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The longitudinal relationship between thigh muscle mass and the development of knee osteoarthritis

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Abstract

Objective—Greater quadriceps strength has been found to reduce risk for symptomatic knee osteoarthritis (SxKOA) and knee joint space narrowing (JSN). However, this finding could relate to muscle mass or activation pattern. The purpose of this study was to assess whether greater thigh muscle mass protects against (1) incident radiographic (RKOA), (2) incident SxKOA or (3) worsening of knee JSN by 30-month follow-up.

Design—Multicenter Knee Osteoarthritis (MOST) study participants, who underwent dual energy x-ray absorptiometry (DXA) at the Iowa site were included. Thigh muscle mass was calculated from DXA image sub-regions. Sex-stratified, knee-based analyses controlled for incomplete independence between limbs within subjects. The effect of thigh lean mass and specific strength as predictors of ipsilateral RKOA, SxKOA and worsening of JSN were assessed, while controlling for age, BMI, and history of knee surgery.

Results—A total of 519 men (948 knees) and 784 women (1453 knees) were included. Mean age and BMI were 62 years and 30 kg/m^2. Thigh muscle mass was not associated with risk for RKOA, SxKOA or knee JSN. However, in comparison with the lowest tertile, those in the highest and middle tertiles of knee extensor specific strength had a lower risk for SxKOA and JSN (OR 0.29–0.68).

Conclusions—Thigh muscle mass does not appear to confer protection against incident or worsening knee OA. These findings suggest that future studies of risk for knee OA should focus on the roles of knee extensor neuromuscular activation and muscle physiology, rather than the muscle mass.

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Keywords

Strength; muscle; knee; osteoarthritis; incidence; progression

INTRODUCTION

Despite the high prevalence of osteoarthritis (OA), the etiology remains poorly understood[1]. A better understanding of knee OA is undoubtedly hindered by its multifactorial nature[2]. Furthermore, risk factors for knee OA, including obesity, previous injury, sex, advancing age, and quadriceps weakness, may differ in their mechanisms of action[3, 4]. Considering the high prevalence and substantial personal and societal burdens[5], the elucidation of potential treatments is paramount[1]. Hence, there is a fundamental need to discover modifiable risk factors.

As quadriceps weakness is a potentially modifiable risk factor for knee OA, it has long been the focus of physical therapy programs[6]. Other risk factors, such as previous injury, sex, and advancing age are not modifiable. In addition, obesity, although amenable to modification, has been shown to have a stronger independent correlation with incidence than progression[3]. Therefore, a better understanding of how quadriceps weakness may contribute to the development of knee OA could enable implementation of innovative clinical therapies that may attenuate risk for onset as well as progression.

Prior to implementation of therapies, it is essential to determine which factors associated with quadriceps weakness—insufficient muscle mass, proprioception, motor unit recruitment, cellular metabolism, excitation-contraction coupling, inhibition of activation due to pain or the presence of an effusion or reduced central activation— may explain the association with development and or progression of knee OA. Previous studies have shown that strength is likely to be of greater importance than proprioception in mediating risk for knee OA[7]. If muscle mass were to explain the relationship between quadriceps strength and risk for knee OA, then programs could be implemented in community-based settings to correct this factor. Therefore, elucidating the longitudinal relationship between muscle mass and knee OA would provide insight into a possible mechanism for the relationship between quadriceps weakness and knee OA onset and progression. It will also help to guide design of clinical therapies aimed at attenuating risk.

This study used dual-energy X-ray absorptiometry (DXA) measurements of thigh lean mass to assess the relationship between thigh muscle mass at baseline and incident radiographic, symptomatic or progressive knee OA by 30-month follow-up. If reduced thigh muscle mass were found to predict development of knee OA, then this would suggest the need to determine the effect of increasing muscle mass on altering risk for knee OA. If, however, thigh muscle mass were found to have little or no longitudinal association with incident or progressive knee OA, then it would suggest that the relationship between strength and knee OA may relate to muscle activation. Therefore, we assessed the association between thigh muscle mass at baseline and development of incident radiographic, symptomatic and progressive knee OA at 30-month follow-up, testing the following hypotheses:

Hypothesis 1: Higher thigh muscle mass at baseline is associated with lower risk for the development of a) incident radiographic tibiofemoral knee OA, b) incident symptomatic whole knee OA and c) worsening OARSI joint space narrowing of the whole knee, tibiofemoral or patellofemoral compartments by 30-month follow-up.

