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Quadriceps Strength and the Risk of Cartilage Loss and Symptom Progression in Knee Osteoarthritis

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Abstract

Objective—To determine the effect of quadriceps strength in individuals with knee osteoarthritis (OA) on loss of cartilage at the tibiofemoral and patellofemoral joints (assessed by magnetic resonance imaging [MRI]) and on knee pain and function.

Methods—We studied 265 subjects (154 men and 111 women, mean ± SD age 67 ± 9 years) who met the American College of Rheumatology criteria for symptomatic knee OA and who were participating in a prospective, 30-month natural history study of knee OA. Quadriceps strength was measured at baseline, isokinetically, during concentric knee extension. MRI of the knee at baseline and at 15 and 30 months was used to assess cartilage loss at the tibiofemoral and patellofemoral joints, with medial and lateral compartments assessed separately. At baseline and at followup visits, knee pain was assessed using a visual analog scale, and physical function was assessed using the Western Ontario and McMaster Universities Osteoarthritis Index.

Results—There was no association between quadriceps strength and cartilage loss at the tibiofemoral joint. Results were similar in malaligned knees. However, greater quadriceps strength was protective against cartilage loss at the lateral compartment of the patellofemoral joint (for highest versus lowest tertile of strength, odds ratio 0.4 [95% confidence interval 0.2, 0.9]). Those with greater quadriceps strength had less knee pain and better physical function over followup ($P < 0.001$).

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AUTHOR CONTRIBUTIONS

Dr. Amin 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. Amin, Baker, Felson.

Acquisition of data. Clancy, Goggins, Guermazi, Grigoryan, Hunter, Felson.

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ROLE OF THE STUDY SPONSOR

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Conclusion—Greater quadriceps strength had no influence on cartilage loss at the tibiofemoral joint, including in malaligned knees. We report for the first time that greater quadriceps strength protected against cartilage loss at the lateral compartment of the patellofemoral joint, a finding that requires confirmation. Subjects with greater quadriceps strength also had less knee pain and better physical function over followup.

The influence of quadriceps strength on knee osteoarthritis (OA), one of the leading causes of disability among elderly persons (1), is unclear. In individuals with knee OA, decreased quadriceps strength is frequently observed (2–8) and has been associated in cross-sectional studies with both greater knee pain and impaired physical function (3,5,9). However, reports from longitudinal studies examining the effect of quadriceps strength on structural progression of knee OA have been conflicting (10–12). Decreased quadriceps strength was associated with increased incident radiographic knee OA in women, but not in men (10). In contrast, among women with established knee OA, quadriceps strength did not affect the risk of radiographic progression (11). Another study suggested that while quadriceps strength was not associated with radiographic progression in most persons, in those with malaligned or lax knees greater quadriceps strength was associated with accelerated radiographic progression (12).

Most studies have evaluated the effect of quadriceps strength on the tibiofemoral joint of the knee. The quadriceps muscle also has important biomechanical effects at the patellofemoral joint (13,14), a site of frequent cartilage loss (15) in addition to pain and disability among persons with knee OA (16,17), yet few studies have examined this knee compartment specifically. Weakness of the vastus medialis obliquus component of the quadriceps muscle has been reported to contribute to lateral subluxation or partial dislocation of the patella (13,14). While a cross-sectional study demonstrated an association between decreased quadriceps strength and lateral patellofemoral radiographic joint space narrowing (18), a longitudinal study revealed no association (12).

Studies to date have focused on the association between quadriceps strength and radiographic progression of joint space narrowing, which is an indirect measure of cartilage loss. Joint space narrowing at the tibiofemoral joint can be caused by meniscal extrusion, not necessarily by cartilage loss (19). Furthermore, radiography is insensitive to loss of cartilage (20); therefore, an effect on cartilage may actually be missed in radiographic studies. In contrast, studies using magnetic resonance imaging (MRI) evaluate loss of cartilage directly. In addition, assessment of quadriceps strength in knee OA necessitates an evaluation of pain and function, the clinically important features of the disease. To our knowledge, the relationship of quadriceps strength to cartilage loss in the knee has not previously been investigated longitudinally with both MRI studies and assessments of knee pain and physical function.

In the present study, we examined how greater quadriceps strength affects loss of cartilage at both the tibiofemoral and patellofemoral joints of the knee, assessed using MRI, as well as how it affects knee pain and physical function, among men and women with established symptomatic knee OA followed up longitudinally. We also explored how knee alignment influences these results.

