity limitations by 1.12 s in the GUG, 5.83 s in the walk test, and 1.25 s in the stair-climb test when their muscle strength decreases by 1 unit of change (1 Nm/kg) over three years.

Moderation by proprioception and laxity

Neither proprioception at T0 nor the interaction between proprioception and change in muscle strength was significantly associated with change in activity limitations (**Table 2**, model 2). The same result was obtained for laxity, with the exception of the walk test (**Table 2**, model 3).

Controlling for confounders

Addition of age, gender, change in pain, and radiographic severity (KL-grade) as predictors in the models, with activity limitations at T1 as dependent variable and activity limitations at T0 and change in muscle strength as independent variables, did not affect the strength of the association between change in muscle strength and performance-based activity limitations by more than 10%. The strength of the association between change in muscle strength and self-reported activity limitations decreased by 13.5%. A positive association was found between change in pain and change in activity limitations measured with the WOMAC-pf, walk test, and stair-climb test (**Table 2**, model 4).

Discussion

We evaluated the association between change in muscle strength and change in activity limitations among participants with early symptomatic knee OA over three years. The main finding was that a decrease in muscle strength was associated with an increase in activity limitations over time, independent of age, gender, change in pain, and radiographic severity. Both proprioception and laxity at T0 did not moderate this association. These results are in line with muscle weakness playing an important role in the development of activity limitations in early knee OA.

Although muscle strength has often been assumed to be a causal factor in the development of activity limitations, the evidence for this is limited.[17,20,21] The present study hypothesized that, if muscle weakness is indeed a causal factor in the development of activity limitations, a decrease in muscle strength will be associated with an increase in activity limitations. This hypothesis was confirmed for three performance tests and a trend was found for the WOMAC-pf. These results add indirect evidence for the causal relationship between a decrease in muscle strength and an increase in activity limitations in early knee OA. This finding has been confirmed in another longitudinal study of our study group in established knee OA (submitted for publication). However, to demonstrate a causal relationship of muscle weakness on activity limitations, further well-designed experimental studies are required, controlling for potential confounders.

Neither proprioception nor laxity at T0 affected the association between change in muscle strength and change in activity limitations. Evidence for the influence of proprioception on the association between muscle strength and activity limitations has been demonstrated in cross-sectional studies.[10,26,42-44] Possibly, moderation by proprioception does exist: this effect could, however, be small – too small to be established in the present longitudinal study. The influence of knee joint laxity on the association between muscle strength and activity limitations has been controversial in cross-sectional studies.[9,11,45] Differences in results could be explained by differences in study population and statistical analysis. In our study, laxity did not moderate the association between change in muscle strength and activity limitations (with the exception of the walk test, which we consider a chance finding).

An increase in knee pain over three years was found to be associated with an increase in activity limitations (with the exception of the GUG test), independent of decrease in muscle strength. This result emphasizes the important role of knee pain in the development of activity limitations in early knee OA.[18] Knee pain and muscle strength are cross-sectionally related, and it has been suggested that muscle strength might be inhibited by knee pain.[46] However, in the present longitudinal study, change in muscle strength and change in knee pain were not associated (Pearson $r = -0.05$, $p = 0.619$; Spearman $r = -0.02$, $p = 0.814$). Thus an increase in knee pain and a decrease in muscle strength are independent factors in the development of activity limitations in early knee OA.

The association of the decrease in muscle strength with the increase in activity limitations was consistent over the various measures of activity limitations. However, the contribution of the decrease in muscle strength to the explained variance in outcome measures was small over three years (approximately 2%, data not shown). This small contribution to the variance in activity limitations should be viewed in the context of an observational study, with a relatively short duration of follow-up, and in an early stage of the disease.

Study limitations

Some limitations to our longitudinal study need mentioning. First, it is possible that a "floor-effect" (= no further improvement possible) or a "ceiling-effect" (= no further deterioration possible) on activity limitations as measured by the WOMAC-pf is responsible for the nearly significant association with change in muscle strength. Eight persons improved on the WOMAC-pf over three years to the minimum score of 0, none deteriorated to the maximum score of 68. After exclusion of these eight participants in regression analyses, the association with change in muscle strength was significant ($B = -8.25$, $p = 0.030$). Second, our data cover only a three-year period. The associations we found might be stronger if the intervals between the assessment of muscle strength and activity limitations were longer. Third, the small sample size may limit the ability to estimate associations with sufficient precision in our models. However, the associations of change in muscle strength with change in activity limitations were persistent in all analyses. Fourth, the present study used only a motion detection test as a measurement of proprioception. Another measurement of proprioception is a position detection test. Both measurements seem to test different aspects of knee proprioception.[47,48] The motion detection test is, however, more reliable than a position detection test.[47] Further studies are needed on the influence of both knee joint motion sense and knee joint position sense on the association between muscle strength and activity limitations. Finally, missing data at T1 might have biased our results, although the implication of such a bias is unknown. Five participants with total joint replacement dropped out of the study. These five participants showed high activity limitations at baseline (data not shown). It is to be expected that these participants would have influenced the results at follow-up by showing stronger associations between change in muscle strength and activity limitations.

The results from the present longitudinal study substantiate that improvement in muscle strength might reduce activity limitations or even prevent the development of activity limitations in the early phases of knee OA. This is in line with the beneficial effects of exercise therapy and physical activity, as observed in clinical trials[4] and observational studies[22] in more developed knee OA.

Conclusions

Overall, it can be concluded that although changes in muscle strength and activity limitations over a three-year period are small, a decrease in muscle strength is associated with an increase in activity limitations in patients with early knee OA. Our results are a step towards understanding the role of muscle weakness in the development of activity limitations in knee OA. To establish the causal role of muscle weakness in activity limitations, further well-designed experimental studies are indicated.

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