Hypothesis 2: Higher estimated thigh muscle specific strength at baseline is associated with lower risk for the development of a) incident radiographic tibiofemoral knee OA, b) incident symptomatic whole knee OA and c) worsening OARSI joint space narrowing of the whole knee, tibiofemoral or patellofemoral compartments by 30-month follow-up.

METHODS

Study Population

The Iowa site of the Multicenter Osteoarthritis (MOST) Study is an NIH-funded longitudinal observational study of 1,507 community-dwelling men and women age 50–79 with knee osteoarthritis or known risk factors for knee osteoarthritis. Subject enrolment has been described previously[8]. Potential participants were identified by mass mailings or advertisements, screened by telephone for known knee OA risk factors including knee injury or surgery or obesity. The Institutional Review Boards (IRB) of the investigators' approved this study. All participants provided written informed consent using IRB-approved consent forms.

Baseline Assessments

Anthropometric Measures—Heights were obtained by stadiometer (Holtain Ltd., Crosswell, Crymych, Pembs., UK) to the nearest 1 mm and body masses were assessed using a balance beam scale to the nearest 0.1 kg by trained and certified staff[9]. Body mass index (BMI, kg/m^2) was calculated from baseline mass in kilograms divided by the square of the height in meters.

Thigh Muscle Mass—Thigh lean body mass (g) was measured using a Hologic QDR 4500W Dual Energy X-ray Absorptiometry (DXA) (Hologic Inc., Bedford, MA: Software Version 12.0). Densitometers were calibrated daily by certified technicians. Participants changed into hospital gowns and removed all external metal artifacts prior to scans. Scans were completed according to manufacturer guidelines. Whole body scans for body composition were conducted in default mode (Array). Operators were trained and certified and performed daily quality control scans as well as cross-calibration scans of phantoms used on both machines. Quality control data were collected using standard quality assurance protocols and reviewed monthly.

Thigh fat-free mass was analyzed by one technician and determined by redefining the region of interest using the manufacturer's body composition analysis software. Lines through the femoral neck parallel to and just proximal to the inter-trochanteric line and through the knee joint line respectively defined the superior and inferior borders of the region of interest. The lateral border was bounded outside of the thigh muscle shadow and the medial border was bounded just medial to the thigh muscle shadow for each thigh (Figure 1). Bone mineral content was subtracted from fat-free mass to obtain thigh muscle mass measurements. Inter-rater reliability of the thigh muscle measurement in our lab by the Shrout-Fleiss single-score method (ICC 2,1) was 0.94.

Specific Strength—Specific strength was defined as peak isokinetic knee extensor strength (as described previously)[10, 11] divided by thigh muscle mass from DXA. Confirmatory analyses adjusted the thigh muscle mass from DXA, using a CT-based quadriceps specific strength validation, to assess for bias in the specific strength measurements in individuals with greater fat mass. These analyses also confirmed whether thigh muscle mass was sufficiently related to quadriceps muscle mass to be used in this predictor[12].

Outcome Assessments

Weight-bearing, semi-flexed posteroanterior (PA) and lateral views of the knees were obtained at baseline, and 30 months according to the MOST radiograph protocol[9]. Radiographs were taken of the contralateral knee in participants with unilateral knee replacement. Two independent readers interpreted and graded radiographs according to Kellgren-Lawrence (KL grade)[13].

The study of incident *radiographic* knee OA included a subset of Iowa MOST participants without pre-existing radiographic knee OA (KL grade of <2)[13] at baseline. Those who developed either radiographic knee OA (KL≥2) or had a knee arthroplasty by follow-up were defined as having incident radiographic knee OA.

