

Association between bone mineral density, lean mass, and fat mass among healthy middle-aged premenopausal women: a cross-sectional study in southern Sri Lanka

Sarath Lekamwasam Æ Thilak Weerathna Æ Mahinda Rodrigo Æ Wasantha Kodikara Arachchi Æ Duminda Munidasa

Received: 7 January 2008 / Accepted: 9 March 2008 Ó The Japanese Society for Bone and Mineral Research and Springer 2008

60

Abstract Associations between lean mass, fat mass, and bone mass have been reported earlier; however, most of those studies have been done in Caucasian populations, and data from Asian countries, especially those in South Asia, are limited. We examined the associations between lean mass, fat mass, bone mineral density (BMD), and bone mineral content (BMC), determined by dual-energy X-ray absorptiometry technology, in a group of healthy, middle-aged, premenopausal female volunteers. The mean (SD) age of the women ($n = 106$) was 42.1 (6.1) years and the mean (SD) body mass index was 24.3 (3.6) kg/m^2 . Total body BMD, total body BMC, and BMD in total spine, total hip, and femoral neck showed statistically significant partial correlations (adjusted for age) with total fat mass ($r = 0.19\text{--}0.43$, $P \leq 0.05$) and lean body mass ($r = 0.28\text{--}0.54$, $P \leq 0.05$). Truncal fat mass correlated positively with total body BMC and BMD at total hip and femoral neck ($r = 0.33\text{--}0.40$, $P \leq 0.001$). When a stepwise regression model was fitted, lean mass remained the strongest predictor of total body BMD, total body BMC, and total spine BMD (regression coefficients = 0.004–0.008 g/cm^2 per

S. Lekamwasam (&) Center for Metabolic Bone Diseases, Faculty of Medicine, Galle 80000, Sri Lanka e-mail: sarathlk@sltnet.lk

T. Weerathna Center for Lipid Disorders, Faculty of Medicine, Galle, Sri Lanka

M. Rodrigo Department of Anatomy, Faculty of Medicine, Galle, Sri Lanka

W. K. Arachchi D. Munidasa Teaching Hospital, Karapitiya, Sri Lanka

$P \leq 0.001$).

1-kg change BMD and BMC increased across the tertiles of lean mass (P trend \backslash 0.05). We show that lean mass is the strongest predictor of total body BMC and BMD at different sites, although positive correlations with fat mass also exist.

Keywords Lean mass Fat mass Bone mineral density Premenopausal women Sri Lanka

Introduction

Although there are various ways to estimate body composition, dual-energy X-ray absorptiometry (DXA) is widely used in research and clinical settings [1]. DXA uses two X-ray beams of different energies; high and low, which are attenuated preferentially while passing through different body compartments. The low-energy beam is attenuated by the soft and bone tissues; the high-energy beam is attenuated only by the bone tissue. The degree of attenuation of the two beams is used to estimate bone mineral content (BMC), bone mineral density (BMD), and fat mass and lean mass. BMD and BMC, which are highly correlated with bone mass [2], are used to determine the fracture risk of an individual with low bone mass [3].

Previous studies have demonstrated significant associations between different body compartments, and some of these associations were age specific [4–7]. In young and premenopausal women, lean mass was the main predictor of BMD [4, 5], whereas in old or postmenopausal women, fat mass predicted BMD better than lean mass [6, 7]. These studies would help in understanding age-related trends in body composition in different populations. Increased fat mass and reduced bone mass have clear clinical consequences, and this information would help in

in lean mass,

Similarly,

crude

1 3

understating the comorbidity associated with osteoporosis or hyperlipidemia.

Studies on body composition among South Asian women are scarce, which may reflect the restricted availability of facilities of estimating body composition in these countries. Women in South Asia can be expected to have associations different from those already reported from Western countries as South Asian women have a different lifestyle, which is associated with a high level of physical activity, marginal nutrition, multiparity, less smoking, and low alcohol consumption. This study was conducted in southern Sri Lanka

using a group of healthy, middle-aged, premenopausal volunteers to examine the associations between lean mass, fat mass, and BMD, and also to determine the strongest predictor of BMD at various sites.

