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Muscle Mass Is More Strongly Related To Hip Bone Mineral Density Than Is Quadriceps Strength Or Activity Level In Adults Over Age 50

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Abstract

This cross-sectional study examined whether reduced hip bone mineral density (BMD) is better explained by isokinetic knee extensor strength (KES), lower limb lean body mass (L-LBM), or activity level (PASE). Through population-based recruitment, 1543 adults without knee osteoarthritis were recruited. For men and women respectively, means $\pm$ SD were: Age 60.8 $\pm$ 8.0 and 61.1 $\pm$ 7.9 years; BMI 29.6 $\pm$ 4.6 and 29.1 $\pm$ 5.4 kg/m²; hip BMD 1.025 $\pm$ 0.138 and 0.895 $\pm$ 0.128 g/cm²; KES 124.9 $\pm$ 41 and 72.7 $\pm$ 22.9 N•m; L-LBM 10.3 $\pm$ 1.5 and 7.0 $\pm$ 1.2 kg; and PASE 206.4 $\pm$ 99.7 and 163.8 $\pm$ 77.0. The relationship between BMD and KES in men ($r=.21$, $p<.002$) and women ($r=.23$, $p<.001$) was significant before adjustment. However, this association was no longer significant after controlling for L-LBM. Even after controlling for age, race, and sex, the association between BMD and KES was better explained by L-LBM (partial $R^2=.14$, $p<.001$) than by PASE (partial $R^2=.00$). Allometric scaling of KES to body size attenuated the association of BMD with KES (Std Beta=.03). The significant association between BMD and L-LBM (Std Beta=.36) remained stronger than that between BMD and weight (Std Beta=.21). Therefore, muscle mass accounted for a greater proportion of the variance in hip BMD than KES or activity level and explained a significant proportion of the association between weight and BMD.

Keywords

Bone mineral density; quadriceps strength; muscle mass; physical activity level; allometric scaling; rehabilitation

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Introduction

Studies have demonstrated that spine extensor muscle weakness is associated with low spine bone mineral density (BMD),(1,2) and spine deformity.(3) However, there are differing results regarding whether knee extensor strength is an independent predictor of BMD.(4) The relationship between BMD and knee extensor strength is of clinical interest since weakness is a possible contributor to increased risk and impact severity of falls,(5) and individuals with low BMD are at greatest risk for fractures with falls. Therefore, an association between these would support a need for knee extensor strengthening in a group with dual risk factors.

To date, populations studied have been mainly normal weight (body mass index $<25 \text{ kg/m}^2$), and this may significantly influence results, considering that increased obesity can be associated with both increased lean body mass (LBM) and lower activity level.(6,7) However, given the fact that 39% of older adults (age ≥ 54 years) in the United States are obese and over 65% meet criteria for being either overweight or obese,(8) there is a need to examine the relationship between BMD and knee extensor strength in a population which includes obese adults.

Study of knee extensor strength must also consider the potential effects of lower limb lean body mass (L-LBM), weight, and age, as these have been shown to be inter-related and also related to hip BMD.(7,9) Activity level, weight, and age may also be related to hip BMD. Using multiple regression models to consider these relationships has revealed that in non-obese women knee extensor strength is strongly related to femoral neck BMD, but not to spinal BMD, suggesting a local effect. Due to the effects of body mass on both strength and BMD, it is appropriate to use allometric scaling to control for the effect of body mass when examining the relation between strength and BMD.(4,10–12) Additionally, to guide therapy to maintain or increase hip BMD, it would be useful first to examine whether there is a relationship between knee extensor strength and BMD and then clarify whether this relationship is better explained by muscle bulk (L-LBM) or physical activity.

The aim of this study was to determine whether there is an association between BMD and several factors that could be targets of rehabilitative interventions: strength, lean body mass and activity, testing the following hypotheses: (1) Knee extensor strength is significantly associated with total hip BMD, (2) Lean body mass in the lower limbs explains the association between knee extensor strength and BMD, (3) Activity level does not account for the relationship between knee extensor strength and BMD, (4) The association between BMD and knee extensor strength is better explained by L-LBM than by activity level. Finally, these results are not modified by either (5) stratifying by BMI or (6) adjusting strength for body size. The present report used cross-sectional data from the initial examination of the Multicenter Knee Osteoarthritis (MOST) Study.