The study of incident *symptomatic* knee OA included Iowa MOST participants who did not have symptomatic knee OA at baseline—lacking the combination of radiographic knee OA (KL grade<2) and frequent knee symptoms (participants answered “No” at either the telephone screen or clinic visit in response to “During the past 30 days, have you had any pain, aching, or stiffness in your knee on most days?”)[10]. Knees were considered to develop incident symptomatic knee OA if they had the combination of radiographic knee OA and frequent knee symptoms at 30-month follow-up.

For the study of worsening JSN, only knees from Iowa MOST participants with an OARSI joint space narrowing score <3 in both the tibiofemoral and patellofemoral compartments were eligible for inclusion[14]. Knees were considered to have worsening JSN if they had an increase in OARSI JSN score in the respective joint or underwent arthroplasty by 30-month follow-up. For whole knee JSN, we used the maximum of the following: medial tibiofemoral JSN (lateral view), lateral tibiofemoral JSN (lateral view), medial tibiofemoral JSN (PA view), lateral tibiofemoral JSN (PA view), and patellar JSN (lateral view). Tibiofemoral JSN was defined as the maximum of the first four.

Statistical Analyses

Participant characteristics were summarized with frequencies (sex, history of surgery) and means (age, BMI, thigh muscle mass). Tertiles of thigh muscle mass and specific strength were generated separately for men and women. Analyses were performed separately for men and women due to the differences in muscle mass by sex and prior evidence for differing relationships between strength and the outcomes in women and men. Analyses of outcomes were limb-based, considering thigh muscle mass and specific strength ipsilateral to each knee. In sex-specific analyses, independent tertiles of thigh muscle mass and specific strength respectively were compared using logistic regression with generalized estimating equations to adjust for the correlation between limbs within participants. Known correlates with thigh muscle mass or knee OA outcomes (age, BMI, and history of knee surgery) were included in all multivariable models: (1) incident radiographic knee OA, (2) incident symptomatic knee OA, (3a) worsening whole knee JSN, (3b) worsening tibiofemoral JSN, (3c) worsening patellofemoral JSN. The lowest tertile of thigh muscle mass and specific strength respectively were the referent groups in each analysis. In considering variables for which adjustment may be indicated, we assessed correlation coefficients between thigh length and thigh muscle mass ($r = 0.01$, $p = 0.518$) and specific strength ($r = -0.03$, $p = 0.051$). As there were not significant relationships detected, thigh length was not entered as a covariate. A second set of confirmatory analyses treated thigh muscle mass and specific strength as continuous predictors of each of the three outcome measures and generated odds ratios for each 1 kg of thigh muscle mass and each 10 Nm/kg of specific strength, while adjusting for age, BMI, and history of knee surgery within each sex. SAS Version 9.2 (SAS

Institute Inc., Cary, NC) was used for all analyses and significance level was considered to be 0.05.

RESULTS

Participant characteristics for each outcome are summarized in Table 1.

Incident Radiographic Tibiofemoral OA

At baseline 528 (73.9%) of male knees and 703 (70.9%) of female knees had a KL grade of 0, while 187 (26.2%) of male knees and 289 (29.1%) of female knees had a KL grade of 1. Tertiles of thigh muscle mass in men were {4,829.8 – 6,753.5 g, 6,762.2 – 7,644.0 g, and 7,647.1 – 10,988.9 g} and in women were {2,769.6 – 4,458.9 g, 4,459.1 – 5,068.5 g, and 5,069.9 – 7,536.3 g}. In comparison with the lowest tertile, risk for incident radiographic OA did not differ in men or women in the highest and middle tertiles of thigh muscle mass (Table 2). In analyses that treated baseline thigh muscle mass as a continuous variable, no association was detected with incident radiographic tibiofemoral OA in women (p=0.5499) or men (p=0.8354).

