

Quadriceps Strength and Osteoarthritis Progression in Malaligned and Lax Knees

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Background: Quadriceps muscle strengthening is a common goal in the management of knee osteoarthritis. In healthy knees, strength protects against new osteoarthritis. In arthritic knees, greater strength may protect joints and thereby delay osteoarthritis progression. Alternatively, in certain joint environments, such as malalignment or laxity, greater strength may translate into damaging joint reaction forces. The relationship between quadriceps strength and progression of knee osteoarthritis may differ according to these factors.

Objective: To determine whether greater quadriceps strength is associated with greater probability of tibiofemoral osteoarthritis progression in malaligned knees and in high-laxity knees.

Design: Prospective, longitudinal cohort study.

Setting: Academic medical center.

Participants: 237 persons with primary knee osteoarthritis, definite tibiofemoral osteophytes, and at least some difficulty with knee-requiring activity. Two hundred thirty completed the 18-month evaluation. The current study primarily involved those without advanced osteoarthritis in either knee ($n = 171$).

Measurements: Quadriceps strength, knee laxity and alignment, and osteoarthritis progression.

Results: The predicted probability of tibiofemoral progression was 0.153 (95% CI, 0.100 to 0.228) in high-strength knees and 0.098 (CI, 0.061 to 0.155) in low-strength knees. In malaligned knees, high strength was associated with a significant increase ($P = 0.03$) in the likelihood of progression (predicted probability, 0.406 [CI, 0.226 to 0.615] vs. 0.187 [CI, 0.081 to 0.375] in high-strength vs. low-strength knees). Strength was also associated with increased likelihood of progression in high-laxity knees ($P = 0.003$ when high laxity was defined as ≥ 6.75 degrees). The probability of patellofemoral progression did not differ between high- and low-strength knees in the full sample or within subsets.

Conclusions: Greater quadriceps strength at baseline was associated with increased likelihood of tibiofemoral osteoarthritis progression in malaligned knees and lax knees. Subset-specific approaches beyond strengthening exercises should be developed to enhance joint-protective muscle activity.

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Knee osteoarthritis is responsible for more chronic disability in elderly persons than any other medical condition (1). Quadriceps strengthening is widely recommended for knee osteoarthritis (2, 3), based on cross-sectional studies identifying strength (maximal voluntary muscle force generation) as a correlate of physical function (4–8) and on trials, predominantly short term, suggesting that quadriceps strengthening reduces pain and improves function (9, 10).

The impact of quadriceps strength on the course of osteoarthritic disease itself is not well understood. A longitudinal study has shown that, in healthy knees, strong quadriceps offer some protection against new osteoarthritis development (11). However, whether quadriceps strength protects against progression or advancement of osteoarthritis in already arthritic knees has not been demonstrated. Brandt and colleagues (12) found no difference in baseline quadriceps strength between those with and those without disease progression. The effect of quadriceps strength on osteoarthritis disease progression is particularly important given the frequency with which quadriceps strengthening exercises are prescribed for persons with knee osteoarthritis.

Muscle effects are less predictable in arthritic knees than in healthy knees. On the positive side, muscle activity promotes cartilage health and stabilizes the joint. During activity, muscles contract at different levels and protective

reflexes are applied to shield knee tissues from injury (13). Coactivation, the dual drive of agonist and antagonist muscles, provides control for the stop and start of motion as well as compensation for gravity. Implicit in the recommendation of quadriceps strengthening for knee osteoarthritis is the assumption that greater strength will enhance these positive effects. If this enhancement comes without cost, greater strength may indeed protect arthritic joints from osteoarthritis progression.

On the negative side, greater quadriceps strength may be associated with forces that could damage the vulnerable articular cartilage of osteoarthritis. The compensatory increase in muscle forces in osteoarthritis may increase the joint reaction force (14). A higher coactivation level in the agonist versus antagonist muscles can impair motion regulation and reduce ligament-protecting actions (13). The net impact of quadriceps strength on osteoarthritis progression depends on which effects—positive or negative—are greater.