Materials and methods

A group of healthy premenopausal female volunteers, aged 30 years or older and living in the neighborhood of the Faculty of Medicine, Galle, Sri Lanka, was included in the study. These volunteers responded to an open invitation displayed in public places within 1 km distance from the faculty. After a brief interview and physical examination, women with history of diabetes, hypertension, chronic renal or liver disease, hyperlipidemia, ischemic heart disease, endocrine diseases, or prolonged inflammatory conditions were excluded from the study. Women using bone-active medications such as systemic corticosteroids, heparin, vitamin D, or pharmacological doses of calcium were also excluded, and 113 women were selected for the study.

All consenting women completed a health-related questionnaire and underwent a detailed physical examination conducted at the Center for Lipid Disorders in the Faculty of Medicine, Galle, during which body measurements such as weight, height, and hip and waist circumference were recorded. All measurements were taken by the same technician, adhering to the standard protocols of defining these measurements. Weight was measured while wearing light clothes and after emptying the urinary bladder. Height was measured using a stadiometer.

A total body DXA scan was performed for all subjects using a Hologic Discovery scanner (Hologic, Bedford, MA, USA). DXA scanning was also performed over the lumbar spine and proximal femur of the nondominant side to estimate BMD in the total spine from L1 to L4 in the anteroposterior projection, total hip, and femoral neck region. The coefficient of variation of BMD measurements in the same machine has been published earlier [8].

Analytical software provided by the DXA manufacturer was used to analyze body composition. All scans were

J Bone Miner Metab **61**

analyzed by the same technician, adhering to the guidelines provided by the manufacturer, and total body bone mineral density, total body bone mineral content, and lean body mass were estimated. Furthermore, total fat mass and the regional fat mass over the abdomen, truncal fat mass, were measured using the same analytical software. Ethical approval for the study was obtained from the local Ethics Review Committee of the Faculty of Medicine, Galle, and all participants signed a consent form at the beginning of the study.

Statistics

Descriptive data of the sample are given as mean (SD) values. Associations between lean body mass, fat mass, BMC, and BMD were examined by partial correlations, after controlling for age. The regression model was fitted with BMD or BMC as the dependent variable and body mass index (BMI), waist–hip ratio, age, lean body mass, and total fat mass as independent variables; weaker variables were excluded in stepwise fashion to find the strongest predictor of BMC or BMD at different sites. Mean BMD across the tertiles of lean body mass, which emerged as the strongest predictor of BMD in the regression model, were compared using analysis of variance (ANOVA), initially unadjusted, and then adjusted for age and BMI. Data were not adjusted for smoking habits or alcohol consumption as only five women had consumed alcohol in the past. No subjects in the study group reported smoking. Two-tailed $P < 0.05$ was taken as the level of statistical significance. The SPSS version 10 for Windows was used for all statistical analyzes.

Results

Fifteen women were excluded and 113 subjects were recruited to the study. Seven DXA images were unsuitable for body composition measurements, and data of 106 women were included in the final analysis. Age of the women in the sample ranged from 30 to 54 years, with a mean of 42.1 (SD 6.1) years. Mean (SD) BMI and waist–hip ratio (WHR) were 24.3 (3.6) kg/m² and 0.87 (0.06), respectively (Table 1). When controlled for age, both lean mass and total fat mass showed positive and significant partial correlations with total body BMC and all BMD measurements. Furthermore, truncal fat mass correlated positively with total body BMC and BMD at total hip and femoral neck (r varied from 0.33 to 0.40; $P < 0.001$) (Table 2).