Tertiles of knee extensor specific strength in men were {3.8123 – 15.0569 Nm/kg, 15.0578 – 19.6333 Nm/kg, and 19.6470 – 33.4144 Nm/kg} and in women were {3.9164 – 12.9780 Nm/kg, 13.0410 – 17.4083 Nm/kg, and 17.4105 – 43.6301 Nm/kg}. In comparison with the lowest tertile, risk for incident radiographic OA did not differ in men and women in the highest and middle tertiles of specific strength (Table 3). In analyses that treated baseline specific strength as a continuous variable, no association was detected with incident radiographic tibiofemoral OA in women (p=0.4801) or men (p=0.8595).

Incident Symptomatic Knee OA

At baseline, 263 male knees (28.1%) had radiographic knee OA (none with daily pain) and 672 male knees did not have radiographic knee OA (11.8% with daily knee pain). At baseline, 446 female knees (32.5%) had radiographic knee OA (none with daily pain) and 927 female knees did not have radiographic knee OA (16.4% with daily knee pain). Tertiles of thigh muscle in men were {4,448.5 – 6,776.1 g, 6,781.8 – 7,667.3 g, and 7,668.7 – 11,139.5 g} and in women were {2,769.6 – 4,467.3 g, 4,467.5 – 5,111.0 g, and 5,111.9 – 8,676.8 g}. In comparison with the lowest tertile, women in the highest and middle tertiles of thigh muscle mass did not differ in risk for incident symptomatic knee OA. Men in the highest tertile of thigh muscle mass also did not differ in risk. However, men in the middle tertile had a lower risk for incident symptomatic knee OA (Table 2). In analyses that treated baseline thigh muscle mass as a continuous variable, no association was detected with incident symptomatic knee OA in women (p=0.4882) or men (p=0.3066).

Tertiles of knee extensor specific strength in men were {3.8123 – 14.8262 Nm/kg, 14.8429 – 19.3522 Nm/kg, and 19.3664 – 33.4144 Nm/kg} and in women were {3.3735 – 12.1415 Nm/kg, 12.1580 – 16.7331 Nm/kg, and 16.7351 – 43.6301 Nm/kg}. In comparison with the lowest tertile, women in the highest and middle tertiles of knee extensor specific strength had a reduced risk for incident symptomatic knee OA. There was also a similar but lesser trend in men (Table 3). Analyses that treated baseline specific strength as a continuous variable confirmed protection against incident symptomatic tibiofemoral OA with OR (95% CI) of 0.33 (0.18, 0.59) per 10 Nm/kg of specific strength in women (p=0.0002) and 0.49 (0.25, 0.97) in men (p=0.0409).

Worsening Joint Space Narrowing

Tertiles of thigh muscle in men were {4,525.4 – 6,801.2 g, 6,802.2 – 7,697.1 g, and 7,697.2 – 11,139.5 g} and in women were {2,769.6 – 4,472.7 g, 4,475.1 – 5,124.1 g, and 5,126.5 – 8,676.8 g}. In comparison with the lowest tertile, women and men in the highest and middle tertiles of thigh muscle mass did not differ in risk for whole knee JSN, tibiofemoral JSN, or patellofemoral JSN (Table 4). In analyses that treated baseline thigh muscle mass as a continuous variable, no association was detected with worsening joint space narrowing in the tibiofemoral, patellofemoral or whole knee in women (p= 0.4602, 0.2149, 0.9429) or men (p=0.0725, 0.1468, and 0.0994).

Tertiles of knee extensor specific strength in men were {3.8123 – 14.8804 Nm/kg, 14.8834 – 19.3973 Nm/kg, and 19.4213 – 33.4144 Nm/kg} and in women were {3.3735 – 12.1178 Nm/kg, 12.1195 – 16.6383 Nm/kg, and 16.6452 – 43.6301 Nm/kg}. In comparison with the lowest tertile, women in the highest and middle tertiles of knee extensor had a reduced risk for whole knee JSN and tibiofemoral JSN, but not patellofemoral JSN (Table 5). Analyses that treated baseline specific strength as a continuous variable confirmed protection against whole knee JSN and tibiofemoral OA with OR (95% CI) of 0.62 (0.43, 0.89) (p=0.0105) and 0.68 (0.46, 1.00) (p=.0500) per 10 Nm/kg of specific strength in women and demonstrated a trend for protection against patellofemoral JSN with OR of 0.63 (0.37, 1.07) (p=0.0859). In men, there was not a significant relationship between knee extensor specific strength and risk for JSN. Treating specific strength as a continuous predictor in men confirmed the lack of association with JSN in the whole knee (p=0.4981), tibiofemoral (p=0.4394) or patellofemoral compartments (p=0.4292).