PATIENTS AND METHODS

Study participants

Study participants were enrolled in a 30-month natural history study of symptomatic knee OA (Boston Osteoarthritis of the Knee Study); their recruitment has been described in detail previously (21,22). Briefly, potential participants had to have answered yes to the following

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2 questions: "Do you have pain, aching or stiffness in one or both knees on most days?" and "Has a doctor ever told you that you have knee arthritis?" A subsequent interview was conducted to exclude other forms of arthritis. All eligible participants had to have an osteophyte seen on radiographs (posteroanterior [PA] weight-bearing, lateral, or skyline views, as previously described [21]) of the more symptomatic knee, be able to walk with or without the aid of a cane, and be willing to participate in the longitudinal study. There were 324 subjects (201 men and 123 women, mean ± SD age 67 ± 9 years) who met the eligibility criteria. All participants met the American College of Rheumatology criteria for symptomatic knee OA (23).

Study overview

Examinations were conducted at baseline and at 15 and 30 months and included knee imaging studies and questionnaires. Subjects were weighed with their shoes off on a balance beam scale, and their height was measured. The Institutional Review Boards of Boston University Medical Center and the Veterans Administration Boston Healthcare System approved the protocol for the baseline and followup evaluations.

Knee MRI protocols

Participants without contraindications underwent MRI of the more symptomatic knee, and this knee was imaged again after 15 and 30 months of followup. MRIs were acquired on a General Electric Signa 1.5-Tesla MRI system (GE Medical Systems, Milwaukee, WI) using a phased-array knee coil. An anchoring device for the ankle and knee was used to ensure uniformity of positioning between patients and for followup. The imaging protocol included sagittal spin-echo, proton-density and T2-weighted images as well as coronal and axial fat-suppressed spin-echo, protondensity and T2-weighted images (repetition time 2200 msec, time to echo 20/80 msec, slice thickness 3 mm, interslice gap 1 mm, 1 excitation, field of view 11–12 cm, matrix 256 × 192 pixels).

Cartilage morphology scoring and assessment of cartilage loss

Cartilage morphology at the tibiofemoral and patellofemoral joints was determined using the Whole-Organ Magnetic Resonance Imaging Score (WORMS) semiquantitative method for assessment of knee OA (24). All MRIs were scored by a total of 3 trained readers who were blinded with regard to quadriceps strength. The majority of subjects (86%) with longitudinal MRIs had them read by both a musculoskeletal radiologist and a musculoskeletal researcher, both from the Osteoporosis and Arthritis Research Group of the University of California, San Francisco, reading each MRI together (20).

Cartilage morphology was scored in all 5 regions of each compartment (medial and lateral) of the tibiofemoral joint (central femur, posterior femur, anterior tibia, central tibia, posterior tibia) (Figure 1). Cartilage morphology of the patellofemoral joint was scored at both surfaces, the patella and anterior femur, for each of the medial and lateral compartments (Figure 1). A scale of 0–6 was used for scoring of cartilage morphology, as follows: 0 = normal thickness and signal; 1 = normal thickness but increased signal on T2-weighted images; 2 = solitary focal defect of <1 cm in greatest width; 3 = areas of partial-thickness defects (<75% of the region) with areas of preserved thickness; 4 = diffuse partialthickness loss of cartilage (≥75% of the region); 5 = areas of full-thickness loss (<75% of the region) with areas of partial-thickness loss; 6 = diffuse full-thickness loss (≥75% of the region) (24). The intraclass correlation coefficient for agreement of cartilage readings ranged from 0.72 to 0.97 for readers (20).

As previously reported, we collapsed the 0–6 scores to 0–4 for analyses (20). The original WORMS scores of 0 and 1 were collapsed to 0, the original scores of 2 and 3 were collapsed to 1, and the original scores of 4, 5, and 6 were considered 2, 3, and 4, respectively, in the new scale. This was done because grades of 1 and 2 were infrequent among the MRIs read in our study population, and grade 1 represents a change in signal in cartilage of otherwise normal morphology, while grades 2 and 3 represent similar types of morphologic abnormalities. Using this new scale, cartilage loss over followup at each region was defined as an increase in cartilage morphology score from baseline to followup, which could range from 0 (no loss) to 4 (maximal loss).

Quadriceps strength measurement

Using a Cybex (Medway, MA) isokinetic dynamometer, baseline quadriceps strength for each leg was measured isokinetically during concentric knee extension at 60°/second. All testing was performed in the morning. Subjects were tested in a seated position with support for the back and stabilizing straps at the level of the chest, pelvis, and thigh. The hip was flexed at 80°. The tibia was strapped to the lever arm, and its axis of rotation was aligned with the anatomic axis of the knee joint. Each subject was allowed 4 practice repetitions, and then the maximal strength (peak torque, in Nm) of 3 repetitions was used. We excluded participants with sufficient knee pain that precluded testing or led to low outlier values. We expressed quadriceps strength relative to body weight (Nm/kg) by dividing the peak torque (Nm) by the participant's body weight (mass) (kg) (10,25).