Which muscle effects prevail is likely to depend on the local mechanical environment. Local factors that alter load distribution, such as laxity and malalignment, influence how well the joint copes with muscle forces. Woo and associates (15) liken this situation to a hammer (muscle) driving a nail (the joint), while a hand (ligaments and, more broadly, local environment) holds the nail in place.

Context

Experts routinely recommend that adults with knee osteoarthritis strengthen leg muscles.

Contribution

This 18-month cohort study of 237 adults with primary knee osteoarthritis found that greater baseline quadriceps strength was associated with greater risk for progressive tibiofemoral joint space narrowing among adults with malaligned or very lax knees.

Implications

Maximization of quadriceps strength in osteoarthritic patients with malaligned or very lax knees may not be joint protective and should be studied in trials that include joint structure outcomes.

Cautions

These results do not imply that physical activity in adults with knee osteoarthritis is harmful.

—The Editors

The stabilizing hand allows greater force from the hammer. In other words, a healthy environment contributes to safe muscle force distribution over the menisci, articular cartilage, and other tissues. However, with laxity or malalignment, muscle forces may increase stress on localized areas of cartilage. Similarly, Marks and colleagues (16) theorized that local joint abnormalities can render muscle forces pathogenic.

Malalignment and laxity are key local abnormalities. Any shift from a neutral hip–knee–ankle alignment alters load distribution; varus and valgus alignments increase medial and lateral compartment forces, respectively (17). Alignment influences the outcome of most knee surgeries, as well as natural disease progression and functional decline in osteoarthritis (18). Knee laxity—abnormal displacement of the tibia with respect to the femur (19)—shifts opposing surfaces of tibiofemoral contact so that congruence is reduced and increases shear and compression forces. Varus–valgus laxity has been linked to greater likelihood of osteoarthritis after ligament injury (20, 21). In other studies, laxity was present in patients with osteoarthritis before full-blown disease and was worsened by aspects of disease (22), was associated with worse function, and altered the strength–function relationship (23).

If greater quadriceps strength improves the load imbalance created by malalignment or attenuated load in malaligned knees, it might protect against osteoarthritis progression in patients with maligned knees. Alternatively, malalignment may alter the line of action of quadriceps forces, distributing them inequitably across the joint surface (16); in this case, strength might increase the likelihood of osteoarthritis progression. In the lax knee, strength might be protective if greater quadriceps strength enhances

dynamic stabilization. However, if the cost of this compensation—that is, greater joint reaction force—exceeds the stabilization benefit, the likelihood of osteoarthritis progression might increase. Our objective was to determine whether greater quadriceps strength was associated with greater probability of tibiofemoral osteoarthritis progression among all knees in persons with osteoarthritis and in two subsets, malaligned knees and high-laxity knees.

METHODS**Participants**

Mechanical Factors in Arthritis of the Knee (MAK) is a natural history study of knee osteoarthritis at Northwestern University in Chicago, Illinois. Participants in MAK were recruited through periodicals targeting senior citizens, 67 neighborhood organizations, the registry of the Northwestern University Buehler Center on Aging, and medical center referrals. Inclusion and exclusion criteria were based on those developed for osteoarthritis progression studies at a workshop sponsored by the National Institute of Arthritis and Musculoskeletal and Skin Diseases and the National Institute on Aging (24). Inclusion criteria were definite osteophyte presence (Kellgren and Lawrence radiographic grade ≥ 2) in one or both knees and at least a little difficulty (Likert category) with at least two items in the Western Ontario and McMaster University osteoarthritis index physical function scale. Exclusion criteria were corticosteroid injection within 3 months, avascular necrosis, rheumatoid or other inflammatory arthritis, periarticular fracture, Paget disease, villonodular synovitis, joint infection, ochronosis, neuropathic arthropathy, acromegaly, hemochromatosis, Wilson disease, osteochondromatosis, gout, pseudogout, osteopetrosis, bilateral total knee replacement, or plan for knee replacement within the next year. Persons with past unilateral knee replacement were eligible if they had osteoarthritis in the nonreplaced knee. The institutional review board of Northwestern University approved the study, and all participants gave informed consent.

