Arthritis & Rheumatism (Arthritis Care & Research)
Vol. 59, No. 7, July 15, 2008, pp 943–951
DOI 10.1002/art.23823

ORIGINAL ARTICLE

Does Knee Malalignment Mediate the Effects of Quadriceps Strengthening on Knee Adduction Moment, Pain, and Function in Medial Knee Osteoarthritis? A Randomized Controlled Trial

BOON-WHATT LIM,[1] RANA S. HINMAN,[1] TIM V. WRIGLEY,[1] LEENA SHARMA,[2] AND KIM L. BENNELL[1]

Objective. **To examine whether the effects of 12 weeks of quadriceps strengthening on the knee adduction moment, pain, and function in people with medial knee osteoarthritis (OA) differ in those with and without varus malalignment.**
Methods. **A single-blind, randomized controlled trial of 107 community volunteers with medial knee OA was conducted. Participants were stratified according to knee malalignment (more varus or more neutral) and then randomized into either a 12-week supervised home-based quadriceps strengthening group or a control group with no intervention. The primary outcome was the knee adduction moment, measured using 3-dimensional gait analysis. Secondary outcomes included the Western Ontario and McMaster Universities Osteoarthritis Index scores (measuring pain and physical function), step test score, stair climb test score, and maximum quadriceps isometric strength. Analyses of covariance were carried out based on intent-to-treat principles.**
Results. **Quadriceps strengthening did not significantly alter the knee adduction moment in either the more malaligned or the more neutral group (unadjusted knee adduction moment 0.12 and 0.05% Nm/BW×HT, respectively). Function did not improve significantly following quadriceps strengthening in either alignment group, but there was a significant improvement in knee pain in the more neutrally aligned group ($P < 0.001$).**
Conclusion. **Quadriceps strengthening did not have any significant effect on the knee adduction moment in participants with either more varus or more neutral alignment. The benefits of quadriceps strengthening on pain were more evident in those with more neutral alignment. Knee alignment thus represents a local mechanical factor that can mediate symptomatic outcome from exercise interventions in knee OA.**

INTRODUCTION

Mechanical factors have been implicated in the etiology and progression of knee osteoarthritis (OA) (1,2). In particular, knee alignment is thought to play an important role (3,4). Knee alignment determines load distribution across the knee. During normal gait, ~70% of knee joint loading passes through the medial compartment (5) due to the ground reaction force passing medial to the knee joint. Malalignment is a local joint factor that can affect how well the knee copes with imposed forces. Varus malalignment, commonly associated with medial tibiofemoral OA, serves to increase the moment arm of the ground reaction force and further increase loading in the medial compartment (6,7). As a result, varus malalignment is a major contributing factor to OA progression in this compartment (4,8,9).

Quadriceps strengthening exercises are commonly prescribed for patients with knee OA because they can reduce pain and improve function (10–12). However, little is known about their effects on knee loading and disease progression, and it is unclear whether these effects are influenced by the presence of knee malalignment. A recent longitudinal study found that greater quadriceps strength at baseline increased the risk of disease progression in patients with malaligned knees but not in those with neu-

ClinicalTrials.gov identifier: NCT00414557.
Supported in part by United Pacific Industries through a grant from the Physiotherapy Research Foundation, Australia.
[1]Boon-Whatt Lim, BSc(Hons)Physio, MSc, Rana S. Hinman, BPhysio(Hons), PhD, Tim V. Wrigley, MSc, Kim L. Bennell, BAppSc(Physio), PhD: Center for Health, Exercise, and Sports Medicine, School of Physiotherapy, The University of Melbourne, Victoria, Australia; [2]Leena Sharma, MD: Feinberg School of Medicine, Northwestern University, Chicago, Illinois.
Address correspondence to Kim L. Bennell, BAppSc (Physio), PhD, Center for Health, Exercise, and Sports Medicine, School of Physiotherapy, The University of Melbourne, 202 Berkeley Street, Carlton 3010, Melbourne, Victoria, Australia. E-mail: k.bennell@unimelb.edu.au.
Submitted for publication September 17, 2007; accepted in revised form February 11, 2008.

trally aligned knees (13). The authors suggested that the inability of malaligned knees to evenly distribute muscle forces could result in greater structural progression in these joints. It is also possible that greater quadriceps strength increases compressive forces across the knee joint (14), and that these effects may be accentuated with knee malalignment. In other words, local joint abnormalities such as malalignment could render muscle forces pathogenic (3,15).

Increased knee joint loading has been associated with an increased risk of disease progression (16). A commonly used surrogate measure of medial knee loading is the external knee adduction moment as determined from 3-dimensional (3-D) gait analysis. The knee adduction moment is directly related to the ratio of medial to lateral joint reaction force, and a higher knee adduction moment is indicative of higher medial compartment joint load (5,14,17). The peak knee adduction moment has been shown to be closely related to both the severity (18) and progression of knee OA (8). Thus, the knee adduction moment is widely accepted as a biomechanical marker of medial knee OA disease progression. To our knowledge, no study to date has evaluated the effects of quadriceps strengthening on the knee adduction moment in people with knee OA.

This study aimed to examine whether the effects of 12 weeks of quadriceps strengthening on the knee adduction moment, pain, and function in people with medial knee OA differ in those with and without varus malalignment. We hypothesized that varus malalignment would attenuate the effects of quadriceps strengthening, resulting in a higher knee adduction moment and poorer symptomatic outcomes.

PARTICIPANTS AND METHODS

Participants. Participants were recruited from the community in Melbourne, Australia through advertisements in newspapers and at local community clubs. All participants had tibiofemoral joint OA in at least 1 knee fulfilling the American College of Rheumatology classification criteria (19). To ensure that participants had medial OA, inclusion criteria were medial knee pain, medial compartment osteophytes, and medial joint space narrowing greater than lateral joint space narrowing (18). Exclusion criteria were a history of lower limb joint replacement, knee surgery within the previous 6 months, intraarticular steroid or hylan G-F 20 injection within the previous 6 months, a systemic arthritic condition, more than 5 degrees of valgus malalignment on radiograph, intention to start or current participation in physiotherapy for knee OA or a lower limb strengthening program, and/or presence of a severe medical condition that precluded safe participation in an exercise program. Ethical approval was obtained from the University of Melbourne Human Research Ethics Committee. Written informed consent was provided by participants.

