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REDUCED QUADRICEPS STRENGTH RELATIVE TO BODY WEIGHT

A Risk Factor for Knee Osteoarthritis in Women?

CHARLES SLEMENDA, DOUGLAS K. HEILMAN, KENNETH D. BRANDT, BARRY P. KATZ, STEVEN A. MAZZUCA, ETHAN M. BRAUNSTEIN, and DONNA BYRD

Objective. **To determine whether baseline lower extremity muscle weakness is a risk factor for incident radiographic osteoarthritis (OA) of the knee.**

Methods. **This prospective study involved 342 elderly community-dwelling subjects (178 women, 164 men) from central Indiana, for whom baseline and followup (mean interval 31.3 months) knee radiographs were available. Lower extremity muscle strength was measured by isokinetic dynamometry and lean tissue (i.e., muscle) mass in the lower extremities by dual x-ray absorptiometry.**

Results. **Knee OA was associated with an increase in body weight in women ($P = 0.0014$), but not in men. In both sexes, lower extremity muscle mass exhibited a strong positive correlation with body weight. In women, after adjustment for body weight, knee extensor strength was 18% lower at baseline among subjects who developed incident knee OA than among the controls ($P = 0.053$), whereas after adjustment for lower extremity muscle mass, knee extensor strength was 15% lower than in the controls (P not significant). In men, in contrast, adjusted knee extensor strength at baseline was comparable to that in the controls. Among the 13 women who developed incident OA, there was a strong, highly significant negative correlation between body weight and extensor strength ($r = -0.740$, $P = 0.003$), that is, the more obese the subject, the greater the reduction of quadriceps strength. In contrast, among the 14 men who developed incident OA, a modest positive correlation existed between weight and quadriceps strength ($r = 0.455$, $P = 0.058$). No correlation between knee flexor (hamstring) strength and knee OA was seen in either sex.**

Conclusion. **Reduced quadriceps strength relative to body weight may be a risk factor for knee OA in women.**

Osteoarthritis (OA) of the knee is the most common cause of chronic disability among the elderly (1). Quadriceps muscle weakness is common in patients with knee OA, in whom it is widely believed to be due to disuse atrophy, consequent to a reduction in loading of the extremity because of joint pain. A recent study of subjects with knee pain found that weakness played a more significant role in disability than the severity of either the pain or the radiographic changes (2).

Although several studies have shown that quadriceps strengthening exercises may ameliorate joint pain in subjects with knee OA (3–6), whether weakness plays an etiologic role in this disease has seldom been considered. However, the quadriceps muscle stabilizes the knee joint (7), and it is plausible that a reduction in the ability of this muscle to respond rapidly to mechanical stresses and to changes in the position of the joint could reduce its efficiency as a shock absorber and its ability to protect the joint from stress (8–10). Given our growing understanding of safe and effective methods for increasing strength among the elderly (11–13), elucidation of the importance of muscle weakness or reduced strength relative to body weight in OA is particularly germane.

We have recently undertaken a prospective study of the relationships among lower extremity muscle

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Douglas K. Heilman, MS, Barry P. Katz, PhD, Steven A. Mazzuca, PhD, Ethan M. Braunstein, MD: Indiana University School of Medicine, Indianapolis; Kenneth D. Brandt, MD: Indiana University School of Medicine, and Indiana University Multipurpose Arthritis and Musculoskeletal Diseases Center, Indianapolis; Donna Byrd, LPN: Indiana University Multipurpose Arthritis and Musculoskeletal Diseases Center, Indianapolis.

Dr. Slemenda is deceased.

Address reprint requests to Kenneth D. Brandt, MD, 541 Clinical Drive, Room 492, Indianapolis IN 46202.

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strength, lean tissue mass, and knee OA among a community cohort of men and women over the age of 65. Our baseline analyses indicated that quadriceps weakness may be present in women with radiographic evidence of knee OA, even in the absence of a history of knee pain and in the presence of normal or increased muscle bulk in the thigh (14). The present report provides evidence that women in the cohort who developed radiographic changes of incident OA were heavier and had greater lower extremity muscle mass but lower knee extensor strength relative to body weight or to lower extremity lean tissue mass at baseline than did women who did not develop radiographic evidence of knee OA. The effects of muscle weakness on the progression of established radiographic changes of OA will be reported elsewhere.