Materials and Methods

Subjects

Subjects were excluded if they had radiographic knee osteoarthritis (Kellgren-Lawrence grade ≥ 2) or knee arthroplasty, possible confounders for the relationship between BMD and both knee extensor strength and L-LBM. Subjects were selected from a population-based cohort of adults, age 50–79, enrolled in the Multicenter Osteoarthritis (MOST) Study, in which eligible participants were targeted to have a body mass index (BMI) over 25 kg/m^2 or prior knee injury or surgery. The MOST Study excluded adults with rheumatoid arthritis or cancer.

Radiograph protocol for assessment of knee osteoarthritis in the MOST study has been described previously.(13) Knee osteoarthritis was defined as Kellgren-Lawrence grade 2 or

greater at standard image size on posteroanterior weight-bearing semi-flexed knee radiographs. (14) All subjects underwent an informed consent process approved by the Institutional Review Boards at each of the investigators' institutions prior to participating in research protocols.

Bone Mineral Density and Body Composition Measurements

Lower limb lean body mass (g) and total hip bone mineral density (g/cm^2) were measured using a Hologic QDR 4500W Dual Energy X-ray Absorptiometry (DXA) (Hologic Inc., Bedford, MA: Software Version 12.0). Scans of the hip were conducted using Fast Array mode unless a subject weighed 170 pounds or greater in which case Array mode was used. Whole body scans for body composition were conducted in default mode (Array) and lower limb lean body mass was obtained by using the body composition analysis software provided by the manufacturer.

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 was collected using standard quality assurance protocols and reviewed monthly by the University of California San Francisco Coordinating Center DXA Quality Assurance Center.

Height and Weight Measurements

Height was measured with a wall-mounted Harpenden stadiometer (Holtain Ltd., Crosswell, Crymych, Pembrokeshire, UK) and followed a written protocol. Height was assessed during full inspiration to the nearest 1 mm. The measurement was repeated twice and if these differed by >3 mm, 2 additional measurements were taken.

Weight was measured with a standard medical beam balance with the certified examiner standing behind the subject. Weight was recorded to the nearest 0.1 kg. The scale was calibrated monthly with a 50 kg weight for accuracy as well as with 5, 10, 15 and 20 kg weights for linearity calibration. Body mass index (BMI) was calculated as weight divided by height squared, and obesity was defined as $\text{BMI} \geq 30 \text{ kg}/\text{m}^2$.(15,16)

Knee Extensor Strength

Concentric knee extensor strength was assessed with a Cybex 350 computerized isokinetic dynamometer (Avocent, Huntsville, AL) at 60 degrees per second and a chair back angle of 85 degrees. HUMAC software version 4.3.2/Cybex 300 for Windows98 Software Package was used for data acquisition. Subjects' knee extensor strength was considered the peak torque in $\text{N}\cdot\text{m}$ obtained over 4 trials. Trained examiners, certified in the standardized MOST strength testing protocol, underwent annual recertification to assure uniformity in following the strength testing protocol and standardized script for subject testing. Examiners calibrated the isokinetic dynamometer position, angular velocity and torque (at 25 and 245 $\text{N}\cdot\text{m}$) monthly. Subject-specific knee extensor strength was defined as the mean of the peak knee extensor strength for both lower limbs.

Participants were excluded from strength testing for a systolic blood pressure greater than 199 mmHg, diastolic blood pressure greater than 109 mmHg, history of cerebral aneurysm, cerebral bleeding within the past six months, back surgery within the previous 3-months, myocardial infarction or cataract surgery within the previous 6-week period, untreated inguinal hernia, or thigh dimensions that precluded use of a thigh strap during the test.