Measurement of alignment at the knee

Alignment at the knee was assessed from long-limb films, which were obtained at the first followup examination with a 14 × 51–inch cassette, using methods previously described (26). Knee alignment was measured from the femoral mechanical axis (the line extended from the femoral head through the center of the knee), where it intersects with the tibial mechanical axis (the line from the center of the ankle to the center of the knee) (varus alignment >0°; valgus alignment <0°).

Knee pain and physical function

At baseline and followup, participants rated the severity of pain in each knee during the past week, which they scored using a 100-mm visual analog scale (VAS) (from 0 [no pain] to 100 [most severe pain possible]). Physical function (Western Ontario and McMaster Universities Osteoarthritis Index [WOMAC] physical function subscale) was assessed using a Likert scale (0–68, with higher scores indicating worse physical function) (27).

Statistical analysis

Statistical analyses were performed using SAS software, release 8.2 (SAS Institute, Cary, NC).

Quadriceps strength and cartilage loss—We created tertiles of quadriceps strength for men and women separately, based on their baseline quadriceps strength relative to body weight (in Nm/kg), of the knee imaged by MRI over followup. We examined the relationship between quadriceps strength and cartilage loss at the medial and lateral compartments separately for each of the tibiofemoral and patellofemoral joints. We used 30-month data unless these were unavailable, in which case we used 15-month data. Cartilage loss was expressed in whole numbers from 0 (no loss) to 4 (maximum loss) and was analyzed as ordered categories using a proportional odds logistic regression model (with a generalized estimating equation correction to account for the association of cartilage loss between regions within a knee compartment) and adjusted for baseline cartilage scores, age, body mass index (BMI), sex, and duration of followup.

Regression models were additionally adjusted for quartiles of alignment. To further explore the effects of more varus alignment (which increases loading at the medial compartment) on cartilage loss at the medial tibiofemoral compartment, we stratified results by ≥5° versus <5° varus alignment, corresponding to the level of malalignment previously reported to be associated with increased radiographic progression with greater quadriceps strength (12). We included alignment as a continuous variable in analyses to ensure that malalignment within these strata was not confounding results. We were unable to evaluate the effect of ≤ −5° of (valgus) malalignment (which increases loading at the lateral compartment) on cartilage loss at the lateral tibiofemoral compartment, since too few knees in the cohort (6%) had this degree of malalignment. The study had 80% power (at $\alpha = 0.05$, 2-sided) to detect a 5.5–10.2% difference in progression rates between those in high and those in low tertiles of quadriceps strength.

Quadriceps strength, knee pain, and physical function—To examine the association between quadriceps strength and knee symptoms, we used the knee-specific VAS pain score for the knee that underwent MRI during followup, as well as the WOMAC physical function subscale score. We used 30-month data unless these were unavailable, in which case we used 15-month data. In a linear regression analysis, we examined the difference in change in scores (defined using the longest available followup) among the sex-specific tertiles of quadriceps strength, adjusted for baseline cartilage scores, age, BMI, sex, and duration of followup. We also examined differences among tertiles of quadriceps strength in mean VAS knee pain and WOMAC physical function subscale scores at baseline as well as at followup, following similar adjustment. We additionally explored the effect of alignment on cartilage loss.

RESULTS

There were 317 participants who had no contraindications to baseline knee MRI, and 277 (87%) underwent followup knee MRI at 15 months, 30 months, or both. There were no differences between those who were and those who were not followed up with respect to age (mean ± SD 66 ± 9 years versus 66 ± 10 years, respectively), baseline BMI (mean ± SD 30.8 ± 5.7 kg/m^2 versus 29.1 ± 5.6 kg/m^2, respectively), Kellgren/ Lawrence (K/L) grade (28) (54% versus 55%, respectively, with K/L grade >2), or quadriceps strength (mean ± SD 0.78 ± 0.33 Nm/kg versus 0.79 ± 0.31 Nm/kg, respectively), but the group not followed up included a higher proportion of men (83% of those not followed up versus 59% of those followed up; $P < 0.01$). We excluded 12 subjects from analyses; 9 of these subjects had no measure of quadriceps strength (see Patients and Methods), and 3 of these subjects had MRIs that were unreadable for cartilage loss. Thus, the final study population included 265 participants.

Of the 265 participants who were included in analyses (154 men and 111 women) (Table 1), alignment data were available for 219 (83%). Characteristics of participants by sex-specific tertile of quadriceps strength are listed in Table 2. (Because the K/L grade is scored based on PA radiograph views only, participants in our study with K/L grades of <2 represent those with OA involving the patellofemoral joint.) Overall, 30-month data were available for 222 subjects (84%), and 15-month data were available for the remainder, and the proportions with 30-month and 15-month followup were similar among the tertiles of quadriceps strength.