Measurement of Key Factors

All measurements were obtained in both knees. Isokinetic quadriceps strength was tested by using a computer-driven isokinetic dynamometer (Cybex, Avocent, Huntsville, Alabama) to assess maximal torque during movement. One tester assessed all participants by following a previously described protocol (23). The computer recorded data in foot-pounds (ft-lbs) and corrected for gravity effects. Reliability, determined by using test repetitions, was high (intra-class correlation coefficients > 0.98) (23).

To assess alignment, a single anteroposterior radiograph of both lower extremities was obtained by using a graduated grid cassette (51 \times 14 inches), adhering to a protocol we have described elsewhere (18). Alignment was defined as the measure of the angle formed by the intersection of the line connecting the centers of the femoral

head and intercondylar notch and the line connecting the centers of the ankle talus and tibial spines (17, 25, 26). Knees were considered “more neutral” if the angle was less than 5 degrees in a varus or valgus direction and “malaligned” if the angle was 5 degrees or more. One experienced reader made all measurements. Reliability, based on a set of radiographs from patients with osteoarthritis (18), was high for varus and valgus alignment (intraclass correlation coefficients, 0.99 and 0.98, respectively).

Varus–valgus laxity was measured with a device designed for the MAK study by Dr. Thomas Buchanan (22, 23). The measurement protocol has been described elsewhere (22, 23). Angular deviation was measured at the foot with application of varus or valgus load. Varus–valgus laxity was analyzed as the sum of varus and valgus rotation for each knee (27–29). Because a definition of high and low laxity is not available, knees in the highest laxity tertile (≥ 5.75 degrees) were designated as high laxity. Laxity measurements were performed by the same examiner and assistant, and reliability was very good in participants with osteoarthritis (within-session intraclass correlation coefficients, 0.85 to 0.96; between-sessions intraclass correlation coefficients, 0.84 to 0.90) (22).

Measurement of Outcome

Knee radiographs were obtained at baseline and at 18 months, following the semi-flexed, fluoroscopically confirmed protocol developed by Buckland-Wright (24, 30, 31). Knee position, beam alignment, markers to account for magnification, and measurement landmarks were specified. The standing semi-flexed position superimposes anterior and posterior medial tibial margins. Knee position was confirmed fluoroscopically before anteroposterior radiographs were taken. To visualize the patellofemoral compartment, weight-bearing, 30-degree flexion, skyline views were obtained (30). Radiographs were obtained in one unit by two trained technicians. Foot maps made at baseline were used at the 18-month evaluation.

We used a consistent approach to define osteoarthritis progression in each compartment, relying on joint space assessment. The primary outcome, tibiofemoral osteoarthritis progression, was defined as an increase in the grade of joint space narrowing in the medial or lateral compartment between baseline and 18 months. Patellofemoral osteoarthritis progression was defined as an increase in the grade of medial or lateral patellofemoral narrowing. The semi-flexed, fluoroscopically confirmed protocol provides appropriate conditions for direct measurement of medial but not lateral or patellofemoral joint space width; no protocol has yet been developed to support lateral or patellofemoral joint space measurement. One experienced reader graded each compartment separately by using the Osteoarthritis Research Society International atlas-based scales (none, possible, definite, severe) developed by Altman and colleagues (32). Intrareader reliability was good ($\kappa = 0.80$ to 0.86) (18).

Measurement of Potential Confounders

Body mass index (BMI) was measured as weight in kilograms divided by the square of the height in meters. Disease severity was assessed by using the Kellgren and Lawrence global scale (0 = normal; 1 = possible osteophytes; 2 = definite osteophytes, possible joint space narrowing; 3 = moderate or multiple osteophytes, definite narrowing, some sclerosis, possible attrition; 4 = large osteophytes, marked narrowing, severe sclerosis, definite attrition). Physical activity was assessed by using the Physical Activity Scale for the Elderly (PASE) (33).