Procedures. We conducted a 12-week, single-blind, randomized controlled trial, outlined in Figure 1. Participants were screened by telephone and those eligible underwent a standardized, extended-view anteroposterior weight-bearing radiograph. The most painful knee, or the dominant knee if both knees were equally severe, was deemed the study knee. Disease severity was assessed using the Kellgren/Lawrence (K/L) scale (20), in which higher grades indicate greater severity. Anatomic knee alignment was determined by a single investigator (B-WL) (intraclass correlation coefficient [ICC] 0.97) using the methods of Moreland et al (21). The anatomic femoral axis was obtained by drawing a line from the center of the tibial spines to a point 10 cm above the joint surface and bisecting the medial-to-lateral width of the femur. Similarly, tibial anatomic axis was obtained by drawing a line from the center of the tibial spines to a point 10 cm below the joint surface and midway between the medial and lateral tibial surfaces. Anatomic knee alignment is represented by the angle subtended at the point where the 2 lines meet in the center of the tibial spines. Mechanical knee alignment was then extrapolated using the following regression equation from Hinman et al (22): mechanical alignment = 0.915 (anatomic alignment) + 13.895. Alignment is reported as the deviation from neutral in the varus direction, and an alignment of 0 degrees indicates a neutrally aligned knee. Although the mechanical axis measured using a full-limb radiograph is considered the gold standard in measuring knee alignment, several studies have found a good to excellent correlation ($r = 0.65–0.88$) between the anatomic axis and the mechanical axis (22–24).

Participants fulfilling eligibility criteria were enrolled in the study and categorized according to alignment. Participants with $\geq$5 degrees varus malalignment were deemed more malaligned, and those with $<$5 degrees malalignment (in either direction) were deemed more neutral (13). Each group was then randomized to receive either quadriceps strengthening or no intervention (control group).

A random table, stratified by alignment (more malaligned or more neutral) in blocks of 6, was used to determine group allocation. An independent researcher not involved in eligibility or outcome assessment randomized participants, and the allocation schedule was concealed from the blinded examiner (B-WL) who carried out the outcome assessments.

This study was powered to detect an interaction effect between alignment and strengthening on the change in knee adduction moment using a two-way analysis of variance (ANOVA) with 80% power and an alpha level of 0.05. We aimed to detect a 10% change in the knee adduction moment between the more malaligned strengthening group and the other 3 groups. This change was decided a priori to be clinically relevant because an increase of this magnitude could increase the odds of progression $\times$ 3.3 (8). Although Thorstensson et al (25) have reported data concerning the effects of strengthening on the knee adduction moment, this was not available at our study outset. Based on our data and that of others (26,27), a 10% change in the knee adduction moment was assumed to be equivalent to an absolute change of 0.4% Nm/BW$\times$HT, with the SD estimated to be 0.4% Nm/BW$\times$HT. Based on these assumptions, a sample size of 49 participants was required