Activity Level

We used a validated survey, the Physical Activity Scale for the Elderly (PASE: New England Research Institute, Watertown, MA) to assess activity.(17)

Statistical Methods

SAS Version 9.1 (SAS Institute Inc., Cary, NC) was used for all analyses and overall significance level was .05. Continuous variables listed below were summarized for each group with means $\pm$ SD. Pearson correlation coefficients were calculated between continuous variables to assess for colinearity prior to multivariate analyses. We performed linear regression with BMD as a continuous dependent variable, and knee extensor strength as a continuous independent variable with covariates: sex, age and race. To address the respective contributions of L-LBM and PASE to the relationship between BMD and knee extensor strength, we performed linear regression analyses.

We also examined categorized BMD in sex-specific strata for pair-wise comparisons. In these parallel analyses, ANOVA was used to examine these associations comparing between strata (i.e. between BMD strata and between BMI strata). Subjects were classified into the following 6 BMD strata: <0.8 , $0.8\leq 0.9$, $0.9\leq 1.0$, $1.0\leq 1.1$, $1.1\leq 1.2$, >1.2 g/cm². In addition to treating BMI as a continuous variable in the overall analysis, relationships between the primary variables of interest were examined for each of the following strata: normal weight (BMI <25 kg/m²), overweight ($25\leq$ BMI <30 kg/m²) and obese (BMI ≥ 30 kg/m²). We calculated the associations between BMD and (1) knee extensor strength and (2) L-LBM within each sex-specific BMD strata, giving 12 correlations for each of these 2 analyses. Tukey's method was used to control for multiple comparisons in the stratified analysis.

To assess whether L-LBM better explains variance in BMD than knee extensor strength, standardized beta estimates were calculated from linear regression analyses. The contributions of (1) L-LBM and (2) knee extensor strength were examined with BMD as a continuous dependent variable. We then tested the hypothesis that the standardized beta (in order to compare strength of associations with BMD on the same scale) would be greater for L-LBM than for knee extensor strength.

Allometric scaling was used to control for the independent effect of body size on knee extensor strength in each of the preceding analyses. Body size was estimated as weight $\times$ height, as reported by Owings *et al.* (4) The scaled relationship between knee extensor strength (KES) and body size (m) is: $KES = S_n m^b$ where S_n is normalized strength for a population. A logarithmic transformation of the equation yields $\ln KES = \ln S_n + b(\ln m)$. Therefore S_n was calculated from the regression line of a scatter plot of KES and weight $\times$ height for the population by $S_n = KES/m^b$. Strength data was scaled by first calculating the scaling parameter (b) by regressing the log of KES on the log of weight $\times$ height. (4) Total hip BMD was then regressed on normalized KES ($KES/[weight \times height]^b$). T-scores and Z-scores were not utilized since our analyses adjusted for age, sex and race and were designed to assess for relationships between bone mineral density and muscle strength and mass.

Results

A cohort of 3026 (1820F; 1206M) adults was recruited to the MOST Study and 1543 met inclusion criteria for this study (Figure 1). Complete data were available for 570 men and 809 women due to either exclusions for safe participation in the isokinetic strength or DXA scan protocols. Sex-specific characteristics for variables of interest are summarized in Table 1.

1. Relationship between knee extensor strength and total hip bone mineral density (BMD)

Mean peak knee extensor strength in men and women in the lowest 2 strata of hip BMD ($<.8$ and $.8-.9$ g/cm²) was significantly lower than that of subjects in each of the other strata (black and charcoal bars in Figure 2). There was a modest association between BMD and knee extensor strength in men ($r=.207$, $p=.0017$) and women ($r=.225$, $p<.0001$) (Figure 3a). After

adjusting for age, race and sex, knee extensor strength continued to be significantly associated with total hip BMD ($R^2=.28$, $p<.0001$).

2. Lower Limb Lean Body Mass (L-LBM) as an Explanatory Factor In The Relationship Between Knee Extensor Strength and BMD

Total hip BMD also was related to L-LBM in men ($r=.42$, $p<.0001$) and women ($r=.44$, $p<.0001$) (Figure 3b). Mean L-LBM was significantly lower in lower strata of hip BMD. Additionally, L-LBM remained significantly associated with BMD after (1) controlling for age and race; (2) controlling for age, race, sex and PASE score; and (3) for men and women separately (for L-LBM: all $p<.0001$).