Statistical Analysis

Participants with advanced osteoarthritis (the most severe grade of joint space narrowing at baseline in any compartment of either knee) were excluded from analysis. Replaced knees were excluded from analyses. We used logistic regression with generalized estimating equations (GENMOD procedure, SAS software, version 8.00, SAS Institute, Inc., Cary, North Carolina) to include data from one or both knees of each participant and thereby test the effect of high versus low strength on likelihood of osteoarthritis progression. An independent working correlation structure was used. Low strength was defined as less than or equal to the median strength of right lower limbs in the sample (47.3 ft-lb). Statistical tests on logistic regression coefficients for strength were based on robust empirical standard error estimates. Analyses were adjusted for potential confounders: age (continuous), BMI (continuous), disease severity using Kellgren and Lawrence grade (categories entered as indicator variables), and physical activity using PASE score (continuous). To illustrate the effect of high versus low strength, we presented the predicted probability of osteoarthritis progression and associated 95% CIs for a person 65 years of age who had a baseline BMI of 30 kg/m², a Kellgren and Lawrence grade of 2, and a median PASE score of 124, based on the estimated logistic model. The relationship between strength and progression was examined in subsets of more neutral, malaligned, low-laxity, and high-laxity knees. Analyses were repeated by using alternative definitions of high laxity.

Role of the Funding Sources

The funding sources had no role in the collection, analysis, and interpretation of the data or in the decision to submit the paper for publication.

RESULTS

We longitudinally followed 237 participants, of whom 7 (3%) did not return at 18 months; 5 had died, and 2 could not be reached. Of the 230 remaining participants, 171 did not have advanced osteoarthritis in any compartment of either knee. Among these 171 participants (126 women, 45 men), mean age (\pm SD) was 64.0 \pm 11.0 years and mean BMI (\pm SD) was 30.0 \pm 5.5 kg/m². At baseline, no participants had a Kellgren and Lawrence grade of 0 for

Table 1. Knees with Tibiofemoral Osteoarthritis Progression according to Baseline Alignment and Strength

Variable	Knees, <i>n</i>	Knees with Osteoarthritis Progression, %
More neutral alignment (<5 degrees)*		
Low quadriceps strength	125	11.2
High quadriceps strength	125	11.2
Malalignment (≥5 degrees)†		
Low quadriceps strength	38	26.3
High quadriceps strength	40	50.0

* 147 participants.

† 59 participants.

right knee osteoarthritis severity, 11 had a grade of 1, 110 had a grade of 2, 50 had a grade of 3, and none had a grade of 4. Sixty-three participants had no joint space narrowing in the right knee at baseline, 60 had mild narrowing, 48 had moderate narrowing, and none had severe narrowing. Mean right-limb quadriceps strength (\pm SD) was 51.8 \pm 28.5 ft-lb, and mean laxity (\pm SD) was 5.32 \pm 2.03 degrees. Right knees were varus in 79 participants, valgus in 71 participants, and neutral in 21 participants. No participants had a knee effusion. These assessments were similar in the left knees. All analyses incorporated data from both knees, using generalized estimating equations. We excluded 14 knees that had previously been replaced, leaving 328 knees for analysis.

Quadriceps strength did not reduce the likelihood of subsequent osteoarthritis progression. After adjustment for age, BMI, disease severity, and physical activity, the predicted probability of progression was slightly greater in knees with higher compared with lower quadriceps strength (0.153 [95% CI, 0.100 to 0.228] vs. 0.098 [CI, 0.061 to 0.155]; $P = 0.09$).