Cartilage loss at the tibiofemoral joint

There were 118 knees (45%) with loss of cartilage at ≥1 of the 5 regions in the medial tibiofemoral compartment. Quadriceps strength did not influence the likelihood of cartilage loss over followup in the medial compartment, in either crude or adjusted analyses (Table 3). Results were consistent between men and women (data not shown). Further adjustment for quartile of alignment did not change the results: for middle strength, odds ratio (OR) 0.7 (95% confidence interval [95% CI] 0.4, 1.3); for high strength, OR 0.9 (95% CI 0.5, 1.7). When we stratified results by ≥5° varus alignment versus <5° alignment, we still observed no association (Table 4).

There were 58 knees (22%) with loss of cartilage at ≥1 region in the lateral tibiofemoral compartment. There was no association between quadriceps strength and cartilage loss in this compartment (Table 3). Adjustment for quartiles of alignment did not change the results (for middle strength, OR 1.3 [95% CI 0.6, 2.7]; for high strength, OR 1.1 [95% CI 0.5, 2.5]). There were very few participants with cartilage loss in this compartment among those with ≥5° varus alignment or even valgus malalignment, which limited our ability to evaluate the possibility of differential effects of strength by alignment within this compartment.

Cartilage loss at the patellofemoral joint

There were 58 knees (22%) with loss of cartilage at either region (patella or anterior femur) in the medial compartment of the patellofemoral joint. We found no association between quadriceps strength and cartilage loss (Table 3), and additional adjustment for quartile of alignment did not change the results (for middle strength, OR 0.9 [95% CI 0.5, 1.8]; for high strength, OR 0.8 [95% CI 0.4, 1.6]). Results were similar when stratified by alignment (Table 4).

There were 50 knees (19%) with loss of cartilage at either region in the lateral compartment of the patellofemoral joint. The proportion of regions within this compartment showing loss of cartilage over followup was less when quadriceps strength was high (Table 3). Further adjustment for quartile of alignment did not change the results (for middle strength, OR 0.5 [95% CI 0.2, 1.1]; for high strength, OR 0.4 [95% CI 0.2, 0.9]). Findings appeared similar when stratified by alignment, although power was limited (Table 4).

Results for the medial and lateral compartments of the patellofemoral joint were also consistent for men and women (data not shown).

Knee pain and physical function findings

Although the change in either knee pain or physical function over followup did not differ significantly by quadriceps strength, participants in the highest tertile of quadriceps strength had significantly less knee pain and better physical function (even following adjustment for confounders) at baseline compared with participants in the lowest tertile of quadriceps strength (Table 5), and these findings persisted at followup (Table 5). Results were similar upon stratification for alignment, although greater quadriceps strength conferred a slightly more favorable effect on pain and physical function among those with <5° of alignment than among those with ≥5° varus alignment (data not shown).

All findings and conclusions regarding cartilage loss and knee symptoms were the same in separate yet identical analyses in which sex-specific tertiles of quadriceps strength (in Nm; not normalized to body weight) were used.

DISCUSSION

Among 265 men and women with symptomatic knee OA, we found that for most compartments of the knee, greater quadriceps strength had no effect on cartilage loss, including in knees with varus malalignment. Interestingly, we found that stronger quadriceps protected against cartilage loss at the lateral compartment of the patellofemoral joint, a finding that needs confirmation. We also found that those with the greatest quadriceps strength had persistently less knee pain and better physical function than those with the least strength, throughout followup.

Skeletal muscles provide shock absorption and distribute load across joints (29). Impaired neuromuscular protective mechanisms from weak quadriceps muscles may lead to failure in dissipating potentially harmful loads during heel-strike (30), thereby initiating or worsening joint damage. Nevertheless, we found no protective effect of greater quadriceps strength on cartilage loss at the load-bearing tibiofemoral joint. Our findings are consistent with those of previous studies showing no overall effect of greater quadriceps strength at the tibiofemoral joint (11,12). While malalignment at the knee is an important risk factor for progression of knee OA (31), we were unable to confirm the finding of greater quadriceps strength increasing the risk of tibiofemoral cartilage loss in malaligned knees (12). Our study was MRI based, so we were able to assess cartilage loss directly. It is not clear whether the lack of weight-bearing imaging by MRI can account for differences. Similar to other studies (11,12), our study was observational; therefore, differences in level and type of physical activity or self-directed exercise programs among those with greater quadriceps strength could have contributed to differences in findings among studies. Similarly, our inability to identify a protective effect of greater quadriceps strength on cartilage at the tibiofemoral joint may be due to an avoidance of injurious activities by those with weaker quadriceps, who, as we have noted, also tend to be less physically active.