Once L-LBM entered the regression model, knee extensor strength no longer was significantly associated with BMD in either sex (Table 2 and Table 3). Controlling for age, race and sex, L-LBM remained significantly associated with BMD in normal weight, overweight, and obese subjects (all $p<.0001$). For each of these BMI strata, knee extensor strength was no longer associated with BMD with L-LBM in the model.

3. Activity as a Factor in the Relationship Between Knee Extensor Strength and BMD

Activity, as measured by PASE, was weakly correlated with total hip BMD in univariate analysis ($r=.17$). However, activity was not significantly associated with BMD after controlling for knee extensor strength, age, race and sex (Table 2).

4. Comparison of L-LBM and Activity as Predictors of hip BMD

As noted above, L-LBM was significantly associated with BMD alone, and after controlling for age, race, sex, knee extensor strength and activity level (Table 2: for L-LBM in each model: all $p<.0001$). In contrast, activity level was not significantly associated with BMD in any of these models. Pearson correlation coefficients comparing L-LBM with knee extensor strength in each BMD strata ranged from .26 to .51 in men and .13 to .59 in women. After controlling for L-LBM, knee extensor strength no longer significantly differed between BMD strata in men or women (Table 3). Standardized beta estimates were consistently higher for L-LBM than for knee extensor strength (Table 3).

5. Effect of BMI on the relationship between knee extensor strength and total hip (BMD)

The association between BMD and knee extensor strength was attenuated among patients in higher BMI strata, with model R^2 for normal weight, overweight and obese of .31, .28, and .19 respectively. Controlling for age, race and sex, knee extensor strength was significantly associated with BMD in normal weight ($p=.0002$) and overweight ($p=.0064$), but not in obese ($p=.1891$) subjects.

6. Allometric scaling of strength relative to body size

Calculation of the allometric scaling parameter (b) revealed an exponent of 0.974 in this population ($\ln[\text{KES}]=.974*\ln[\text{weight} \times \text{height}]-7.09$). Compared with the correlation between BMD and non-normalized knee extensor strength ($r=.41$ $p<.0001$), the correlation between BMD and knee extensor strength normalized for body size ($r=.14$ $p<.0001$) was diminished, indicating that body size accounted for much of the correlation between BMD and knee extensor strength.

Additional analyses confirmed that body size was a better predictor of BMD than either knee extensor strength or knee extensor strength normalized for body size. Assessment of which component of body size explained BMD best was conducted by regressing BMD on knee extensor strength, L-LBM, weight and height. This regression confirmed that knee extensor

strength was not associated with BMD after controlling for anthropometric variables (weight, height and L-LBM). Standardized beta estimate was greatest for L-LBM, indicating that L-LBM accounted for a greater proportion of the variance in BMD than did either weight or height (Table 4).

Discussion

The results of this study support a positive association between knee extensor strength and BMD, in non-obese individuals. However, the association between knee extensor strength and total hip BMD was explained best by lower limb lean body mass (L-LBM), and L-LBM accounted for a higher amount of the variance in BMD than did knee extensor strength. Therefore, the varying results regarding the relationship between hip BMD and knee extensor strength in prior studies may have been due to not considering the role of L-LBM.

Our results may have differed from prior studies that examined the relationship between BMD and strength due to differences in the age of subjects studied. Studies of older adults have reported that low knee extensor strength is associated with low BMD,(18,19) although these did not control for L-LBM. In contrast, studies of adults under age 42 have suggested that physical activity is a better predictor of BMD than is knee extensor strength.(20–22) Similarly, studies of younger athletic men have revealed that, although knee extensor strength is associated with BMD at the hip, activity level predicts this relationship better than either knee extensor strength or lean body mass (LBM).(23)

Alternatively, differences between our results and those of prior studies may stem from measurements used. For example, use of isometric strength testing provides strength data at only 90°, (18) an angle that may be relevant only for standing from a seated position. However, use of isokinetic strength testing allowed measurement of knee extensor strength at multiple angles and angular velocities, providing knee extensor strength data potentially more relevant to standing, ambulation, and fall risk.