In the regression analysis, lean body mass remained the strongest predictor of total body BMC, total body BMD,

1 3

J Bone Miner Metab

6 2

and spine BMD. During this process, the model excluded the weak predictors such as age, BMI, waist–hip ratio, and total fat mass. However, BMD in the total hip and femoral neck showed less strong associations with the lean body mass, and in these sites BMI was the strongest determinant.

Independent of age, BMI, and total fat mass, a change of lean body mass by 1 kg was

0.002 0.002 0.4 0.004 0.002 0.056

BMI body mass index, BMD bone mineral density

^a Data are adjusted for age, BMI, and truncal and total fat mass ^b P values indicate statistical significance of regression coefficients

Table 2 Age-adjusted partial correlations between bone mineral density (BMD), bone mineral content (BMC), lean body mass, and total fat mass in 106 women included in the analysis

Total body BMC

0.87 (P < 0.001) –

Total spine BMD

0.63 (P < 0.001) 0.61 (P < 0.001) –

Total hip BMD

0.72 (P < 0.001) 0.66 (P < 0.001) 0.49 (P < 0.001) –

--

Femoral neck BMD

0.68 (P < 0.001) 0.68 (P < 0.001) 0.52 (P < 0.001) 0.83 (P < 0.001) –

-

Total fat mass

0.19 (P = 0.047) 0.41 (P < 0.001) 0.21 (P = 0.032) 0.43 (P < 0.001) 0.43 (P < 0.001) –

Lean body mass mass

Total body BMD Total body BMC Total spine BMD Total hip BMD Femoral neck BMD Total fat mass

Lean body mass

Truncal fat 0.28 0.17

(P = 0.004) (0.080) 0.54 0.33 (P \ 0.001) (\0.001) 0.22 0.17

(P = 0.02) (0.085) 0.37 0.038 (P \ 0.001) (\0.001) 0.40 0.40

(P \ 0.001) (\0.001) 0.69 0.84 (P \ 0.001) (\0.001)

0.58 (\0.001)

1 3

Table 4 Crude and adjusted (age, BMI) mean (SD) BMC and BMDs in the tertiles of the lean body mass

J Bone Miner Metab **63** P^a

0.62 \0.001 0.002 0.054 \0.001 0.001

0.04

0.065 \0.001 0.039 \0.001

0.04

Age (years)	Lean mass (g)	TBBMD ^b	TBBMD ^c	TBBMC ^b	TBBMC ^c	TSBMD ^b	TSBMD ^c	THBMD ^b	THBMD ^c	FNBMD ^b	FNBMD ^c
-------------	---------------	--------------------	--------------------	--------------------	--------------------	--------------------	--------------------	--------------------	--------------------	--------------------	--------------------

The lower third of lean mass (n = 35)

42.6 (1.03) 31466 (601.7) 1.024 (0.014) 1.030 (0.018) 1628.15 (33.33) 1636.13 (42.63) 0.876 (0.023) 0.884 (0.023) 0.862 (0.015) 0.891 (0.018) 0.701 (0.015) 0.730 (0.018)

The middle third of lean mass (n = 36)

41.3 (1.02) 35484 (593.3) 1.082 (0.014) 1.086 (0.016) 1812.77 (32.86) 1823.48 (38.27) 0.943 (0.022) 0.956 (0.021) 0.941 (0.015) 0.952 (0.016) 0.784 (0.015) 0.785 (0.016)

The upper third of lean mass (n = 35)

42.6 (1.03) 41407 (601.7) 1.088 (0.014) 1.081 (0.018) 1906.13 (33.33) 1885.24 (42.65) 0.950 (0.023) 0.939 (0.023) 0.962 (0.015) 0.928 (0.018) 0.805 (0.015) 0.787 (0.018)

TBBMD total body BMD, TBBMC total body ^a P contrasts mean differences between the three groups and estimation by analysis of variance (ANOVA) ^b Crude values ^c Age- and BMI-adjusted values expressed in g/cm²

Discussion

In the current study, we observed positive and significant correlations between lean mass, fat mass, BMC, and BMD measured at various sites. Lean mass emerged as the strongest predictor of total body BMC, total body BMD, and spine BMD. The categorical analysis showed a pattern in which the highest BMC and BMD were seen among women with higher lean mass and the lowest BMC and BMD were seen among women with lower lean mass; all these associations were independent of age and BMI.