We did find a protective effect of greater quadriceps strength on the lateral compartment of the patellofemoral joint, which is a novel observation. As part of 1 of the 4 quadriceps muscles, the vastus medialis obliquus pulls the patella medially in the femoral trochlea (13,14). Weakness of the vastus medialis obliquus predisposes to lateral subluxation or partial dislocation of the patella (13,14). A stronger quadriceps may represent, in part, a stronger vastus medialis obliquus, preventing excessive lateral excursion of the patella and thereby preventing excess cartilage loss in this compartment. It may also be a reason that less severe knee pain and better physical function were noted among our study participants in the highest tertile of quadriceps strength, but this requires further investigation. Our findings, which include an association of greater quadriceps strength with less knee pain and physical limitation over followup, suggest that greater quadriceps strength has an overall beneficial effect on symptomatic knee OA.

Our study has limitations. While OA in the community is more common among women, we had more men than women in our study since participants were recruited largely from the Veterans Administration. Although this was a relatively large longitudinal MRI study of knee OA, we still had only a modest number of participants to permit analyses of all potential confounders. Residual confounding by age and BMI remains a possibility. We do not have a measure of knee laxity. We were unable to evaluate the possibility of an interaction between quadriceps strength and activity level. Alignment data were available for most, but not all, study participants. We had too few individuals with valgus malalignment to explore its relationship to quadriceps strength and cartilage loss at the lateral tibiofemoral compartment. While we have information on analgesic use, it was still too limited to adequately assess its influence on our findings regarding knee symptoms. We did observe, however, that the proportion of participants reporting analgesic use, regardless of the indication, was similar across quadriceps strength groups (data not shown).

Finally, it is important to note that the focus of this study was quadriceps strength, and not strengthening or exercise. While our findings suggest that maintaining strong quadriceps is of benefit to those with knee OA, further work is needed to determine the type and frequency of exercise regimen that will be both safe and effective.

Although there have been several short-term exercise trials that have shown improved quadriceps strength and beneficial effects on knee pain and function (18,32–35), consistent with our observations, most were of limited duration, which precluded an assessment of cartilage loss. One 18-month trial of low-intensity aerobic and resistive training in knee OA demonstrated that both types of exercise regimens resulted in an improvement in symptoms and physical function over followup compared with the control group; however, no differences were seen among groups in radiographic scores (36). Interestingly, knee flexion strength was better in both exercise groups relative to controls, but knee extension strength was similar at followup in all 3 groups. A more recent trial of quadriceps strengthening exercise failed to demonstrate a protective effect on progression of joint space narrowing (37); however, not only was it a radiographic study, but the exercise intervention also failed to produce an improvement in quadriceps strength. Ideally, clinical trials designed to study the influence of quadriceps strengthening exercises on progression of symptomatic knee OA would include MRI for longitudinal assessment of cartilage loss, both at the tibiofemoral and patellofemoral joints, as well as an assessment of the degree to which quadriceps strength is improved by the exercise intervention.

In summary, in men and women with symptomatic knee OA, we found no association between quadriceps strength and cartilage loss at the tibiofemoral joint, including in malaligned knees. However, greater quadriceps strength, which may prevent lateral offset and tilt of the patella, protected against cartilage loss at the lateral compartment of the patellofemoral joint, a frequent site of symptom generation in knee OA. Subjects with greater quadriceps strength were also more likely to have less knee pain and better physical function. Our results suggest that strong quadriceps muscles have an overall beneficial effect on knee OA.