We determined the proportion of knees with disease progression according to baseline alignment and strength (Table 1). In more neutral knees, quadriceps strength had no effect on progression (11.2% in high- and low-strength knees). However, disease progression was substantially more likely in high-strength versus low-strength malaligned knees (50.0% vs. 26.3%). We next determined the proportion of knees with disease progression according to

Table 2. Knees with Tibiofemoral Osteoarthritis Progression according to Baseline Laxity and Strength

Variable	Knees, <i>n</i>	Knees with Osteoarthritis Progression, %
Low laxity (<5.75 degrees)*		
Low quadriceps strength	98	14.3
High quadriceps strength	120	19.2
High laxity (≥5.75 degrees)†		
Low quadriceps strength	65	15.4
High quadriceps strength	45	24.4

* 127 participants.

† 71 participants.

baseline laxity and strength (Table 2). High strength versus low strength at baseline was associated with increased progression in low-laxity (19.2% vs. 14.3%) and high-laxity (24.4% vs. 15.4%) knees.

We used logistic regression to statistically test the relationship between strength and tibiofemoral progression in the alignment (Table 3) and laxity (Tables 4 and 5) subsets. Predicted probabilities are provided to illustrate these results. There was no evidence of a protective effect of strength on progression in any knee subset. In contrast, in malaligned knees (Table 3), strength was associated with a significant increase in the likelihood of disease progression. As shown in Table 4, strength in high-laxity knees was associated with an increased likelihood of progression that approached significance. When the cutoff for high laxity was increased to at least 6.75 degrees (Table 5), the association became significant.

The predicted probability of patellofemoral progression did not differ between high- and low-strength knees, either in the full sample or within knee subsets. Knee pain during strength testing was infrequent, and adjustment for pain did not alter our results. Strength, alignment, laxity, BMI, and physical activity were also measured at 18 months. Except for laxity, which increased by 1.8 degrees, mean change in each of these factors was small. Modest correlations existed between baseline values of strength and laxity ($r = -0.29$), alignment and laxity ($r = 0.18$), and strength and physical activity ($r = 0.29$) but were not of sufficient magnitude to influence interpretation of results.

When analyses were repeated in women only, results were similar in high-laxity knees. For high versus low strength, the P value was 0.03 when high laxity was defined as at least 5.75 degrees and 0.001 when high laxity was defined as at least 6.75 degrees. Results were also similar in malaligned knees but were not statistically significant, possibly reflecting the small number of knees in this subset. Because our study included much fewer men than women, it was not feasible to confirm results in men only.

Our sample had a high average BMI. Therefore, it was important to determine whether our results persisted in nonobese participants. In participants with BMIs less than 30 kg/m² ($n = 117$), progression was more likely in high-strength malaligned knees ($P = 0.06$) and high-strength, high-laxity knees ($P = 0.03$ when high laxity was defined as ≥ 5.75 degrees; $P = 0.05$ when high laxity was defined as ≥ 6.75 degrees) than in low-strength knees.

DISCUSSION

Greater quadriceps strength at baseline did not protect against subsequent progression of knee osteoarthritis and, in malaligned knees and in lax knees, was associated with increased likelihood of tibiofemoral osteoarthritis progression. Strength was not associated with increased or decreased likelihood of osteoarthritis progression in more neutrally aligned or low-laxity knees. These results suggest

Table 3. Predicted Probability of Osteoarthritis Progression for High versus Low Strength according to Baseline Alignment

Baseline Alignment	Participants/Knees, n/n	Predicted Probability of Osteoarthritis Progression Adjusted for Age, Body Mass Index, Disease Severity, and Physical Activity*		
		High Strength	Low Strength	P Value†
More neutral (<5 degrees)	147/250	0.079 (0.045–0.136)	0.090 (0.050–0.155)	>0.2
Malaligned (≥5 degrees)	59/78	0.406 (0.226–0.615)	0.187 (0.081–0.375)	0.03

* For a knee with Kellgren and Lawrence grade 2 in a person 65 years of age with a body mass index of 30 kg/m² and a Physical Activity Scale for the Elderly score of 124. Values in parentheses are 95% CIs.