Generally, BMI is considered a surrogate of the global adiposity or total fat mass. However, both lean mass and total BMC contribute to the weight of the person, which is used in calculating BMI. Therefore, BMI partly reflects the changes in lean mass and total BMC. In our study sample, BMI was more representative of total fat mass ($r = 0.89$) than either lean mass ($r = 0.66$) or total BMC ($r = 0.66$). We believe that when results were adjusted for BMI, it actually tested the effect of total fat mass on the analysis. In support of this, we did not see a change in the results when the categorical analysis was adjusted for the total fat mass.

A similar association between BMD and lean mass has been demonstrated among young or premenopausal women [4, 5], and it has been observed among healthy women [4–7] as well as in women with rheumatoid arthritis [9]. In contrast, fat mass showed a stronger association with BMD in postmenopausal or older women [6, 7].

Although current literature demonstrates an association between lean mass and BMD or BMC, especially among young women, the exact mechanism underlying this

association is not clear. The role of insulin-like growth factors and circulating adiponectin has been discussed [10, 11]. Physical activity appears to be the most plausible link between these measures. Physical activity has a positive influence on both BMD and lean mass [12, 13]. Compared to less physically active women, women who were more active had a stronger association between lean mass and BMD [14]. Less physical activity in old age may disrupt this association, allowing the fat mass to be the main predictor of bone density in postmenopausal women. If physical activity is the underlying mechanism between lean mass and bone density, the association can be expected to be more prominent among males. However, studies involving men are limited [15].

In our data collection, we had categorized our subjects as “very active,” “moderately active,” or “less active” depending on their current physical activities. Most of the women (80 subjects) were found to be in the “moderately active” group, and the data did not change materially when adjusted for their physical activity. This, we believe, is the result of inadequacy of recording the physical activity of our subjects.

Aromatization of estrogen precursors in the peripheral adipose tissue and skin is the main

source of estrogen in postmenopausal women. The concentration of circulating estrogens in postmenopausal women increases according to body weight and age [16]. Common biallelic polymorphism of the aromatase gene was found to be associated with significant differences in bone mass and fracture occurrence [17]. Therefore, women with higher fat mass are likely to have higher circulating estrogen levels and

13

BMC, TSBMD total

spine BMD, THBMD total hip BMD, FNBMD femoral neck BMD

J Bone Miner Metab

64

higher BMD. This mechanism may explain the association between BMD and fat mass in postmenopausal women.

The role of vitamin D in the association between lean mass and BMD should be examined. Although association between serum vitamin D level and BMD or fracture occurrence is well established [18], it is also known that vitamin D polymorphism is associated with strength of major skeletal muscles such as the quadriceps and hamstrings in premenopausal women [19]. Hypovitaminosis D leading to low BMD and low lean mass is a possible link between these two measures. Vitamin D deficiency or insufficiency is prevalent in many countries in Europe as well as in Asia [18].

The link between lean body mass and BMD has several clinical applications. When low BMD is associated with low muscle mass, the risk of fracture is relatively higher as sarcopenia would increase the risk of falls. This association has been shown in epidemiological studies where low BMI appeared as a risk factor for fractures, and low BMI in these patients may represent the combination of low bone and muscle mass [20]. As BMD and lean mass are positively related, interventions meant to improve muscle mass would simultaneously improve BMD. The association between physical activities and fractures has been shown previously [21]. Various forms of forces, such as torsion and traction, applied by muscles during physical activities would facilitate the accumulation of bone materials under the periosteum, leading to increased cortical thickness. Bradney et al. [22] found more cortical thickness and increased section modulus in the proximal femur in growing subjects allocated to moderate exercise program.