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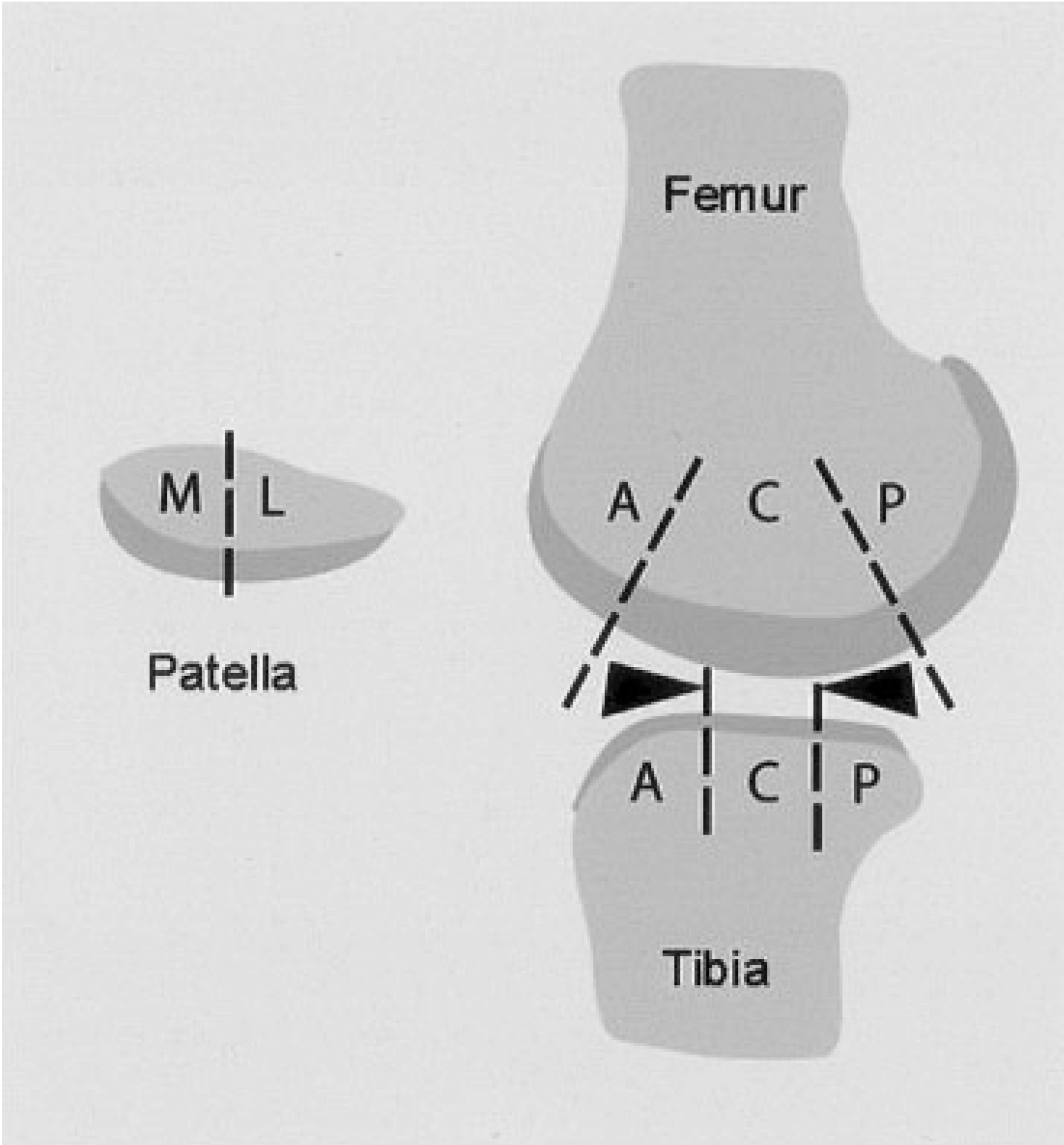

Figure 1.
Diagram of the knee (sagittal view) and patella illustrating the 5 cartilage plates of the tibiofemoral joint (central femur, posterior femur, anterior tibia, central tibia, posterior tibia) and 4 plates of the patellofemoral joint (medial and lateral patella and anterior femur). M = medial; L = lateral; A = anterior; C = central; P = posterior. Reproduced, with permission, from ref. 38.

Table 1

Baseline characteristics of the 265 men and women with symptomatic knee osteoarthritis*

	All (n = 265)	**Men (n = 154)†**	**Women (n = 111)†**
Age, years	67 ± 9	68 ±9	64 ±9
BMI, kg/m^2	31.5 ± 5.8	31.0 ± 4.7	32.2 ± 7.0
K/L grade ≥2, %	77	70	87
Maximal cartilage morphology scores ≥1 at any region, %‡§			
Tibiofemoral joint			
Medial compartment	83	82	86
Lateral compartment	61	56	69
Patellofemoral joint			
Medial compartment	85	81	91
Lateral compartment	75	68	84
Quadriceps strength, Nm	67.2 ± 29.5	78.8 ± 30.2	51.1 ± 19.3
Quadriceps strength relative to body weight, Nm/kg	0.78 ± 0.33	0.88 ± 0.34	0.64 ± 0.24
Knee alignment, degrees¶	3.7 ± 5.7	5.0 ± 5.8	2.0 ± 5.3
Knee alignment ≥5° varus, %¶	40	48	29
VAS pain score, 0–100 mm	43.7 ± 25.1	45.2 ± 26.0	41.6 ± 23.9
WOMAC physical function subscale score, 0–68	23.8 ± 11.5	24.5 ± 11.4	22.7 ± 11.7

*Except where indicated otherwise, values are the mean ± SD. BMI = body mass index; K/L = Kellgren/Lawrence; VAS = visual analog scale; WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index.