SUBJECTS AND METHODS

Study population. To obtain a sample of independent-living elderly subjects, we conducted brief telephone interviews with residents of households in central Indiana who were selected through modified random-digit dialing methods to increase the sampled proportion of subjects over the age of 65, as described previously (14). All subjects were independent, community-based individuals who met minimal criteria for participation in this study (e.g., they were willing and able to provide informed consent and to undergo the strength assessments and other evaluations described below). Subjects were excluded if they had amputations of both lower extremities, had undergone total knee arthroplasty, or had had a recent cerebrovascular accident or myocardial infarction. Four hundred sixty-two subjects (~55% of all who were eligible) agreed to participate and completed the baseline examinations described below.

Baseline and followup standing anteroposterior radiographs of both knees were available for 342 (74%) of the 462 subjects in the cohort. The mean interval between the baseline and followup radiographic examination was 31.3 months (median 31.9 months, range 21.3–40.2 months). The severity of OA in the tibiofemoral compartments was graded independently by a musculoskeletal radiologist (EMB) and a rheumatologist (KDB), according to Kellgren and Lawrence (K/L) criteria (15). Followup radiographs were read without knowledge of the grade assigned at the baseline examination. Any discrepancies in grading were resolved by mutual reexamination of the image by the 2 readers until agreement was reached. A K/L grade ≥2 for either knee was required in order to classify the subject as having "OA."

Because this paper deals with incident (and not prevalent) OA, the data presented below are confined to the 280 subjects (141 women, 139 men) in whom the baseline radiograph showed no evidence of OA (i.e., K/L grade 0 or 1) in one or both knees (Table 1). Among these subjects, baseline radiographs showed normal findings bilaterally in 237 (113 women, 124 men) and unilaterally in 43 (28 women, 15 men). Six additional subjects (2 women, 4 men) whose radiographs showed unilateral knee OA at baseline, but whose followup radiographs were read as bilaterally normal (presumably because of differences in radioanatomic positioning between the 2 examinations) were excluded from analysis.

Table 1. Baseline radiographic characteristics of the 342 subjects for whom paired knee radiographs were available and in whom one or both knees were radiographically normal at baseline examination

Baseline radiographic status	No. of subjects		
	Women	Men	Total
Bilaterally normal	113	124	237
Unilateral OA	28	15	43*
Left leg normal	14	9	
Right leg normal	14	6	
Bilateral OA	35	21	56
Total	178	164	342

* Baseline radiographs of 6 additional subjects (4 men and 2 women) showed unilateral knee osteoarthritis (OA; Kellgren/Lawrence grade 2 in 5 and grade 3 in 1), but followup radiographs were bilaterally normal.

Classification of subjects with respect to incident OA. Based on the findings in followup radiographs, the 280 subjects with normal findings on at least 1 baseline knee radiograph were classified as having "no incident OA" or "incident OA." The former group comprised 219 subjects (107 women, 112 men) in whom both the baseline and followup knee radiographs showed normal findings bilaterally (designated hereafter as the "controls") and 34 subjects (21 women, 13 men) in whom one knee was radiographically normal at both examinations, while the other knee showed evidence of OA at both time points (Table 2).

The group classified as having incident OA included subjects in whom both knees were radiographically normal at baseline, but whose followup examination showed either unilateral (n = 13) or bilateral (n = 5) OA, and those with unilateral OA at baseline whose followup radiograph showed bilateral OA (n = 9).

Lower extremity muscle strength. The strength of each leg was evaluated separately with an isokinetic dynamometer (KIN-COM 500H; Chattecx, Hixson, TN). Pilot testing of several subjects was performed to ensure that any problems with the testing protocol were eliminated before the start of the study. All subjects were given the same instructions before testing and the same prompting during testing, and received visual feedback of their level of torque generation. To familiarize them with the operation of the dynamometer before formal testing began, subjects were allowed several submaximal practice efforts, following which the best of 3 maximal efforts was recorded for flexion and extension at both 60° and 120° per second. The interval between contractions was ~20 seconds. To obtain the best possible representation of strength for each subject, aborted efforts were repeated. Testing was performed by a research nurse trained in isokinetic strength testing (DB).