DISCUSSION

Thigh muscle mass was not found to be associated with development of incident or worsening knee OA over 30 months. However, consistent with the findings of prior studies of knee extensor strength[10, 11], specific strength was unrelated to subsequent development of incident radiographic knee OA, but was related to both incident symptomatic knee OA in both sexes and to tibiofemoral and whole knee JSN worsening in women. The longitudinal relationships between specific strength (strength/muscle mass) and incident symptomatic knee OA as well as worsening JSN, in the absence of relationships between muscle mass and these outcomes suggests that greater weakness than would be expected from the amount of muscle mass present explains the relationship between strength and these outcomes. In other words, rather than muscle mass, it appears to be other contributors that explain the mechanism by which strength is longitudinally associated with reduced risk for incident symptomatic knee OA in men and women and progressive knee OA in women.

Knee extensor muscle strength has been associated with risk for incident symptomatic knee OA[10, 16], as well as knee joint space narrowing[11]. However, it was previously unknown whether these relationships may be due to diminished muscle mass, impaired or asynchronous muscle activation, greater antagonist co-activation, or alterations in neuromuscular physiology. The results of the current study have clarified that thigh muscle mass assessed by DXA does not explain risk for these outcomes. One exception was the finding that men in the middle tertile of muscle mass had a reduced risk for incident symptomatic knee OA. However, this isolated finding appears neither externally consistent with the other findings, nor internally consistent. There was no linear trend with the other categories and an association was not supported in analyses that treated muscle mass as a continuous variable. Therefore, there is insufficient evidence to conclude that a true association exits. The absence of a longitudinal relationship between muscle mass and incident and worsening knee OA in this observational study, in the context of associations between specific strength (strength/mass), suggests that future studies should focus on better clarifying whether muscle activation (including the role of pain in inhibiting or modifying activation) or neuromuscular physiology (e.g. cell metabolism, calcium ion release or excitation-contraction coupling) may better explain the mechanism of the association of strength and specific strength with risk for knee OA.

These results are consistent with those of other studies that have found impaired neuromuscular activation to be associated with knee OA. Mairet *et al.* reported that neuromuscular efficiency (the ratio of maximum voluntary contraction to electromyographic activity) was lower in the rectus femoris and vastus medialis of limbs with knee OA[17]. That study also found that measures of muscle architecture—fascicle length and pennation angle—did not explain the weakness present in the context of knee OA, providing further evidence that the weakness observed with knee OA is better explained by neuromuscular activation than by muscle architecture. In another study, the central activation ratio explained 40% of the variance in quadriceps strength in limbs with KL grade 4 knee OA, demonstrating that muscle activation was a greater determinant of weakness than quadriceps lean cross sectional area in limbs with severe knee OA[18]. These observational findings also are consistent with interventional findings that EMG biofeedback appears to enhance quadriceps strengthening in adults with knee OA[19].

The finding that quadriceps specific strength is predictive of worsening JSN over time in women, but not in men is consistent with a number of other studies of strength and risk for knee OA[10, 11, 20]. Reasons for apparent differences between men and women could relate to biomechanical or neuromuscular factors or could relate to strength capacity being closer to a threshold for risk[21, 22]. Studies have revealed that women typically have less than 60 percent of the quadriceps strength of men, despite no significant difference in body mass index (a measure of relative body size)[11, 23]. This reduction in measured strength could result from reduced muscle mass and lever arms, but also may relate to impaired activation, as women presenting for total knee arthroplasty have been reported to have lower quadriceps activation levels than men[24]. Whether there is a lower strength reserve or lower level of muscle activation in women, if there is a threshold for strength necessary to protect the knee joint, then women would be closer than men to this threshold, and crossing it could compromise their ability to protect their knee joints.