†Fifty-eight percent of subjects were men and 42% of subjects were women.

‡Baseline maximal cartilage morphology score at ≥1 of the 5 regions within a compartment.

§Equivalent to cartilage morphology score of ≥2 (on a 0–6 scale) determined using the original Whole-Organ Magnetic Resonance Imaging Score.

¶Values above 0° indicate a more varus alignment (which increases loading at the medial compartment of the knee), while values below 0° indicate a more valgus alignment (which increases loading at the lateral compartment of the knee). Alignment data were available for 219 of the 265 participants (83%).

Table 2

Baseline characteristics of the 265 men and women with symptomatic knee osteoarthritis by sex-specific tertile of quadriceps strength[*]

	Sex-specific tertile of quadriceps strength		
	Low (n = 88)	**Middle (n = 89)**	**High (n = 88)**
Quadriceps strength, Nm/kg			
All subjects[†]	0.45 ± 0.16	0.77 ± 0.16	1.11 ± 0.23
Men[†]	0.50 ± 0.17	0.88 ± 0.10	1.25 ± 0.19
Women[†]	0.38 ± 0.11	0.62 ± 0.06	0.91 ± 0.12
Age, years[†]	70 ± 9	66 ±9	64 ±9
Women, %	42	42	42
BMI, kg/m^2[†]	33.5 ± 7.0	31.9 ± 4.8	29.1 ± 4.4
K/L grade ≥2, %[†]	86	71	74
Maximal cartilage morphology scores ≥1 at any region, %[‡§]			
Tibiofemoral joint			
Medial compartment	87	89	82
Lateral compartment[†]	72	65	52
Patellofemoral joint			
Medial compartment	90	87	80
Lateral compartment	83	72	69
Knee alignment, degrees[¶]	4.4 ± 7.0	4.0 ± 5.8	2.9 ± 4.3
Knee alignment ≥5° varus, %[¶]	46	42	32
Physical activity score for the elderly[†]	103.4 ± 72.9	134.3 ± 96.4	158.7 ± 79.6
VAS pain score, 0–100 mm[†]	52.7 ± 25.1	42.9 ± 23.6	35.6 ± 24.1
WOMAC physical function subscale score, 0–68[†]	29.4 ± 9.9	23.4 ± 10.7	18.4 ± 11.2

[*]Except where indicated otherwise, values are the mean ± SD. See Table 1 for definitions.

[†]Statistically significant difference ($P < 0.05$) between at least 2 of the tertiles.

[‡]Baseline maximal cartilage morphology score at ≥1 of the 5 regions within a compartment.

[§]Equivalent to cartilage morphology score of ≥2 (on a 0–6 scale) determined using the original Whole-Organ Magnetic Resonance Imaging Score.

[¶]Values above 0° indicate a more varus alignment (which increases loading at the medial compartment of the knee), while values below 0° indicate a more valgus alignment (which increases loading at the lateral compartment of the knee). Alignment data were available for 219 of the 265 participants (83%).

Table 3

Risk of cartilage loss at the knee in the 265 men and women with symptomatic knee osteoarthritis by sex-specific tertile of quadriceps strength*

	Sex-specific tertile of quadriceps strength		
	Low (referent)	**Middle**	**High**
Tibiofemoral joint			
Medial compartment			
Regions with cartilage loss, %	21.6	17.1	19.8
Crude OR (95% CI)†	1.0	0.8 (0.5, 1.3)	1.0 (0.6, 1.6)
Adjusted OR (95% CI)‡	1.0	0.8 (0.5, 1.4)	1.0 (0.5, 1.8)
Lateral compartment			
Regions with cartilage loss, %	7.6	8.2	7.1
Crude OR (95% CI)†	1.0	1.3 (0.6, 2.5)	1.1 (0.6, 2.2)
Adjusted OR (95% CI)‡	1.0	1.3 (0.6, 2.7)	1.1 (0.5, 2.5)
Patellofemoral joint			
Medial compartment			
Regions with cartilage loss, %	14.3	13.2	11.5
Crude OR (95% CI)†	1.0	0.9 (0.5, 1.7)	0.7 (0.4, 1.4)
Adjusted OR (95% CI)‡	1.0	0.9 (0.5, 1.8)	0.8 (0.4, 1.6)
Lateral compartment			
Regions with cartilage loss, %	17.1	9.9	8.8
Crude OR (95% CI)†	1.0	0.6 (0.3, 1.2)	0.5 (0.2, 0.9)
Adjusted OR (95% CI)‡	1.0	0.5 (0.2, 1.1)	0.4 (0.2, 0.9)

*OR = odds ratio; 95% CI = 95% confidence interval.

†Adjusted for baseline cartilage scores only.