Subjects were studied when they were in a seated position, with the pad on the lever arm applied to the tibia 3 inches above the tibiotalar joint. Knee flexion was carried

Table 2. Development of incident OA in subjects in whom one or both knees were radiographically normal at baseline examination

Classification	Radiographic Status		Subjects		
	Baseline	Follow-up	Women	Men	Total
No incident OA	Bilaterally normal	Bilaterally normal	107	112	219
No incident OA	Unilateral OA	Unilateral OA	21	13	34
Incident OA	Bilaterally normal	Unilateral OA	5	8	13
Incident OA	Bilaterally normal	Bilateral OA	1	4	5
Incident OA	Unilateral OA	Bilateral OA	7	2	9
Total			141	139	280*

* Baseline radiographs of 6 additional subjects (4 men and 2 women) showed unilateral knee osteoarthritis (OA; Kellgren/Lawrence grade 2 in 5 and grade 3 in 1), but followup radiographs were bilaterally normal.

through a range of 10–80°. Peak torque was recorded in both the concentric and eccentric mode. Because testing in the eccentric mode yielded greater variability among the values for the 3 contractions, only the results of testing in the concentric mode are reported below. For the same reason, only the results of testing at 60°/second are shown below.

Because the purpose of the present study was to examine the effect of strength on incident OA, in each case, the strength data presented below are those for the extremity in which the baseline knee radiograph was normal. For subjects in whom both knees were radiographically normal at baseline, the strength data for each knee were utilized.

Lower extremity lean tissue mass. Total body dual x-ray absorptiometry (DXA) scans were obtained on all subjects at baseline with a Lunar-DPX-L instrument (Lunar, Madison, WI). Right and left lower extremities were analyzed separately for total and regional body composition, including body fat, mineral, and lean components. The lean (i.e., nonfat, nonmineral) component, which is essentially muscle, is hereafter referred to as "muscle." The lower extremity was defined as all tissue below a diagonal line drawn outward and upward from the groin area through the femoral neck. In each case, the DXA data for lower extremity muscle mass reported below are for the same extremity for which strength data are provided.

Knee pain. Knee pain was evaluated at baseline, using the pain subscale of the Western Ontario and McMaster Universities Osteoarthritis Index (16), which assesses the severity of knee pain during 5 activities (walking on a flat surface, going up or down stairs, lying in bed at night, sitting or lying down, and standing upright). Pain was assessed in each knee separately. Responses to each question about the severity of knee pain were recorded on a categorical scale as none, mild, moderate, severe, or extreme. Each category was assigned a corresponding numerical score from 1 to 5, yielding a pain scale range of 5–25. Participants who rated the severity of their pain as moderate or greater ($\geq$3) for any of the 5 activities on more than half of the days in the month preceding the evaluation were considered to have "pain."

Level of physical activity. Subjects were also asked at baseline to grade their level of physical activity (walking, participation in sports, physical labor) relative to that of others of similar age, as follows: "much less active," "a little less active," "about the same," "a little more active," or "much more active."

Statistical analysis. All analyses were performed separately for women and men. Statistical significance is noted where $P < 0.05$. Subjects were categorized into 1 of 3 groups: 1) the baseline and followup knee radiographs were both normal bilaterally (controls), 2) 1 knee was radiographically normal at both examinations (unilateral OA), or 3) incident OA developed in one or both knees. One-way analysis of variance was used to compare age and body weight among the 3 groups. Measures of strength were recorded separately for each leg. Strength data for both legs were included for all control subjects and for the affected leg(s) for the other 2 groups. Data for the contralateral extremity of subjects who had unilateral OA at baseline were excluded from analysis because we considered that they were not "normal" controls.