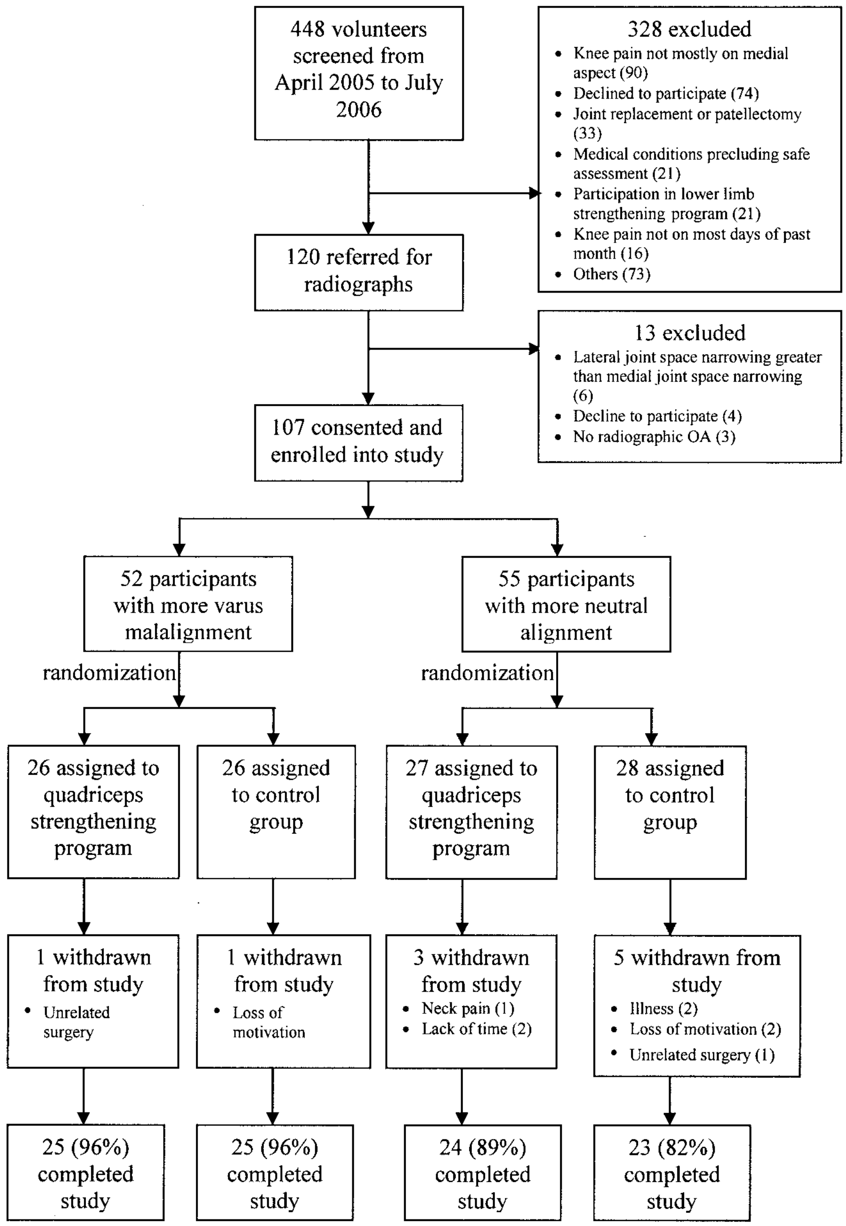

Figure 1. Flowchart of participants through the study. OA = osteoarthritis.

and this was increased to 107 to account for dropouts and the chance of a larger variance than anticipated a priori.

Methods. Six experienced musculoskeletal physiotherapists supervised the home-based quadriceps strengthening program. Participants were taught 5 quadriceps strengthening exercises (Table 1) to be performed on the study leg 5 days a week for 12 weeks using ankle weights and a black Thera-Band (Hygenic Corporation, Akron, OH). Participants visited the physiotherapists a total of 7 times (during weeks 1, 2, 3, 4, 5, 7, and 10), and exercise loads were progressed when participants could comfortably achieve the given dosages. Participants in the control group were not given any intervention and were asked to avoid starting any new treatment or exercise program.

Participants were assessed at baseline and week 13. The following information was obtained: age, sex, height, body mass, body mass index (BMI), presence of unilateral or bilateral symptoms, and duration of symptoms.

The primary outcome measure was the peak external knee adduction moment, which was measured using a Vicon 612 motion analysis system (Vicon, Oxford, UK) with 8 cameras (120 Hz M2) and 2 force plates (AMTI Inc., Watertown, MA) embedded in the center of a walkway. Twenty retroreflective markers were placed over standardized anatomic landmarks, and inverse dynamics were used to calculate external joint moments about an orthogonal axis system located in the distal segment of the joint (28).

Participants walked in their own low-heeled shoes over an 8-meter walkway at a self-selected pace and a standardized pace of 1 meter/second until 5 acceptable trials were

Table 1. Quadriceps exercises*

1. Long arc knee extension using ankle weight in sitting position from 90 degrees to 0 degrees knee flexion.
2. Inner range knee extension using ankle weight over fulcrum in supine lying or long sitting position from 30 degrees to 0 degrees knee flexion.
3. Straight leg raise using ankle weight in supine lying or elbow-supported supine lying position.
4. Isometric knee extension at 30 degrees knee flexion using ankle weight in sitting position.
5. Isometric knee extension at 60 degrees knee flexion using Thera-Band in sitting position.

* Each exercise was performed in a controlled manner at a self-determined pace. Two sets of 10 repetitions were performed for the first 2 weeks, and 3 sets of 10 repetitions thereafter. Exercises were performed 5 days of each week, with 2 rest days determined by the participants according to their symptoms.

recorded for each person. For standardized trials, participants were given verbal feedback to remain within 10% of the required pace. Walking speed was measured using photoelectric beams (Jaycar Electronics, Melbourne, Victoria, Australia) attached to a stopwatch and placed 4 meters apart in the middle of the 8-meter walkway. All markers were applied by the same examiner (B-WL), and participants wore the same shoes at baseline and followup. Test–retest reliability in our laboratory was excellent with this procedure in 11 knee OA patients tested 1 week apart (ICC 0.96–0.97).

The Likert version of the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) was used to assess knee pain and physical function (29). Each subscale of the WOMAC questionnaire was transformed to a 100-point scale for ease of interpretation, with higher scores indicating worse pain or function.

The step test (30) was used to assess dynamic standing balance. Participants were instructed to maintain balance on the study leg while stepping the contralateral leg on and off a 15-cm step as many times as possible in 15 seconds without any weight transfer to the stepping leg. The stair climb test (31) was used to assess function. Participants were instructed to ascend and descend a 6-step set of stairs at their own pace, and the total time taken was recorded.

Quadriceps strength was assessed isometrically at 60 degrees knee flexion in the sitting position using a Kin-Com 125-AP dynamometer (Chattecx Corporation, Hixson, TN). A submaximal warm up was followed by 3 maximal 5-second contractions with a 15-second rest interval in between each (32). The highest peak force of the 3 trials was multiplied by the lever length (in meters) to obtain the maximum torque, which was then normalized by body mass (Nm/kg). The test–retest reliability for this measure in our laboratory in 10 knee OA patients tested 1 week apart is excellent (ICC 0.93).

To monitor compliance, strengthening participants kept a training diary; compliance rate was deemed 100% if the participant had completed 5 days of exercises per week over 12 weeks (total of 60 exercise days). Cointervention and adverse effects of the strengthening program were also recorded.

Statistical analyses. We used SPSS software, version 15.0 (SPSS, Chicago, IL) to undertake statistical analyses on an intent-to-treat basis using the last observation carried forward method to impute data missing at reassessment. One-way ANOVA was used to examine baseline comparability across groups and Tukey honest significant difference post hoc analyses were performed where results were significant. Chi-square tests were used to determine baseline comparability for categorical data. For each participant, change scores for each dependent variable were calculated by subtracting the score at followup from that at baseline.

Two-way ANOVA was performed to examine the main effect of alignment and strengthening, and their interaction effect, on change scores. Analyses were repeated for each change score, adjusting for potential confounders using analyses of covariance. Knee adduction moment was reanalyzed using age, sex, disease severity, baseline knee adduction moment, change in walking speed, and change in knee pain as covariates. Knee pain, function, and quadriceps strength were reanalyzed using age, sex, BMI (except quadriceps strength), disease severity, and baseline score of the variable as covariates.