In our study, a change of 1 kg in lean mass was associated with a change of 0.004–0.008 g/cm² in BMD in different sites. An increase of lean mass by 5 kg would result in a

0.04 g/cm² increase in total spine BMD, which would represent a 4.3% difference when expressed as a percentage of the mean total spine BMD of the sample. Further, this would approximate to one-third of the SD of lumbar spine BMD of the study sample. This degree of BMD difference could be clinically important. In epidemiological studies, a 1 SD decrease of lumbar spine BMD doubled the risk of vertebral fractures [3]. In a previous analysis, although a 10% loss of bone mass in the vertebrae doubled the risk of vertebral fractures, a 10% loss of bone mass in the hip increased the risk of hip fracture by 2.5-fold [23]. Hence, the 4.3% change in spine BMD associated with a 5-kg change in lean mass would be clinically relevant.

The current study has a few limitations. Our sample size was relatively small, and selection bias could have occurred at the time of recruitment. Most of the women belonged to the working class, engaged in sedentary office work, and

would not represent the normal community. This factor was evident in our results, as they mostly belonged to the “moderately physically active” category. We had no detailed estimation of their current and past activities to adjust our data for physical activities.

In summary, results of our study showed a positive correlation between lean mass, fat mass, and bone mass in these healthy, middle-aged, premenopausal female volunteers. Of all the measurements examined, lean mass was the strongest predictor of BMD or BMC, and this association was independent of age and BMI. Physical activity and vitamin D status appear to be the most plausible explanations of this association. This finding is clinically relevant as women with low BMD would have an added risk of fracture because of associated sarcopenia leading to falls. Interventions such as physical activity may simultaneously modify both these risk factors.

Acknowledgments The authors acknowledge the technical assistance of Ms. Anuradha Wickramasekara, Irosha Siribaddana, Kumudinae de Silva, and Sunethra Weererathna during this study.

References

1. Mitchell AD, Scholz AM, Pursel VG, Evock-Clover CM (1998) Composition analysis of pork carcasses by dual-energy X-ray absorptiometry. *J Anim Sci* 76:2104–2114
2. Nagy TR, Clair AL (2000) Precision and accuracy of dual-energy X-ray absorptiometry for determining in vivo body composition of mice. *Obes Res* 8:392–398
3. Kanis JA, Gluer CC (2000) An update on the diagnosis and assessment of osteoporosis with densitometry. Committee of Scientific Advisors, International Osteoporosis Foundation. *Osteoporos Int* 11:192–202
4. Liu JM, Zhao HY, Ning G, Zhao YJ, Zhang LZ, Sun LH, Xu MY, Chen JL (2004) Relationship between body composition and bone mineral density in healthy young and premenopausal Chinese women. *Osteoporos Int* 15:238–242
5. Li S, Wagner R, Holm K, Lehotsky J, Zinaman MJ (2004) Relationship between soft tissue body

composition and bone mass in perimenopausal women. *Maturitas* 47:99–105

6. Ijuin M, Douchi T, Matsuo T, Yamamoto S, Uto H, Nagata Y (2002) Difference in the effects of body composition on bone mineral density between pre and postmenopausal women. *Maturitas* 43:239–244
7. Douchi T, Oki T, Nakamura S, Ijuin H, Yamamoto S, Nagata Y (1997) The effect of body composition on bone density in pre and postmenopausal women. *Maturitas* 27:55–60
8. Lekamwasam S, Rodrigo M, Arachchi WK, Munidasa D (2007) Measurement of spinal bone mineral density on a Hologic Discovery DXA scanner with and without leg elevation. *J Clin Densitom* 10:170–173
9. Sahin G, Guler H, Incel N, Sezgin M, As I (2006) Soft tissue composition, axial bone mineral density, and grip strength in postmenopausal Turkish women with early rheumatoid arthritis: is lean body mass a predictor of bone mineral density in rheumatoid arthritis? *Int J Fertil Womens Med* 51:70–74
10. Reid IR, Evans MC, Cooper GJ, Ames RW, Stapleton J (1993) Circulating insulin levels are related to bone density in normal postmenopausal women. *Am J Physiol* 265:E655–E659