Linear models were constructed to test for differences in strength-related variables among the 3 groups of subjects, adjusted for left–right differences. The generalized estimating equations (GEE) approach (17) was incorporated in these models to adjust the hypothesis tests for correlations between observations on the same participant (i.e., right and left leg values). The group means in Tables 3 and 4 were obtained from the linear models and were adjusted for the relative proportion of left and right legs. Standard errors for these means were calculated after adjusting for the correlation between values for the same subject by use of a formula based on clustered samples (18). Pearson correlation coefficients were used to quantify the associations among continuous variables, and P values were calculated based on GEE when multiple observations from the same subject were included, to account for correlations between knees.

RESULTS

Baseline demographics and characterization of subjects. The mean ($\pm$SD) age of the study subjects at the time of enrollment was 70.8 $\pm$ 4.6 years (women 70.4 $\pm$ 4.6 years; men 71.2 $\pm$ 4.7 years) (Table 3). Eighty-nine percent of the women and 95% of the men were Caucasian.

The present study confirms previous observations (19,20) of the relationship of obesity to knee OA.

Table 3. Characterization of subjects in relation to their radiographic status at baseline and followup examination

Category	No. of subjects	No. of knees	Age, mean ± SD years	Body weight, mean ± SD kg	Lower extremity muscle mass, mean ± SEM kg	Correlation of lower extremity muscle mass with body weight	
						r	*P*
Women							
Normal bilaterally at baseline and followup	107	214	70.8 ± 4.8	66.13 ± 10.70	6.28 ± 0.07	0.595	0.001
Unilateral OA at baseline and followup	21	21	69.1 ± 2.3	77.14 ± 15.88*	6.86 ± 0.18†	0.850	0.001
Incident OA‡	13	14	69.6 ± 4.6	81.15 ± 16.89*	6.96 ± 0.96§	0.744	0.002
Men							
Normal bilaterally at baseline and followup	112	224	70.8 ± 4.7	82.04 ± 10.16	9.55 ± 0.11	0.718	0.001
Unilateral OA at baseline and followup	13	13	73.2 ± 4.4	88.92 ± 13.16	9.62 ± 0.30	0.748	0.003
Incident OA¶	18	15	71.9 ± 4.9	85.79 ± 16.70	9.39 ± 0.38	0.831	0.001

* $P < 0.001$ versus subjects whose knee radiographs were normal at both baseline and followup.
† $P = 0.002$ versus subjects whose knee radiographs were normal at both baseline and followup.
‡ For the women, includes 5 subjects who were radiographically normal at baseline and developed unilateral knee osteoarthritis (OA), 1 who was bilaterally normal at baseline and developed bilateral knee OA, and 7 who had unilateral knee OA at baseline and bilateral knee OA at followup.
§ $P = 0.003$ versus subjects whose knee radiographs were normal at both baseline and followup.
¶ For the men, includes 8 subjects who were radiographically normal at baseline and developed unilateral knee OA, 4 who were bilaterally normal at baseline and developed bilateral knee OA, and 2 who had unilateral knee OA at baseline and bilateral knee OA at followup.

Women with knee OA in our cohort were, on average, heavier than the female controls. Women who developed incident disease were, on average, 23% heavier than the controls (i.e., those without radiographic evidence of OA at either the baseline or the followup examination) (Table 3), while those with stable unilateral knee OA were, on average, 17% heavier ($P < 0.001$ for both). Men with OA were also slightly heavier than the male controls, but the association of knee OA with increased body weight was not statistically significant in men.

Lower extremity muscle mass. Baseline muscle mass in the radiographically normal lower extremity of women who developed incident knee OA was 11% greater than that in the female controls ($P = 0.003$) (Table 3); in women with stable unilateral knee OA, lower extremity muscle mass was ~9% greater ($P = 0.003$). As expected, muscle mass in the radiographically normal extremity was greater in men than in women. However, the values in men who had knee OA at baseline or who developed OA during the study were not significantly different from the value in the controls.

In both sexes, lower extremity muscle mass correlated strongly with body weight (Table 3). This association was apparent in the control subjects as well as in those with OA. Thus, the lower extremity muscle mass of heavier subjects, regardless of whether they had OA, tended to be greater than that of those who weighed less.