Correlations between BMD and knee extensor strength in men and women in our study were similar to those reported in other studies that examined proximal muscle strength and hip region BMD ($r = .19-.28$).(24,25) Additionally, the relationship that we detected was similar to findings of a study of similarly aged group of women with rheumatoid arthritis. (26) In that study, isokinetic knee extensor strength was found to have a partial r of 0.30, significant independent of age, height, weight or disease-related factors. Although corticosteroid use was considered as a covariate in those analyses, L-LBM was not considered, so it is not known whether knee extensor strength would have remained a significant predictor of BMD after controlling for L-LBM.

Our findings were concordant with those reported for the more racially diverse Health ABC cohort in which L-LBM was a significant independent contributor to overall BMD across race and sex.(25) However, our study found a significant association between L-LBM and hip BMD in both men and women, whereas in Health ABC, a study of adults aged 70–79 years, this was found only in men. Considering that our subjects were younger than those in Health ABC may explain some of this discordance for women. These results, as well as those of our study, suggest that maintenance or increase of hip BMD might be attained through maintenance or increase of L-LBM.(25)

An interesting aspect of these results was that following allometric scaling of strength relative to body size (weight $\times$ height), Knee extensor strength no longer significantly predicted hip BMD. This finding concurs with results reported by Owings *et al.*(4) Our findings that body weight and height accounted for 27% and 4% of the variance in hip BMD also were very similar to Owings' findings (30% and 10% respectively). The repetition of these findings strengthens

our belief that it is appropriate to scale strength to body size. It is also in agreement with numerous epidemiological studies which found that body weight was the strongest predictor of variance in BMD in models tested.(27,28) This was particularly the case at weight-bearing sites. Finally, the result of our calculation of the allometric scaling parameter for our population (0.974) was very close to the theoretical value of 1.0 for muscle torque,(11) supporting construct validity for the methods used.

In contrast to reports in which activity level accounted for the relationship between knee extensor strength and BMD in younger women,(23) in our sample of older adults, activity level by PASE was not a significant predictor of BMD. The absence of an association between PASE score and BMD after controlling for muscle parameters was consistent with prior studies. Neither knee extensor strength, nor activity level on the Northwick Park activity index was found to be significantly associated with BMD in older women (mean age 80) who had sustained hip fractures.(29) In that study, there was a possibility that the relationship could have been confounded by the recent injury and the associated change in lifestyle. The repetition of these findings in the current study strengthens the conclusion that overall activity level was not significantly associated with BMD. This finding also suggests that, in contrast to high intensity exercise which has been related to increasing femoral neck BMD,(30,31) activity level rated by the PASE and Northwick Park indices may not be sufficient to affect hip BMD.

Other investigators suggested that BMD and knee extensor strength may be related through genetic factors that influence the size of muscles and bones.(26) Our study extended prior knowledge not only by confirming that body weight is associated with BMD to a greater degree than knee extensor strength, but also by finding that lower limb muscle bulk better explained variance in hip BMD than knee extensor strength, height or even weight. Additionally, after controlling for L-LBM, activity score was not significantly associated with hip BMD. These results suggest that increasing muscle bulk may be a more effective strategy than increasing activity to increase hip BMD in interventional studies.

A strength of this study was the volume of data and inclusion of subjects with BMD over the range of 0.44–1.45g/cm². Our population, enriched with overweight and obese subjects, allowed examination of the relationship between L-LBM, knee extensor strength, and BMD in these heavier groups, which is important because these factors are also associated with higher BMI. Although prior studies of healthy women demonstrated a relationship between BMD and knee extensor strength,(21,32) to our knowledge, the finding that knee extensor strength is not a significant predictor of BMD in obese adults has not been reported previously. This finding may indicate that increased body weight sufficiently loads the skeleton to maintain higher hip BMD in obese adults, whereas loading by the pull of the knee extensors is a more significant contributor to maintaining higher BMD in non-obese adults. Longitudinal study of the temporal relationship between measures of strength and body weight and measure of hip BMD may help to clarify the mechanism for this pattern.