One potential reason for reduced specific strength is pain inhibiting muscle activation. As described previously[10, 11], data from participants who reported knee pain that interfered with their ability to perform the isokinetic strength test were not included, as these strength measures both by the participants' reports and by examination of the data were found to be inaccurate measures of muscle strength (e.g. magnitudes smaller than the torque due to the weight of the limb). However, it is possible that some participants had knee pain of a level that led to inhibition of muscle activation, but was of an insufficient severity to prompt them to report inability to push during the test. These data were included, as excluding these or adjusting for pain could have prevented detection of an association between low strength per unit muscle mass and the outcomes of interest. Further study is necessary to determine the role of pain and other factors in explaining the mechanism for the associations detected.

This study advanced understanding of a potential mechanism for the longitudinal relationship between knee extensor strength and risk for incident symptomatic and progressive knee OA. The sample size and the ability to distinguish muscle from the fat and mineral components were stregnths of this study. However, there are some important limitations to the accuracy of muscle mass estimations using DXA[28–30], relating to the inclusion of an increased proportion of non-contractile lean components of adipose tissue in more obese adults. In a prior study in which the entire thigh region of interest was sampled on DXA scans, the error in estimates of lean mass was found to be attenuated by using a correction factor (eliminating the error due to greater fat tissue in obese participants)[12]. However, in our current study, rather than including the entire thigh in the region of interest, we excluded extramuscular adipose tissue medial and lateral to the muscle shadow when selecting the thigh muscle subregions. Although some adipose tissue remained anterior and posterior to the muscle, error in the estimates of muscle mass were minimized by excluding much of the excess adipose tissue present in obese participants. Confirmatory analyses, in which we corrected for thigh fat mass both in and around the muscle,[12] revealed that correction of the DXA measurement of muscle mass was unnecessary. The correction factors were based upon specific strength when segmenting the quadriceps muscle, while excluding fat mass on CT scan, in comparison with when using DXA with the fat mass included. Use of these validated correction factors in the current study, in which much of the fat mass was excluded from the region analyzed, resulted in odds ratios and 95% confidence intervals with very similar magnitudes and statistical significance, confirming that the results were not due to error in the predictor measures. These consistent results also support that the use of thigh muscle mass rather than isolated quadriceps muscle mass did not interfere with assessment of relationships between muscle mass or specific strength and the outcomes. This was possible due to the high correlation between quadriceps muscle mass and thigh muscle mass once fat mass is sufficiently excluded[12].

CONCLUSIONS

A strength of this study was that it was conducted in the same cohort in which prior studies of the relationship between knee extensor strength and knee OA were conducted. This enables inferences regarding the mechanism for those associations. Although greater knee extensor strength and specific strength are associated with a lower risk for symptomatic knee OA and worsening JSN in women in this cohort, greater thigh muscle mass does not appear to be associated with a lower risk for incident or worsening knee OA. These findings suggest that future studies of risk for knee OA should focus on clarifying the role of neuromuscular activation and physiology of the knee extensor muscles.