† Obtained from logistic regression testing in which the quadriceps strength effect equaled zero.

that the positive actions of the quadriceps muscle on knee function are not translated by greater strength into a beneficial change in disease course.

Our findings are consistent with those of Brandt and colleagues (12), who reported no difference in baseline quadriceps strength between persons with progressive versus nonprogressive tibiofemoral osteoarthritis over an average of 32 months. In a study of incident osteoarthritis, quadriceps strength protected against new knee osteoarthritis in women (11). In contrast to these findings for the knee, Chaisson and colleagues (34) found that grip strength was associated with an increased risk for incident osteoarthritis at the metacarpophalangeal joints in women and the proximal interphalangeal joints, metacarpophalangeal joints, and thumb base in men.

Together, the studies of Brandt and colleagues (11, 12) and Chaisson and colleagues (34) show that the effect of strength may differ between joint sites and according to baseline joint status, that is, whether the joint is relatively healthy (as in studies of incident osteoarthritis) or arthritic (as in studies of osteoarthritis progression). Our results demonstrate that the relationship between strength and progression can differ within a joint site according to attributes of the local environment. Muscle forces that are beneficial in the nondiseased knee may have adverse effects in the more vulnerable osteoarthritic knee that neutralize the benefits of strength or, in some knee subsets, have a net negative effect.

In knees with low laxity or more neutral alignment, strength was not associated with an increased or decreased likelihood of progression, suggesting a balance between positive and negative consequences of strength. Our findings in malaligned knees support Marks and colleagues' theory (16) that such knees are less able to evenly distribute

muscle forces. In high-laxity knees, our findings support that muscle-related dynamic stabilization increases the joint reaction force (14). In terms of the natural history of osteoarthritis, our results indicate that strength does not mechanically compensate for the ill effects of malalignment or laxity on disease outcome.

We examined the relationship between strength at baseline and change in osteoarthritic disease over an 18-month period. The only other longitudinal report of the strength–progression relationship also examined strength at baseline (12). A next step, more feasible within a strengthening intervention trial, would be to examine the effect of an increase in strength on subsequent disease progression. This was not possible in our study because strength was examined at baseline and progression, between baseline and 18 months. It is difficult, however, to believe that a strength increase could delay disease progression in malaligned or lax knees when greater baseline strength was associated with a worse outcome.

Limitations of our study include the fact that our sample was not population based. However, participants were recruited from a variety of community sources as well as a medical center and are likely to be comparable to persons in the general population who receive widespread recommendations on quadriceps strengthening from providers and the lay literature. To date, laxity and full-limb alignment have not been described in population-based studies of knee osteoarthritis. It is unclear what constitutes high versus low quadriceps strength in persons with established mild to moderate knee osteoarthritis; in this report, we applied the sample median. Analyses using alternative definitions of high strength yielded similar results. The sex distribution of our sample allowed us to confirm findings separately in women, but not in men.

Table 4. Predicted Probability of Osteoarthritis Progression for High versus Low Strength according to Laxity at Baseline

Laxity at Baseline	Participants/Knees, n/n	Predicted Probability of Osteoarthritis Progression Adjusted for Age, Body Mass Index, Disease Severity, and Physical Activity*		
		High Strength	Low Strength	P Value†
Low laxity (<5.75 degrees)	127/218	0.124 (0.068–0.218)	0.103 (0.057–0.179)	>0.2
High laxity (≥5.75 degrees)	71/110	0.178 (0.078–0.357)	0.074 (0.032–0.164)	0.05

* For a knee with Kellgren and Lawrence grade 2 in a person 65 years of age with a body mass index of 30 kg/m² and Physical Activity Scale for the Elderly score of 124. Values in parentheses are 95% CIs.

† Obtained from logistic regression testing in which the quadriceps strength effect equaled zero.