RESULTS

Of the 107 participants enrolled in the study, 97 returned for reassessment, representing a completion rate of 91% (Figure 1). The mean ± SD compliance rate was 89 ± 21% for the more malaligned group and 86 ± 22% for the more neutral group. More malaligned participants started with an average exercise load of 3.5 kg and attained 5.7 kg at week 12. More neutrally aligned participants started with an average exercise load of 2.7 kg and ended with 5.8 kg. Although participants were discouraged from seeking additional treatment, 14 strengthening participants (8 more malaligned, 6 more neutrally aligned) and 8 control participants (5 more malaligned, 3 more neutrally aligned) reported performing other low-intensity exercises such as walking during the study.

Among strengthening participants with more malaligned knees, 4 reported increased knee pain and 2 reported increased hip/groin pain that were attributed to the intervention. Among strengthening participants with more neutral alignment, 3 had increased knee pain and 1 reported neck pain due to awkward exercise positioning. Only the participant with neck pain withdrew from the study. Two participants (1 from each alignment group) stopped the strengthening program at week 2 due to increased knee pain but returned for reassessment.

Demographic and anthropometric characteristics of the participants are shown in Table 2. As expected, both of the more malaligned groups had greater varus malalignment than the more neutral groups ($P < 0.001$ for both post hoc tests) and there was a significant association between malalignment and disease severity ($P < 0.001$). In the more malaligned group, 63% of participants had a K/L grade of 4, compared with 20% in the more neutral group. The more malaligned strengthening group was significantly older than the more neutral control group ($P = 0.020$).

Table 2. Characteristics of participants at baseline*

Characteristic	Strengthening group (n = 53) More malaligned (n = 26)	Strengthening group (n = 53) More neutrally aligned (n = 27)	Control group (n = 54) More malaligned (n = 26)	Control group (n = 54) More neutrally aligned (n = 28)
Age, years	67.2 ± 6.7	64.1 ± 9.3	66.6 ± 8.9	60.8 ± 7.8
Female, no. (%)	13 (50)	17 (63)	12 (46)	17 (61)
Height, meters	1.67 ± 0.10	1.65 ± 0.10	1.66 ± 0.08	1.64 ± 0.11
Body mass, kg	78.7 ± 13.0	79.2 ± 15.9	83.4 ± 16.6	76.6 ± 15.6
BMI, kg/m^2	28.2 ± 3.7	29.0 ± 5.2	30.3 ± 5.3	28.4 ± 5.0
Physical activity level†	161.3 ± 63.8	159.5 ± 77.4	172.4 ± 101.6	185.2 ± 81.0
Symptom duration, years	5.9 ± 5.5	6.1 ± 5.0	8.4 ± 6.6	6.4 ± 3.9
Bilateral symptom, no. (%)	11 (42)	9 (33)	8 (31)	13 (46)
Disease severity, no. (%)‡				
K/L grade 2	4 (15)	12 (44)	3 (12)	15 (54)
K/L grade 3	8 (31)	7 (26)	4 (15)	10 (36)
K/L grade 4	14 (54)	8 (30)	19 (73)	3 (11)
Varus malalignment, degrees	6.7 ± 1.7	1.2 ± 1.9	6.9 ± 2.0	1.6 ± 1.8
Quadriceps strength, Nm/kg	1.38 ± 0.52	1.32 ± 0.57	1.46 ± 0.54	1.12 ± 0.49
Knee adduction moment, %Nm/BW×HT	4.28 ± 0.63	3.58 ± 0.94	3.97 ± 0.57	3.91 ± 1.01
WOMAC pain score§	33.1 ± 15.4	35.7 ± 14.6	39.2 ± 14.0	34.6 ± 16.2
WOMAC function score§	31.4 ± 17.4	33.2 ± 15.4	38.5 ± 14.5	36.1 ± 15.7
Self-selected walking speed, meters/second	1.18 ± 0.18	1.22 ± 0.25	1.19 ± 0.21	1.22 ± 0.18
Step test, no.	13 ± 3	12 ± 3	14 ± 3	13 ± 3
Stair climb test, seconds	12.4 ± 4.3	12.0 ± 4.8	12.0 ± 3.1	12.5 ± 5.5

* Values are the mean ± SD unless otherwise indicated. BMI = body mass index; K/L grade = Kellgren/Lawrence grade; WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index.
† Measured using the Physical Activity Scale for the Elderly (0–400, higher scores indicate greater activity).
‡ On the K/L scale, higher scores indicate greater osteoarthritis severity.
§ The WOMAC ranges from 0–100, with higher scores indicating worse symptoms.

Groups were similar at baseline with regard to all outcome measures except knee adduction moment, which differed only between the more malaligned strengthening group and the more neutral strengthening group ($P = 0.011$).

Quadriceps strength. There was a significant main effect for strengthening but no significant interaction effect, suggesting that participants in the strengthening group had a significantly greater increase in quadriceps strength irre-

Table 3. Effect of quadriceps strengthening and knee alignment on mean change in quadriceps strength and knee adduction moment*

	Strengthening More malaligned	Strengthening More neutrally aligned	Control More malaligned	Control More neutrally aligned	*P* Main effect of alignment	*P* Main effect of strengthening	*P* Interaction effect
Quadriceps strength, Nm/kg							
Baseline	1.38 ± 0.52	1.32 ± 0.57	1.46 ± 0.54	1.12 ± 0.49			
Followup	1.67 ± 0.66	1.68 ± 0.61	1.45 ± 0.57	1.18 ± 0.53			
Unadjusted mean change	0.29 ± 0.05	0.36 ± 0.05	−0.01 ± 0.05	0.05 ± 0.05	0.204	< 0.001†	0.900
Adjusted mean change‡	0.28 ± 0.05	0.36 ± 0.05	0.04 ± 0.06	0.01 ± 0.05	0.673	< 0.001†	0.298
Knee adduction moment, % Nm/BW×HT							
Baseline	4.28 ± 0.63	3.58 ± 0.94	3.97 ± 0.57	3.91 ± 1.01			
Followup	4.40 ± 0.76	3.63 ± 1.11	3.91 ± 0.71	3.79 ± 1.11			
Unadjusted mean change	0.12 ± 0.09	0.05 ± 0.09	−0.05 ± 0.09	0.06 ± 0.09	0.804	0.398	0.303
Adjusted mean change§	0.10 ± 0.09	0.06 ± 0.09	−0.01 ± 0.10	0.02 ± 0.10	0.997	0.431	0.736