Knee extensor strength. Despite the increase in lower extremity muscle mass associated with the greater body weight of subjects with OA, the mean knee extensor strength of men and women with OA was not greater at baseline than that of the respective controls (Table 4); indeed, relative to their body weight, women with incident OA or with stable unilateral OA were weaker than the female controls.

Because of the strong correlation between body weight and lower extremity muscle mass (Table 3), between-group comparisons of baseline strength of the radiographically normal extremity were made also after adjustment for body weight and for muscle mass (Table 4). In both instances, the mean value for adjusted strength was 15–18% lower among women who developed incident OA than among the controls ($P = 0.053$ and $P = 0.085$, respectively). An intermediate value was found for women with unilateral knee OA at baseline who did not develop incident OA ($P = 0.055$, for weight-adjusted strength).

In contrast, among men who developed incident OA, adjusted extensor strength at baseline was not significantly different from that of the controls (Table 4). Baseline adjusted strength values for the radiographically normal knee of the 13 men with stable unilateral OA were similar to those in this subgroup of women in the cohort, with weight-adjusted strength ~15% lower than that in the male controls, and strength adjusted for muscle mass ~9% lower (P not significant in both instances).

Although the between-sex differences with re-

Table 4. Peak extensor strength at 60°/second generated by extremity with radiographically normal knee at baseline and relationship of peak strength to body weight and to lower extremity lean tissue mass

Category	No. of subjects	No. of knees	Peak extensor strength, mean ± SEM lb-ft	Peak knee extensor strength (lb-ft) per kg of body weight, mean ± SEM	Peak knee extensor strength (lb-ft) per kg of lower extremity muscle mass, mean ± SEM	Correlation of body weight with peak extensor strength		Correlation of body weight with peak extensor strength per kg of lower extremity muscle mass	
						r	*P*	r	*P*
Women									
Normal bilaterally at baseline and followup	107	214	36.86 ± 1.02	0.57 ± 0.02	5.92 ± 0.17	−0.004	0.985	−0.206	0.013
Unilateral OA at baseline and followup	21	21	35.26 ± 2.44	0.48 ± 0.04*	5.27 ± 0.43	−0.274	0.229	−0.456	0.038
Incident OA†	13	14	33.38 ± 3.06	0.47 ± 0.07‡	5.01 ± 0.60§	−0.740	0.003	−0.828	0.001
Men									
Normal bilaterally at baseline and followup	112	224	53.15 ± 1.63	0.65 ± 0.02	5.58 ± 0.17	0.222	0.005	−0.038	0.560
Unilateral OA at baseline and followup	13	13	48.44 ± 4.54	0.55 ± 0.06	5.06 ± 0.51	0.258	0.395	−0.015	0.962
Incident OA¶	14	18	51.78 ± 3.64	0.61 ± 0.04	5.58 ± 0.43	0.455	0.058	0.016	0.951

* $P = 0.055$.
† For the women, includes 5 subjects who were radiographically normal at baseline and developed unilateral knee osteoarthritis (OA), 1 who was bilaterally normal at baseline and developed bilateral knee OA, and 7 who had unilateral knee OA at baseline and bilateral knee OA at followup.
‡ $P = 0.053$.
§ $P = 0.085$.
¶ For the mean, includes 8 subjects who were radiographically normal at baseline and developed unilateral knee OA, 4 who were bilaterally normal at baseline and developed bilateral knee OA, and 2 who had unilateral knee OA at baseline and bilateral knee OA at followup.

spect to baseline-adjusted strength were not statistically significant, perhaps because of the relatively small number of subjects with incident OA in each group, the trend manifest in women with incident OA—toward a decrease in knee extensor strength, adjusted for either body weight or for lower extremity muscle mass—reflects a pattern clearly different from that seen in men with incident knee OA.

Correlations between body weight and knee extensor strength. Sharp between-sex differences were also noted with regard to the correlation between mean knee extensor strength and body weight (Table 4). Among the male controls, a modest positive correlation existed between body weight and knee extensor strength ($r = 0.222$, $P = 0.005$). No such relationship was apparent, however, among the female controls ($r = -0.004$, $P = 0.985$). Furthermore, among women with incident OA, a highly significant negative correlation existed between extensor strength and body weight ($r = -0.740$, $P = 0.003$) whereas the correlation among men with incident OA was positive but did not quite reach statistical significance ($r = 0.455$, $P = 0.058$, Table 4).