‡Adjusted for baseline cartilage scores, age, body mass index, sex, and duration of followup.

Table 4

Risk of cartilage loss by sex-specific tertile of quadriceps strength, stratified by knee alignment*

	Knee alignment ≥5° varus†			Knee alignment <5°‡		
	Low quadriceps strength (referent)	**Middle quadriceps strength**	**High quadriceps strength**	**Low quadriceps strength (referent)**	**Middle quadriceps strength**	**High quadriceps strength**
Tibiofemoral joint						
Medial compartment						
Regions with cartilage loss, %	39.2	29.2	32.2	14.4	10.2	12.4
Crude OR (95% CI)§	1.0	0.6 (0.3, 1.4)	0.6 (0.2, 1.5)	1.0	0.7 (0.3, 1.6)	0.9 (0.4, 2.0)
Adjusted OR (95% CI)¶	1.0	0.6 (0.3, 1.3)	0.6 (0.2, 1.6)	1.0	0.8 (0.3, 2.4)	1.1 (0.3, 3.4)
Lateral compartment						
Regions with cartilage loss, %	5.3	3.9	0.8	12.6	10.6	10.2
Crude OR (95% CI)§	1.0	NA	NA	1.0	1.1 (0.4, 2.6)	1.1 (0.5, 2.3)
Adjusted OR (95% CI)¶	1.0	NA	NA	1.0	1.4 (0.6, 3.2)	1.7 (0.7, 3.9)
Patellofemoral joint						
Medial compartment						
Regions with cartilage loss, %	19.6	14.0	15.6	10.8	12.8	9.9
Crude OR (95% CI)§	1.0	0.6 (0.2, 1.8)	0.5 (0.2, 1.8)	1.0	1.2 (0.4, 3.3)	0.9 (0.3, 2.4)
Adjusted OR (95% CI)¶	1.0	0.6 (0.2, 1.6)	0.5 (0.1, 2.5)	1.0	1.2 (0.4, 3.9)	0.8 (0.2, 2.6)
Lateral compartment						
Regions with cartilage loss, %	15.4	12.3	6.5	19.0	6.9	10.6
Crude OR (95% CI)§	1.0	0.8 (0.2, 2.8)	0.4 (0.1, 1.5)	1.0	0.4 (0.1, 1.1)	0.5 (0.2, 1.3)
Adjusted OR (95% CI)¶	1.0	0.9 (0.2, 3.2)	0.5 (0.1, 3.1)	1.0	0.3 (0.1, 0.9)	0.4 (0.1, 1.3)

*OR = odds ratio; 95% CI = 95% confidence interval; NA = not available.

†Eighty-seven knees had ≥5° varus alignment (30, 32, and 25 knees in the low, middle, and high quadriceps strength tertiles, respectively).

‡One hundred thirty-two knees had <5° alignment (35, 44, and 53 knees in the low, middle, and high quadriceps strength tertiles, respectively).

§Adjusted for baseline cartilage scores only.

¶Adjusted for baseline cartilage scores, age, body mass index, sex, duration of followup, and alignment.

Table 5

Knee pain and physical function by sex-specific tertile of quadriceps strength[*]

	Sex-specific tertile of quadriceps strength		
	Low (referent)	**Middle**	**High**
VAS pain score, 0–100 mm			
Baseline[†]	50.8 (44.1, 57.4)	40.8 (34.6, 46.9)	35.1 (28.5, 41.7)
Followup[†]	51.3 (44.6, 57.9)	36.1 (29.9, 42.2)	35.6 (29.0, 42.2)
Change	0.9 (−6.5, 8.3)	−2.9 (−9.6, 3.8)	2.3 (−5.0, 9.5)
WOMAC physical function subscale score, 0–68			
Baseline[‡]	30.2 (27.3, 33.2)	23.9 (21.2, 26.6)	20.3 (17.4, 23.2)
Followup[‡]	30.7 (27.4, 34.0)	23.6 (20.6, 26.5)	21.7 (18.5, 24.9)
Change	1.0 (−1.8, 3.8)	−0.05 (−2.6, 2.5)	1.7 (−1.0, 4.5)

[*]Values are mean scores (95% confidence intervals) adjusted for age, BMI, sex, duration of followup, and cartilage scores. See Table 1 for definitions.

[†]Statistically significant difference among tertiles of quadriceps strength ($P = 0.002$, $P = 0.0003$, and $P = 0.4$ for baseline, followup, and change, respectively, in VAS pain scores).

[‡]Statistically significant difference among tertiles of quadriceps strength ($P < 0.0001$, $P < 0.0001$, and $P = 0.5$ for baseline, followup, and change, respectively, in WOMAC physical function subscale scores).