* Values are the mean ± SD unless otherwise indicated. Baseline and followup values are unadjusted. Mean change is calculated as the followup value minus the baseline value.
† Values are significant.
‡ Adjusted for age, sex, disease severity (Kellgren/Lawrence [K/L] grade), and baseline quadriceps strength.
§ Adjusted for age, sex, disease severity (K/L grade), baseline knee adduction moment, change in walking speed, and change in Western Ontario and McMaster Universities Osteoarthritis Index pain score.

Table 4. Effect of quadriceps strengthening and knee alignment on mean change in pain and function*

	Strengthening		Control		P		
	More malaligned	More neutrally aligned	More malaligned	More neutrally aligned	Main effect of alignment	Main effect of strengthening	Interaction effect
WOMAC pain score†							
Baseline	33.1 ± 15.4	35.7 ± 14.6	39.2 ± 14.0	34.6 ± 16.2			
Followup	28.5 ± 16.9	22.8 ± 16.9	36.2 ± 16.2	33.6 ± 15.4			
Unadjusted mean change	−4.6 ± 2.5	−13.0 ± 2.3	−3.1 ± 2.68	−0.7 ± 2.5	0.231	0.007‡	0.033‡
Adjusted mean change§	−6.3 ± 2.4	−11.7 ± 2.3	−4.5 ± 2.5	1.0 ± 2.4	0.981	0.002‡	0.024‡
WOMAC function score†							
Baseline	31.4 ± 17.4	33.1 ± 15.4	38.5 ± 14.5	36.1 ± 15.7			
Followup	29.3 ± 15.6	24.0 ± 18.1	36.5 ± 18.2	32.4 ± 15.5			
Unadjusted mean change	−2.1 ± 2.1	−9.2 ± 2.1	−2.0 ± 2.1	−3.7 ± 2.0	0.036‡	0.179	0.197
Adjusted mean change§	−3.7 ± 2.1	−8.4 ± 2.0	−3.3 ± 2.1	−1.9 ± 2.1	0.476	0.086	0.130
Step test, no.							
Baseline	13 ± 3	12 ± 3	14 ± 3	13 ± 3			
Followup	14 ± 3	14 ± 4	14 ± 4	14 ± 3			
Unadjusted mean change	1 ± 3	2 ± 2	0 ± 3	1 ± 2	0.062	0.065	0.904
Adjusted mean change§	1 ± 2	1 ± 2	1 ± 3	0 ± 3	0.871	0.079	0.465
Stair climb test, seconds							
Baseline	12.4 ± 4.3	12.0 ± 4.8	12.0 ± 3.1	12.5 ± 5.5			
Followup	11.8 ± 4.2	11.0 ± 4.8	12.7 ± 3.8	11.8 ± 4.8			
Unadjusted mean change	−0.6 ± 0.5	−0.9 ± 0.5	0.7 ± 0.5	−0.8 ± 0.5	0.082	0.156	0.261
Adjusted mean change§	−0.8 ± 0.5	−0.8 ± 0.5	0.0 ± 0.5	0.0 ± 0.5	0.998	0.087	0.886

* Baseline and followup values are unadjusted and expressed as mean ± SD. Mean change is calculated as the followup value minus the baseline value and expressed as mean ± SE. WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index.
† The WOMAC ranges from 0–100, with higher scores indicating worse symptoms.
‡ Significant main or interaction effect.
§ Adjusted for age, sex, disease severity (Kellgren/Lawrence grade), body mass index, and baseline score.

spective of alignment group (Table 3). Results were similar with adjustment for confounders. The adjusted mean change in quadriceps strength was 0.28 Nm/kg (20%) for the more malaligned strengthening group and 0.36 Nm/kg (27%) for the more neutral strengthening group.

External knee adduction moment. Similar results were obtained for gait trials at self-selected and standardized paces, and therefore only results from self-selected trials are presented. There was no main effect of either alignment or strengthening on the knee adduction moment (Table 3). There was also no interaction effect. Results were unchanged when adjusted for covariates.

Knee pain and function. Quadriceps strengthening led to a significant improvement in knee pain in only the more neutrally aligned participants (Table 4). There was a significant main effect for strengthening and a significant interaction effect, both with and without adjustment for confounders. In the more neutral group, strengthening participants reported a significant pain reduction compared with control participants (adjusted difference 12.7; $P < 0.001$). There was no significant pain reduction in the more malaligned group (adjusted difference 1.8; $P = 0.592$). Although there was a significant effect of alignment on unadjusted WOMAC physical function scores, the effect was not present after adjusting for covariates. Regarding observed functional outcomes, there were no significant main or interaction effects evident (Table 4).

DISCUSSION

The aim of this study was to examine whether the effects of quadriceps strengthening on the knee adduction moment, pain, and function in medial knee OA differ according to malalignment. Our results showed that strengthening did not alter the knee adduction moment after 12 weeks in either the more malaligned or the more neutral groups. It is unlikely that this nonsignificant finding is due to insufficient power. The sample size of 107 in this study is greater than the 49 required to detect an interaction effect between alignment and strengthening. Post hoc power analyses using the actual pooled estimate of the intragroup SD (which was 0.47 instead of the predicted 0.40) revealed that we had 96% power to detect the stipulated minimum interaction effect size with our final sample size of 97 participants (excluding dropouts). Although it is possible that much smaller changes in the knee adduction moment may have gone undetected by this study, the clinical relevance of smaller changes is unclear.