Correlations between body weight and extensor strength adjusted for lower extremity muscle mass. Further emphasis of the above differences between men and women with knee OA is provided by the correlation between body weight and extensor strength, adjusted for lower extremity muscle mass. Notably, among the female controls a modest negative relationship existed ($r = -0.206$, $P = 0.013$); however, among women who developed incident OA, the negative association was much stronger ($r = -0.828$, $P = 0.001$). An intermediate value was obtained for those women with unilateral OA at baseline who did not subsequently develop OA in the contralateral knee ($r = -0.456$, $P = 0.038$) (Table 4). In marked contrast, among men, no significant correlation existed between weight and extensor strength adjusted for muscle mass.

Knee flexor strength. Peak knee flexor (hamstring) strength at baseline among subjects who developed incident OA was similar to that for the controls (women 16.68 ± 6.83 lb-ft versus 19.34 ± 3.75 lb-ft, $P = 0.35$; men 21.45 ± 7.46 lb-ft versus 27.43 ± 14.27 lb-ft, $P = 0.23$). In contrast to the reduction in adjusted knee extensor strength among women who developed OA, no association was apparent between knee flexor (hamstring) strength and OA in either sex.

Knee pain and level of physical activity. Because pain may affect the strength of a voluntary quadriceps contraction (21), it is relevant that knee pain during the month preceding the baseline examination was relatively uncommon in our subjects. Among the controls, 21% of

the 107 women and 13% of the 112 men reported knee pain. In comparison, 3 of the 13 women (23%) and 2 of the 14 men (14%) who developed incident OA described knee pain. Notably, among women who developed incident OA, mean quadriceps strength was *greater* in those who reported pain than in those who did not.

As indicated above, the DXA data did not support the hypothesis that quadriceps weakness among the women who developed incident OA was due to loss of lower extremity muscle bulk, as might have been expected with disuse atrophy. In support of the DXA results, the quadriceps weakness in these women did not appear to be associated with a decline in their level of physical activity. In response to our query regarding their activity, 67% of the women and 89% of the men who developed incident OA considered themselves to be more active than others of their age, in the control group 74% of the women and 68% of the men considered themselves to be more active. Furthermore, among both men and women who developed knee OA, quadriceps strength adjusted for body weight was as great among those who considered themselves to be less active than their peers as among those who considered themselves to be more active.

DISCUSSION

Our cross-sectional analysis (14) of this community-based cohort of elderly subjects showed that even in the absence of knee pain and muscle atrophy, quadriceps weakness was common among women with radiographic evidence of knee OA. The present longitudinal study shows that among women in that cohort whose baseline knee radiograph showed normal findings but who developed radiographic evidence of knee OA over the next 2–3 years, baseline quadriceps strength, relative to body weight or to lower extremity muscle mass, was 15–18% lower than that in women whose knee radiograph findings remained normal (Table 4). This was not true for men, however, in whom baseline quadriceps strength was not a predictor of incident radiographic OA. The decrease in baseline quadriceps strength among women who developed incident knee OA approached, but did not quite reach, significance ($P = 0.055$) (Table 4), perhaps due to the relatively small number of subjects in this subgroup (n = 13). That possibility requires further study.

Because the strength data reported herein are limited to concentric contraction, it should be noted that concentric shortening of the quadriceps is important in stabilizing the knee during ambulation, whereas eccentric lengthening would be relevant, for example, to descending stairs. It should also be noted that the peak torque measurements reported herein were obtained at a relatively slow speed (60°/second), whereas many functional activities occur at faster speeds. However, values for extensor torque at 120°/second demonstrated greater variability from contraction to contraction within subjects, presumably due to the difficulty encountered by our subjects at the higher speed.