A limitation to this study was that, due to the selective recruitment of overweight and obese subjects, body weight was skewed upwards compared with the general population. Future study should be longitudinal to clarify causal relationships and should also aim to recruit subjects over a broad range of BMI and BMD. Another limitation may be that activity was measured by self-report at one time point, rather than by an objective measure of physical activity over a longer period of time.

The results of this study suggest that increasing muscle bulk, for example through lower limb resistance training, may be more effective for increasing hip BMD than increasing overall physical activity. This inference is supported by evidence that change in BMD with exercise correlates with the amount of weight lifted.(33) Considering that muscle bulk-forming exercise

has a dose-response relationship with BMD, strategies to preserve hip BMD might best target L-LBM.

Conclusion

Lower hip BMD, a risk factor for fall-related fractures, appears to be associated with low L-LBM, and this lower muscle mass accounts for a greater proportion of the variance in hip BMD than knee extensor strength or activity level. Increasing muscle bulk should be examined longitudinally to assess whether BMD can be maintained or increased, with the goal of reducing falls and fracture-related morbidity.

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Figure 1.
Subject Inclusion and Exclusion

Figure 2.
Distributions of Knee Extensor Strength and L-LBM by BMD Group

Figure 3.

Figure 3a: Association Between BMD and Strength (KES)

Figure 3b: Association Between BMD and L-LBM

Table 1

Subject Characteristics (mean±SD)

	Men (N=653)	Women (N=890)	All (N=1543)
Age (years)	60.8 ± 8.0	61.1 ± 7.9	61.0 ± 8.0
Body Mass Index (kg/m ²)	29.6 ± 4.6	29.1 ± 5.4	29.3 ± 5.1
Hip Bone Mineral Density (g/cm ²)	1.025 ± 0.138	0.895 ± 0.128	0.950 ± 0.147
Knee Extensor Strength (N•m)	124.9 ± 41.0 ^a	72.7 ± 22.9 ^a	94.4 ± 40.8
Lower Limb Lean Body Mass (g)	10269.7 ± 1475.4	6973.5 ± 1170.7	8359.3 ± 2087.4
Physical Activity Scale for the Elderly	206.4 ± 99.7	163.8 ± 77.0	181.8 ± 89.8

^aStrength measurement was available for 578 men and 812 women.

Table 2

Overall Regression Analyses

Dependent Variable	Independent Variables	R ²
BMD	KES	.05
BMD	KES, age, race, sex	.28
BMD	KES, age, race, sex, PASE	.28
BMD	KES, age, race, sex, L-LBM	.31
BMD	KES, age, race, sex, L-LBM, L-LBM*sex	.37
BMD	KES, age, race, sex, L-LBM, L-LBM*sex, PASE	.37

Note: L-LBM*sex represents the interaction between L-LBM and sex

Table 3

Comparison of Stratified Regression Models

Model	R ²	β Estimates
BMD = KES (age, race)	Men: .04 Women: .12	KES: .16 KES: .15
BMD = L-LBM (age, race)	Men: .17 Women: .25	L-LBM: .39 L-LBM: .39
BMD = KES, L-LBM (age, race)	Men: .17 Women: .25	KES: .01; L-LBM: .39 KES: .02; L-LBM: .39
BMD = KES, L-LBM (age, race)	Normal weight: .35 Overweight: .31 Obese: .26	KES: .16; L-LBM: .39 KES: .05; L-LBM: .38 KES: -.05; L-LBM: .48

Table 4

Standardized Estimates for Full Model

Variable	Standardized β Estimate	Partial R^2 (Type II)	p-value
KES	0.02773	0.0005	0.3973
Sex	-0.11456	0.0052	0.0078
Age	-0.12275	0.0185	<.0001
Race	0.03677	0.0021	0.0911
PASE	0.02281	0.0007	0.3228
Weight	0.21361	0.0185	<.0001
Height	-0.12659	0.0084	0.0007
L-LBM	0.36319	0.0210	<.0001