There are few studies examining biomechanical or structural effects of strengthening interventions in knee OA. A small uncontrolled study (33) evaluated the effect of 8 weeks of supervised lower limb strength and neuromuscular control exercises on the knee adduction moment (measured during one-leg chair rise and in walking) in 13 patients with early knee OA. Similar to our findings, the authors found that peak knee adduction moment during gait was not significantly altered at the completion of the exercise program. The observed mean change of 0.02 Nm/kg was equivalent to a ~3.8% increase in knee adduction moment, which is similar to our results. However, the authors found a 14% reduction in the knee adduction moment measured during one-leg chair rise. The authors postulated that this reduction may be due to hip or ankle compensation altering the lever arm of the ground reaction force. It is unclear why such a change did not occur during walking.

The knee adduction moment is widely considered a biomarker of disease progression. Only 1 study has evaluated effects of lower limb strengthening on the radiographic progression of knee OA over 30 months in 221 older adults (34). In participants with established knee OA, mean loss of joint space width was 37% less (0.34 mm versus 0.54 mm) in the strength training group compared with the control group, which was performing range of motion exercises, but the results were not significant (P = 0.136). However, several methodologic issues prevented a definitive conclusion, one of which was that the strength training group actually lost quadriceps and hamstring strength over 30 months (35). As the knee adduction moment was not measured, it is unclear whether changes in muscle strength were related to changes in joint loading. Our intervention resulted in an average quadriceps strength gain of 28.7%, which enables us to better evaluate the effect of quadriceps strength gain on knee loading.

We used the knee adduction moment as a surrogate measure of medial knee joint loading. However, we cannot exclude an effect of quadriceps strengthening on compressive force across the knee, which would also serve to increase knee load and thus increase the risk of disease progression over time. Because the quadriceps muscle spans the knee joint, the contraction of the muscle will bring the joint articular surfaces together, causing an axial compressive loading force (36). Therefore, although contraction of the quadriceps muscle can dynamically stabilize the knee and increase knee stiffness (37) prior to heel strike, it does so at the expense of greater compression forces through the knee joint (14). Although our study did not find any significant increase in knee adduction moment following strengthening, it is possible that overall compressive force acting across the knee may increase with a quadriceps strengthening program, and this may have deleterious consequences for disease progression.

Our study is the first to specifically evaluate the impact of quadriceps strengthening on pain and function according to knee malalignment. We found that quadriceps strengthening reduced pain in people with more neutral knee alignment but not in those with more malalignment, despite similar baseline pain and comparable gains in quadriceps strength. This finding may, in part, be due to the improvement in pain observed in the more malaligned control group but not in the more neutral control group. Although studies have shown that increased quadriceps strength improves pain in heterogeneous OA samples (10–12), the mechanism behind pain improvement is poorly understood (38).

There are a number of possible explanations for our results. Stronger quadriceps help to improve joint stability, absorb shock, and attenuate ground reaction forces during gait (39), and this may subsequently improve knee pain. This mechanism may be less effective in malaligned knees, possibly due to damaged mechanoreceptors from stretched joint capsules or due to ligaments producing abnormal afferent signals that decrease quadriceps contraction (40). It is feasible that knee malalignment could alter the line of action of the quadriceps force and that this could increase compression forces on localized areas of articular cartilage (13,41), thereby exacerbating knee pain in this group. Varus malalignment has been associated with the presence of medial patellofemoral joint OA (42), and the contraction of the quadriceps increases patellofemoral joint compression (43). Therefore, the nature of the exercises may well predispose malaligned participants to greater patellofemoral joint compression, thus exacerbating knee pain.

We did not find any significant effect of quadriceps strengthening on physical function in either alignment group, despite a substantial quadriceps strength increase postintervention. This is in contrast with other studies (11,44,45) that have demonstrated improvements in WOMAC function scores after a home-based strengthening program. Unlike the present study, which specifically prescribed isolated open kinetic chain quadriceps strengthening, exercise interventions in other studies involved other lower limb muscle groups in addition to the quadriceps. Therefore, it is possible that greater quadriceps strength alone may not affect overall physical function. The nonfunctional nature of the prescribed exercises may also contribute to the lack of improvement in physical function. However, the exercises were deliberately designed to isolate the quadriceps, given that this was the research question. Our nonsignificant finding for function is not likely to be due to insufficient power; a post hoc power analysis showed that ≥67 participants would be needed to detect a significant interaction effect of alignment and strengthening of a clinically relevant magnitude (9.1 units on the WOMAC) at 80% power (46).

A strength of our study is its design, which allowed the effects of quadriceps strengthening to be compared between the strengthening and control groups while minimizing the potential effects of confounders. Stratification of participants by alignment further enabled the effects of quadriceps strengthening to be differentiated according to knee alignment. Our exercise protocol was targeted specifically at the quadriceps muscle and we were successful in achieving a substantial increase in quadriceps strength. More malaligned participants in our study achieved a 20% in quadriceps strength compared with 27% for more neutrally aligned participants. These strength increases were within the range reported by other home-based strengthening studies (11,44).

However, there are also several limitations to our study. Marker placements used in the 3-D gait analysis have the potential to account for some change in the knee adduction moment over time. Although having standardized anatomic landmarks all placed by the same blinded examiner minimized these errors, as indicated by the excellent reliability of this measurement, it is unknown whether the ideal measure of knee adduction moment without any measurement error could have detected a change in knee adduction moment in the strengthening groups. Furthermore, the presence of a higher baseline knee adduction moment in the more malaligned participants, although understandable given their more varus malalignment, could result in a ceiling effect which may have prevented a higher knee adduction moment increase in the malaligned strengthening group. It should be highlighted that the use of high-intensity isolated quadriceps strengthening in this study does not represent usual clinical practice for managing knee OA, which typically involves functional closed kinetic chain exercises that target multiple muscle groups. Therefore, the results of this study cannot be extrapolated to strengthening exercises using lower exercise loads and involving different muscle groups. In addition, stronger hip abductors have been associated with a reduced risk of knee OA progression in the ipsilateral knee (47), and therefore the results may be different with the addition of hip exercises to the exercise protocol.