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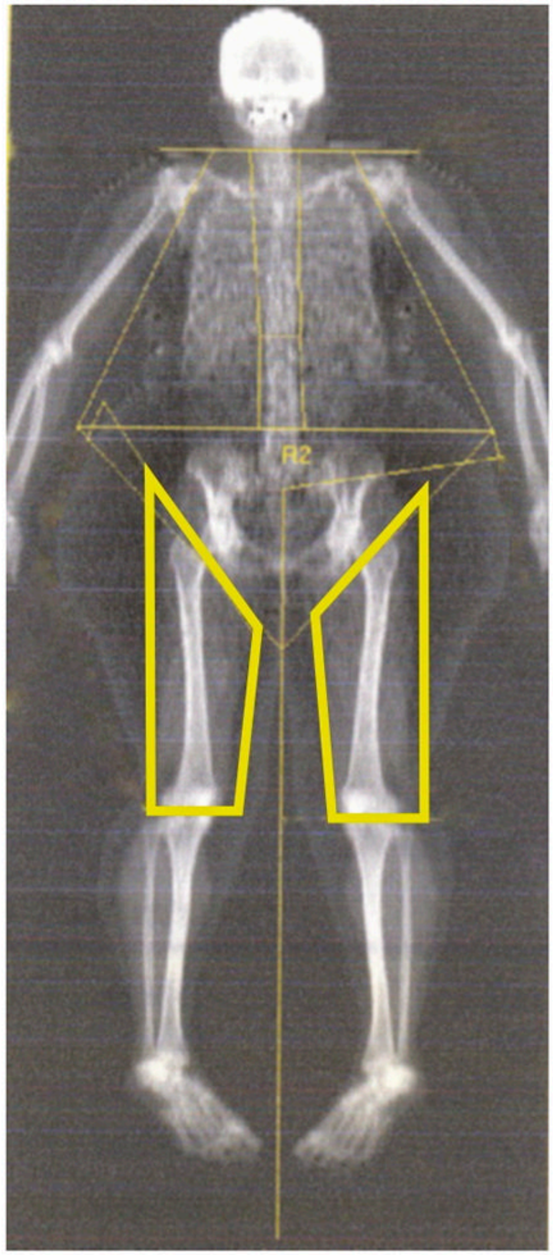

Figure 1.
Regions of Interest for Thigh Muscle Mass Measurements

Table 1

Characteristics of Participants Included in Each Analysis

	Characteristic	Incident Radiographic Knee OA	Incident Symptomatic Knee OA	Worsening Joint Space Narrowing
Men	**Participants (Knees)**	428 (715 knees)	519 (935 knees)	514 (948 knees)
	Age (mean±SD)	61.6±7.6 years	62.5±7.9 years	62.3±7.9 years
	BMI (mean±SD)	29.8±4.9 kg/m^2	30.1±5.0 kg/m^2	30.0±5.0 kg/m^2
	Surgery	6.3% (45 knees)	10.6% (99 knees)	11.3% (107 knees)
Women	**Participants (Knees)**	585 (992 knees)	769 (1373 knees)	784 (1453 knees)
	Age (mean±SD)	61.7±7.8 years	62.6±7.9 years	62.5±7.9 years
	BMI (mean±SD)	29.6±5.5 kg/m^2	30.3±5.9 kg/m^2	30.4±6.0 kg/m^2
	Surgery	4.9% (49 knees)	6.8% (93 knees)	8.1% (117 knees)

Table 2

Associations between thigh muscle mass and incident radiographic and incident symptomatic knee OA

	Sex-specific tertiles of thigh muscle mass	OR (95% CI) for Incident Radiographic Knee OA {N}	OR (95% CI) for Incident Symptomatic Knee OA {N}
Men	**Highest**	1.09 (0.41, 2.89) {n=238; 8.0%}	0.71 (0.34, 1.50) {n=312; 7.4%}
	Middle	0.88 (0.37, 2.07) {n=239; 5.4%}	0.45 (0.22, 0.92) {n=312; 4.5%}
	Lowest	Reference {n=238; 5.5%}	Reference {n=311; 10.3%}
	P for linear trend	0.8491	0.2952
Women	**Highest**	0.87 (0.42, 1.82) {n=331; 9.7%}	0.73 (0.39, 1.35) {n=458; 9.0%}
	Middle	0.96 (0.50, 1.85) {n=331; 8.8%}	1.03 (0.61, 1.73) {n=458; 10.0%}
	Lowest	Reference {n=330; 7.9%}	Reference {n=457; 9.4%}
	P for linear trend	0.7093	0.3435

Table 1: Sex-specific odds ratios (95% confidence intervals) for by tertile of thigh muscle mass, adjusted for age, BMI, history of knee surgery {Number of observations; % with outcome}

Table 3

Associations between specific strength and incident radiographic and incident symptomatic knee OA