Table 5. Predicted Probabilities of Osteoarthritis Progression for High versus Low Strength for High-Laxity Knees with Alternative Definitions of High Laxity

Definition of High Laxity at Baseline	Participants/Knees, n/n	Predicted Probability of Osteoarthritis Progression Adjusted for Age, Body Mass Index, Disease Severity, and Physical Activity*		
		High Strength	Low Strength	P Value†
≥4.75 degrees	104/168	0.158 (0.086–0.273)	0.099 (0.052–0.181)	0.16
≥5.75 degrees	71/110	0.178 (0.078–0.357)	0.074 (0.032–0.179)	0.05
≥6.25 degrees	60/91	0.176 (0.065–0.395)	0.069 (0.024–0.181)	0.09
≥6.75 degrees	49/70	0.307 (0.101–0.637)	0.041 (0.009–0.168)	0.003

* For a knee with Kellgren and Lawrence grade 2 in a person 65 years of age with a body mass index of 30 kg/m² and a Physical Activity Scale for the Elderly score of 124. Values in parentheses are 95% CIs.

† Obtained from logistic regression testing in which the quadriceps strength effect equaled zero.

Strengthening exercise is recommended to reduce pain and improve physical function in knee osteoarthritis, but there is minimal information on its long-term impact (3). Numerous short-term trials demonstrate benefits of exercise; however, when restricted to strengthening exercise exclusively, effect sizes were small (9, 10). In another trial with 18-month follow-up, Ettinger and colleagues found that strengthening exercise led to modest improvement in function (35). There are several possible reasons for a smaller than expected effect in short- and long-term studies. Strength may be less important than aerobic capacity or psychosocial factors in long-term function. Osteoarthritis-associated impairments, such as laxity, may limit the impact of strength on function. Also, strength may have a negative effect on osteoarthritis disease course in certain knee subsets, which ultimately reduces its beneficial effect on function.

Our results raise questions about the use of quadriceps strengthening. First, they question the assumption that greater strength enhances muscle activity in a way that benefits disease course or causes no harm in all patients with osteoarthritis. Second, our results suggest that strength maximization is not likely to have a beneficial disease-modifying effect in persons with osteoarthritis and malaligned or lax knees. Third, the relationship between strength and osteoarthritis progression hinges on local environment and may not be reducible to a simple tenet or strengthening prescription. Fourth, concomitantly dealing with the negative effects of muscle forces may make strengthening exercise more effective as a strategy to prevent disability. Our results have implications for quadriceps strengthening in knee osteoarthritis but not for other forms of exercise or physical activity.

Because trends in osteoarthritis management favor generic, minimally supervised exercise, our findings are timely. The availability of resistance exercise equipment in fitness clubs creates opportunities for additional unsupervised strengthening exercise and contributes to assumptions that such exercise is without risk and that “more” must be better. These assumptions may lead to knee exercises performed under high load. In the future, clinical trials that include a strengthening intervention should ex-

amine the impact of a strength increase on joint structure within alignment and laxity subsets. Strength maintenance programs tailored to knee subsets should be developed.

Muscle-enhancing interventions, rather than exercises focused solely on strengthening, should also be further developed. Such interventions might directly target specific joint-protective muscle actions while safely maintaining strength, possibly through supervised, balanced agonist–antagonist (quadriceps–hamstring) exercise; exercise that targets separate components of the quadriceps; exercises that improve muscle endurance; gait training; exercise that enhances quadriceps action during common tasks; and exercise that improves proprioceptive accuracy. Future studies should also develop approaches coupling muscle enhancement with other interventions that improve load distribution and stabilize the knee. Such approaches may better capitalize on the beneficial effects of strong muscles while neutralizing the deleterious effects of muscle forces, thereby delaying osteoarthritis progression. In our study, greater quadriceps strength at baseline was associated with increased likelihood of tibiofemoral osteoarthritis progression in malaligned knees and in lax knees. These results support the need to develop subset-specific approaches to enhance joint-protective muscle activity.

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