This is the first study to demonstrate that subgroups within knee OA may respond differently to strengthening exercises with regard to pain reduction. Our findings suggest that the use of exercises focusing on quadriceps strength may not improve pain in more malaligned people. Such individuals may benefit more from functional exercises emphasizing neuromuscular control and coordination (48), but the effects of such a program have not been evaluated in a malaligned population. The findings of our study reinforce those by other authors (9,13,48) indicating that treatment of knee OA should be tailored to the individual and that factors such as knee alignment should be considered.

In conclusion, we found that quadriceps strengthening did not have any significant effect on knee adduction moment in participants with either more malaligned or more neutrally aligned knee OA. However, the benefits of quadriceps strengthening on pain were more evident in those with more neutral alignment. Future studies evaluating the efficacy of interventions should stratify analyses by local factors, particularly knee malalignment.

AUTHOR CONTRIBUTIONS

Dr. Bennell 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 design. Lim, Hinman, Wrigley, Sharma, Bennell.

Acquisition of data. Lim, Wrigley.

Analysis and interpretation of data. Lim, Hinman, Wrigley, Sharma, Bennell.

Manuscript preparation. Lim, Hinman, Wrigley, Sharma, Bennell.

Statistical analysis. Lim.

Acquisition of funding. Bennell.

REFERENCES

1. Sharma L. The role of proprioceptive deficits, ligamentous laxity, and malalignment in development and progression of knee osteoarthritis. J Rheumatol Suppl 2004;70:87–92.
2. Jackson BD, Wluka AE, Teichtahl AJ, Morris ME, Cicuttini FM. Reviewing knee osteoarthritis: a biomechanical perspective. J Sci Med Sport 2004;7:347–57.
3. Sharma L. The role of varus and valgus alignment in knee osteoarthritis [editorial]. Arthritis Rheum 2007;56:1044–7.
4. Sharma L, Song J, Felson DT, Cahue S, Shamiyeh E, Dunlop DD. The role of knee alignment in disease progression and functional decline in knee osteoarthritis [published erratum appears in JAMA 2001;286:792]. JAMA 2001;286:188–95.
5. Andriacchi TP. Dynamics of knee malalignment. Orthop Clin North Am 1994;25:395–403.
6. Kettelkamp DB, Wenger DR, Chao EY, Thompson C. Results of proximal tibial osteotomy: effects of tibiofemoral angle, stance-phase flexion-extension, and medial-plateau force. J Bone Joint Surg Am 1976;58:952–60.
7. Marquet P. Biomechanics of the knee: with applications to the pathogenesis and the surgical treatment of osteoarthritis. Berlin: Springer-Verlag; 1984.
8. Miyazaki T, Wada M, Kawahara H, Sato M, Baba H, Shimada S. Dynamic load at baseline can predict radiographic disease progression in medial compartment knee osteoarthritis. Ann Rheum Dis 2002;61:617–22.
9. Felson DT, Goggins J, Niu J, Zhang Y, Hunter DJ. The effect of body weight on progression of knee osteoarthritis is dependent on alignment. Arthritis Rheum 2004;50:3904–9.
10. Van Baar ME, Assendelft WJ, Dekker J, Oostendorp RA, Bijlsma JW. Effectiveness of exercise therapy in patients with osteoarthritis of the hip or knee: a systematic review of randomized clinical trials. Arthritis Rheum 1999;42:1361–9.
11. O'Reilly SC, Muir KR, Doherty M. Effectiveness of home exercise on pain and disability from osteoarthritis of the knee: a randomized controlled trial. Ann Rheum Dis 1999;58:15–9.
12. Bischoff HA, Roos EM. Effectiveness and safety of strengthening, aerobic, and coordination exercises for patients with osteoarthritis. Curr Opin Rheumatol 2003;15:141–4.
13. Sharma L, Dunlop DD, Cahue S, Song J, Hayes KW. Quadriceps strength and osteoarthritis progression in malaligned and lax knees. Ann Intern Med 2003;138:613–9.
14. Schipplein OD, Andriacchi TP. Interaction between active and passive knee stabilizers during level walking. J Orthop Res 1991;9:113–9.
15. Marks R, Kumar S, Semple J, Percy JS. Quadriceps femoris activation in healthy women with genu-varum and women with osteoarthrosis and genu-varum. J Electromyogr Kinesiol 1994;4:153–60.
16. Andriacchi TP, Mundermann A, Smith RL, Alexander EJ, Dyrby CO, Koo S. A framework for the in vivo pathomechanics of osteoarthritis at the knee. Ann Biomed Eng 2004;32: 447–57.
17. Zhao D, Banks SA, Mitchell KH, D'Lima DD, Colwell CW Jr, Fregly BJ. Correlation between the knee adduction torque and medial contact force for a variety of gait patterns. J Orthop Res 2007;25:789–97.
18. Sharma L, Hurwitz DE, Thonar EJ, Sum JA, Lenz ME, Dunlop DD, et al. Knee adduction moment, serum hyaluronan level, and disease severity in medial tibiofemoral osteoarthritis. Arthritis Rheum 1998;41:1233–40.
19. Altman R, Asch E, Bloch D, Bole G, Borenstein D, Brandt K, et al. Development of criteria for the classification and reporting of osteoarthritis: classification of osteoarthritis of the knee. Arthritis Rheum 1986;29:1039–49.
20. Kellgren JH, Jeffrey MR, Ball J. The epidemiology of chronic rheumatism: atlas of standard radiographs. Oxford: Blackwell Scientific; 1963.
21. Moreland JR, Bassett LW, Hanker GJ. Radiographic analysis of the axial alignment of the lower-extremity. J Bone Joint Surg Am 1987;69:745–9.
22. Hinman RS, May RL, Crossley KM. Is there an alternative to the full-leg radiograph for determining knee joint alignment in osteoarthritis? Arthritis Rheum 2006;55:306–13.
23. Kraus VB, Vail TP, Worrell T, McDaniel G. A comparative assessment of alignment angle of the knee by radiographic and physical examination methods. Arthritis Rheum 2005;52: 1730–5.
24. Issa SN, Dunlop D, Chang A, Song J, Prasad PV, Guermazi A, et al. Full-limb and knee radiography assessments of varus-valgus alignment and their relationship to osteoarthritis disease features by magnetic resonance imaging. Arthritis Rheum 2007;57:398–406.