	Sex-specific tertiles of specific strength	OR (95% CI) for Incident Radiographic Knee OA {N}	OR (95% CI) for Incident Symptomatic Knee OA {N}
Men	**Highest**	0.99 (0.43, 2.27) {n=217; 6.0%}	0.55 (0.27, 1.09) {n=284; 5.3%}
	Middle	1.05 (0.48, 2.30) {n=217; 6.5%}	0.53 (0.28, 1.01) {n=284; 5.6%}
	Lowest	Reference {n=216; 6.5%}	Reference {n=284; 11.3%}
	P for linear trend	0.9870	0.0720
Women	**Highest**	0.78 (0.39, 1.55) {n=313; 8.0%}	0.29 (0.16, 0.55) {n=432; 4.6%}
	Middle	0.76 (0.43, 1.33) {n=314; 8.0%}	0.38 (0.23, 0.61) {n=433; 6.5%}
	Lowest	Reference {n=313; 9.9%}	Reference {n=432; 16.0%}
	P for linear trend	0.4739	<0.0001

Table 2: Sex-specific odds ratios (95% confidence intervals) for by tertile of specific strength, adjusted for age, BMI, history of knee surgery {Number of observations; % with outcome}

Table 4

Association between thigh muscle mass and joint space narrowing

	Sex-specific tertiles of thigh muscle mass	OR (95% CI) for worsening whole knee JSN	OR (95% CI) for worsening TF JSN	OR (95% CI) for worsening PF JSN
Men	**Highest** (n=316)	1.50 (0.92, 2.45) {25.6%}	1.53 (0.92, 2.54) {25.3%}	2.41 (0.77, 7.47) {2.5%}
	Middle (n=316)	1.33 (0.87, 2.04) {21.8%}	1.30 (0.83, 2.03) {20.3%}	1.40 (0.45, 4.34) {1.9%}
	Lowest (n=316)	Reference {18.4%}	Reference {17.1%}	Reference {1.9%}
	P for linear trend	0.1064	0.0975	0.1357
Women	**Highest** (n=484)	0.87 (0.58, 1.32) {27.1%}	0.85 (0.55, 1.30) {24.2%}	0.98 (0.47, 2.05) {6.2%}
	Middle (n=485)	0.79 (0.55, 1.12) {21.7%}	0.71 (0.48, 1.03) {17.7%}	1.16 (0.63, 2.13) {6.4%}
	Lowest (n=484)	Reference {23.6%}	Reference {20.7%}	Reference {5.2%}
	P for linear trend	0.4748	0.4073	0.9786

Table 3: Sex-specific odds ratios (95% confidence intervals) for by tertile of thigh muscle mass, adjusted for age, BMI, history of knee surgery {Number of observations; % with outcome}

Table 5

Associations between specific strength and joint space narrowing

	Sex-specific tertiles of specific strength	OR (95% CI) for worsening whole knee JSN	OR (95% CI) for worsening TF JSN	OR (95% CI) for worsening PF JSN
Men	**Highest** (n=286)	1.29 (0.83, 2.00) {22.7%}	1.31 (0.83, 2.05) {21.7%}	0.54 (0.16, 1.87) {1.4%}
	Middle (n=286)	1.08 (0.71, 1.63) {21.3%}	1.12 (0.73, 1.70) {20.6%}	0.24 (0.05, 1.08) {0.7%}
	Lowest (n=286)	Reference {23.1%}	Reference {21.7%}	Reference {3.5%}
	P for linear trend	0.2594	0.2443	0.2678
Women	**Highest** (n=455)	0.60 (0.41, 0.88) {18.5%}	0.62 (0.41, 0.94) {15.4%}	0.72 (0.36, 1.42) {4.4%}
	Middle (n=455)	0.63 (0.45, 0.87) {21.1%}	0.68 (0.49, 0.95) {18.7%}	1.03 (0.56, 1.87) {6.6%}
	Lowest (n=454)	Reference {30.8%}	Reference {26.2%}	Reference {6.6%}
	P for linear trend	0.0072	0.0186	0.3656

Table 4: Sex-specific odds ratios (95% confidence intervals) for by tertile of specific strength, adjusted for age, BMI, history of knee surgery {Number of observations; % with outcome}