13

-
11. Jurimae J, Rembel K, Jurimae T, Rehand M (2005) Adiponectin is associated with bone mineral density in perimenopausal women. *Horm Metab Res* 37:297–302
 12. Bembien DA, Feters NL, Bembien MG, Nabavi N, Koh ET (2000) Musculoskeletal responses to high- and low-intensity resistance training in early postmenopausal women. *Med Sci Sports Exerc* 32:1949–1957
 13. Andreoli A, Monteleone M, Van Loan M, Promenzio L, Tarantino U, De Lorenzo A (2001) Effects of different sports on bone density and muscle mass in highly trained athletes. *Med Sci Sports Exerc* 33:507–511
 14. Douchi T, Matsuo T, Uto H, Kuwahata T, Oki T, Nagata Y (2003) Lean body mass and bone mineral density in physically exercising postmenopausal women. *Maturitas* 45:185–190
 15. Reid IR, Plank LD, Evans MC (1992) Fat mass is an important determinant of whole body bone density in premenopausal women but not in men. *J Clin Endocrinol Metab* 75:779–782
 16. Bulun SE, Zeitoun K, Sasana H, Simpson ER (1999) Aromatase in aging women. *Semin Reprod Endocrinol* 4:349–358
 17. Zarrabeitia MT, Hernandez JL, Valero C, Zarrabeitia AL, Garcia-Unzueta M, Amado JA, Gonzalez-Macias J, Riancho JA (2004) A common polymorphism in the 5′-untranslated region of the aromatase gene influences bone mass and fracture risk. *Eur J Endocrinol* 150:699–704
 18. Viapiana O, Gatti D, Rossini M, Idolazzi L, Fracassi E, Adami S (2007) Vitamin D and fractures: a systematic review. *Reumatismo* 59:15–19

19. Grundberg E, Brandstrom H, Ribom EL, Ljunggren O, Mallmin H, Kindmark A (2004) Genetic variation in the human vitamin D receptor is associated with muscle strength, fat mass and body weight in Swedish women. *Eur J Endocrinol* 150:323–328
20. De Laet C, Kanis JA, Oden A, Johanson H, Johnell O, Delmas P, Eisman JA, Kroger H, Fujiwara S, Garnero P, McCloskey EV, Mellstrom D, Melton LJIII, Meunier PJ, Pols HA, Reeve J, Silman A, Tenenhouse A (2005) Body mass index as a predictor of fracture risk: a meta-analysis. *Osteoporos Int* 16:1330–1338
21. Kanis J, Johnell O, Gullberg B, Allander E, Elffors L, Ranstam J, Dequeker J, Dilsen G, Gennari C, Vaz AL, Lyritis G, Mazzuoli G, Miravet L, Passeri M, Perez Cano R, Rapado A, Ribot C (1999) Risk factors for hip fracture in men from southern Europe: the MEDOS study. *Mediterranean Osteoporosis Study. Osteoporos Int* 9:45–54
22. Bradney M, Pearce G, Naughton G, Sullivan C, Bass S, Beck T, Carlson J, Seeman E (1998) Moderate exercise during growth in prepubertal boys: changes in bone mass, size, volumetric density, and bone strength: a controlled prospective study. *J Bone Miner Res* 13:1814–1821
23. Klotzbuecher CM, Ross PD, Landsman PB, Abbott TAI, Berger M (2000) Patients with prior fractures have an increased risk of future fractures: a summary of the literature and statistical synthesis. *J Bone Miner Res* 15:721–739