25. Thorstensson CA, Roos EM, Petersson IF, Ekdahl C. Six-week high-intensity exercise program for middle-aged patients with knee osteoarthritis: a randomized controlled trial. BMC Musculoskelet Disord 2005;6:27.
26. Prodromos CC, Andriacchi TP, Galante JO. A relationship between gait and clinical changes following high tibial osteotomy. J Bone Joint Surg Am 1985;67:1188–94.
27. Schnitzer TJ, Popovich JM, Andersson GB, Andriacchi TP. Effect of piroxicam on gait in patients with osteoarthritis of the knee. Arthritis Rheum 1993;36:1207–13.
28. Davis RB III, Ounpuu S, Tyburski D, Gage JR. A gait data collection and reduction technique. Hum Mov Sci 1991;10: 575–87.
29. Bellamy N, Buchanan WW, Goldsmith CH, Campbell J, Stitt LW. Validation study of WOMAC: a health status instrument for measuring clinically important patient relevant outcomes to antirheumatic drug therapy in patients with osteoarthritis of the hip or knee. J Rheumatol 1988;15:1833–40.
30. Hill K, Bernhardt J, McGann AM, Maltese D, Berkovits D. A new test of dynamic standing balance for stroke patients: reliability, validity, and comparison with healthy elderly. Physiother Can 1996;48:257–62.
31. Rejeski WJ, Ettinger WH, Schumaker S, James P, Burns R, Elam JT. Assessing performance-related disability in patients with knee osteoarthritis. Osteoarthritis Cartilage 1995;3:157–67.
32. Bennell KL, Hinman RS, Metcalf BR, Buchbinder R, McConnell J, McColl G, et al. Efficacy of physiotherapy management of knee joint osteoarthritis: a randomized, double-blind, placebo controlled trial. Ann Rheum Dis 2005;64:906–12.
33. Thorstensson CA, Henriksson M, von Porat A, Sjodahl C, Roos EM. The effect of 8 weeks of exercise on knee adduction moment in early knee osteoarthritis: a pilot study. Osteoarthritis Cartilage 2007;15:1163–70.
34. Mikesky AE, Mazzuca SA, Brandt KD, Perkins SM, Damush T, Lane KA. Effects of strength training on the incidence and progression of knee osteoarthritis. Arthritis Rheum 2006;55: 690–9.
35. Bennell K, Lim BW. Does strength training affect the incidence and progression of knee osteoarthritis? [abstract]. Nat Clin Pract Rheumatol 2007;3:134–5.
36. Andriacchi TP, Andersson GB, Ortengren R, Mikosz RP. A study of factors influencing muscle activity about the knee joint. J Orthop Res 1984;1:266–75.
37. Olmstead TG, Wevers HW, Bryant JT, Gouw GJ. Effect of muscular activity on valgus varus laxity and stiffness of the knee. J Biomech 1986;19:565–7.
38. Creamer P, Hunt M, Dieppe P. Pain mechanisms in osteoarthritis of the knee: effect of intraarticular anesthetic. J Rheumatol 1996;23:1031–6.
39. Mikesky AE, Meyer A, Thompson KL. Relationship between quadriceps strength and rate of loading during gait in women. J Orthop Res 2000;18:171–5.
40. Hurley MV, Scott DL, Rees J, Newham DJ. Sensorimotor changes and functional performance in patients with knee osteoarthritis. Ann Rheum Dis 1997;56:641–8.
41. Marks R. The effects of 16 months of angle-specific isometric strengthening exercises in midrange on torque of the knee extensor muscles in osteoarthritis of the knee: a case study. J Orthop Sports Phys Ther 1994;20:103–9.
42. Elahi S, Cahue S, Felson DT, Engelman L, Sharma L. The association between varus-valgus alignment and patellofemoral osteoarthritis. Arthritis Rheum 2000;43:1874–80.
43. Grelsamer RP, Klein JR. The biomechanics of the patellofemoral joint. J Orthop Sports Phys Ther 1998;28:286–98.
44. Baker KR, Nelson ME, Felson DT, Layne JE, Sarno R, Roubenoff R. The efficacy of home-based progressive strength training in older adults with knee osteoarthritis: a randomized controlled trial. J Rheumatol 2001;28:1655–65.
45. Thomas KS, Muir KR, Doherty M, Jones AC, O'Reilly SC, Bassey EJ. Home-based exercise program for knee pain and knee osteoarthritis: randomized controlled trial. BMJ 2002; 325:752–6.
46. Tubach F, Ravaud P, Baron G, Falissard B, Logeart I, Bellamy N, et al. Evaluation of clinically relevant changes in patient reported outcomes in knee and hip osteoarthritis: the minimal clinically important improvement. Ann Rheum Dis 2005;64: 29–33.
47. Chang A, Hayes K, Dunlop D, Song J, Hurwitz D, Cahue S, et al. Hip abduction moment and protection against medial tibiofemoral osteoarthritis progression. Arthritis Rheum 2005; 52:3515–9.
48. Fitzgerald GK, Oatis C. Role of physical therapy in management of knee osteoarthritis. Curr Opin Rheumatol 2004;16: 143–7.