With respect to the use of DXA for measuring lower extremity muscle mass, precise measurements of lean mass had previously required measurement of total body potassium, body density (underwater weighing), or other similarly difficult measures. The development of DXA, however, has made possible the accurate, rapid, noninvasive measurement of lean tissue mass (nearly all of which is muscle). The precision of the DXA method is excellent; Fuller et al (22) found a standard deviation of 0.25 kg of muscle, with a coefficient of variation of 1.7%, for the difference between duplicate estimates of skeletal muscle mass in the legs of 28 subjects. Mazess et al (23) obtained similar results. Specifically, the DXA data may be used to suggest whether weakness associated with OA is due to a loss of muscle bulk, i.e., atrophy. They therefore complement our measurements of quadriceps strength.

Consistent with previous reports (19,20), increased body weight was associated with radiographically defined incident knee OA in women, in whom the association was highly significant (Table 3). This relationship was much less striking and not statistically significant in men. In both sexes, however, body weight correlated strongly with muscle mass in the radiographically normal lower extremity (Table 3); muscle mass can increase not only as a result of physical activity, but also because of the requirement for supporting an increase in adipose tissue. However, the greater baseline lower extremity muscle mass in women who developed incident OA was not accompanied by an increase in raw extensor strength. Indeed, a strong *negative* correlation existed between body weight and extensor strength among women who developed incident OA ($r = -0.740$, $P = 0.003$) (Table 4).

The basis for the reduced quadriceps strength relative to body weight that we found in both women with stable unilateral OA and in those with incident knee OA is unclear. In normal subjects, the strength of voluntary isometric and lower-velocity isokinetic contraction of the quadriceps has been shown to diminish after vigorous exercise (24). Whether the chronic burden of obesity in subjects with knee OA exerts a similar

effect is unknown. Hurley and Newham (21) have shown that the strength of maximum isometric and isokinetic voluntary contraction of the quadriceps in subjects with knee OA is lower than that in controls and has attributed this to reflex inhibition of muscle contraction (21). In any case, the absence of a decrease in weight-adjusted strength in the hamstring muscles and the increase in lower extremity lean tissue mass argue against disuse atrophy as the basis for the reduced quadriceps strength relative to body mass among women with OA in our cohort.

We also consider it unlikely that the reduction in quadriceps strength in our cohort was due to inhibition of quadriceps contraction by joint effusion (21). Although our subjects did not undergo a physical examination of the knee at baseline, clinically apparent effusions are present in a relatively small proportion of *clinic patients* with knee OA. We presume that the prevalence was even lower among our community-based subjects, almost none of whom were taking nonsteroidal antiinflammatory drugs.

Consistent with the positive correlation between body weight and lower extremity muscle mass in the present study, lean body mass was also shown to be greater in obese than in nonobese young Japanese men (25). In that study, strength tended to diminish as the percentage of body fat increased. Although a trend toward this inverse relationship was noted in our older adult males, it was not significant (Table 4); however, among the women with OA in our cohort, and especially among women with incident OA, the negative correlation between body weight and knee extensor strength was striking.

Obese subjects have been shown to exhibit weakness not only in isometric knee extensor strength, but also in hand grip and trunk extension (25). This generalized weakness has been attributed to "weak will power," i.e., failure of the subject to overextend himself during physical activity. Dekker et al (26) have hypothesized that muscle weakness serves as a mediating factor between negative affect and joint pain and disability in subjects with OA; i.e., that a negative affect (defined as "a broad range of aversive mood states, including anger, distrust, scorn, guilt, fearfulness, and depression") (27) enhanced the avoidance of pain-related activities. They considered that the resultant low activity level induced muscle weakness, leading to instability of the joint, and therefore pain and disability. Even after controlling for radiographic severity of disease, psychological variables have been shown to be strong predictors of functional impairment and pain in patients with OA of the knee or hip (28). It is also possible, however, that changes in muscle induced by inactivity or due to metabolic effects related to obesity lead to muscle weakness. It is notable, therefore, that our subjects who developed incident OA perceived their level of physical activity to be greater—not less—than that of their peers, and that among the women who developed incident OA, those who reported knee pain had greater quadriceps strength than those without knee pain.

Among women in our cohort who developed incident OA, baseline knee extensor strength adjusted for lower extremity muscle mass also tended to be lower than in the controls (Table 4), although the difference was not significant, perhaps because of the relatively small number of women with OA. Notably, however, among women, a strong negative relationship existed between weight and extensor torque per kg of lower extremity muscle ($r = -0.828$, $P = 0.001$ for those with incident OA; $r = -0.456$, $P = 0.038$ for those with radiographically stable unilateral disease) (Table 4). This negative correlation did not exist in men with OA.

By what mechanism might quadriceps weakness or reduced quadriceps strength relative to body mass lead to knee OA? Although hamstring activity decelerates the forward swing of the leg, at the end of swing, the leg is pulled toward the ground (toward heel-strike) by gravity, assisted by continuous hamstring action. Quadriceps action at this point retards the rate of descent, acting to brake the fall of the leg. Furthermore, because the quadriceps is important in providing anteroposterior stability to the knee (7), quadriceps weakness may alter sites of mechanical loading of the joint surface, resulting in damage to the articular cartilage. Experimental paralysis of the quadriceps in a normal subject was shown to result in a marked heel-strike transient and an estimated 5-fold increase in forces acting at the knee at touchdown (29). Among subjects with normal knee radiographs, those with knee pain were found to exhibit a significantly greater heel-strike transient than those without knee pain (10). Those authors suggested that the gait pattern in the former group, the consequence of which was repeated impact loading of the lower extremity, led to a "pre-osteoarthritic" state, although no evidence was provided that the subjects with knee pain developed OA or that the increased heel-strike transient was the cause, rather than the result, of knee pain. Experimentally, some support exists for this hypothesis: rabbits subjected to repeated acute (50 ms) impact loading of the knee incurred damage to articular cartilage and subchondral bone (30), while impulsive loads of greater magnitude, if applied more gradually (500 ms),

were innocuous (Radin E: personal communication). Very rapid application of load does not allow sufficient time for the periarticular muscles, the major shock absorbers protecting the joint, to absorb the load through eccentric contraction (8,9). Why some normal subjects generate a large heel-strike transient when walking while others do not is also unknown, but may reflect individual differences in central program generators, i.e., neurologic mechanisms based in the central nervous system which coordinate complex limb movements during gait (31).

It was recently shown that the prevalence of heel-strike transients and the rate of loading of the knee were lower in strength-trained female athletes (weightlifters) than in sedentary women (32). The difference between the 2 groups with respect to the rate of loading of the knee was statistically significant. Whether the risk of knee OA in these strength-trained women is lower (after controlling for knee injury) than in the other groups remains to be determined.

Finally, the importance of muscle spindles (sensory nerve endings within muscle) in modulating muscle tone in response to changes in the position of a limb, thereby protecting the joint from injury, has received attention recently (7). Joint position sense, measured both as the ability to reproduce passive positioning and to detect the onset of movement (kinesthesia), was significantly impaired in normal subjects after completion of a strenuous exercise protocol (33). Hence, maintenance of quadriceps strength appears to be important also in preserving the integrity of protective muscular reflexes.

A variety of evidence suggests that the pathogenesis of knee OA in women may be different from that in men. For example, in women, knee OA tends to be more strongly associated with obesity and to be bilateral, whereas in men, OA is more likely to be related to prior trauma and to be unilateral (34). Although the association between knee OA and obesity is well-established, the mechanism by which they are related is unclear. Both biomechanical and metabolic mechanisms have been postulated. Martin et al (35) found recently that after adjustment for age and for obesity, metabolic correlates of obesity (measurements of glucose and lipid metabolism) did not exhibit an independent association with knee OA, thus indirectly favoring a mechanical basis.

Our data suggest that among women with incident OA, the greater their body weight, the poorer their quadriceps function. Regardless of the cause, our findings raise the possibility that the well-recognized association of obesity with knee OA in women is mediated through quadriceps weakness. Studies of the relationship between quadriceps strength and incident OA in a greater number of subjects than in our cohort are required to address this issue.

In conclusion, it should be emphasized that quadriceps strength can be increased by training even in the very elderly (11–13)—that subset of the population at greatest risk for OA. Our results raise the possibility that interventions which strengthen the quadriceps could mitigate joint pathology in individuals predisposed to knee OA. That possibility is now under investigation.

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