Paper

Lean mass predicts the size-dependent and size-adjusted BMD better than fat mass in premenopausal females: a cross-sectional analysis

Lekamwasam S[1]**, Nanayakkara P G C J**[2]**, Liyanage C**[3]

Journal of the Ceylon College of Physicians, 2014, **45**, 22-27

Abstract

Introduction: In the human body, the influence of lean and fat masses on the bone tissue is unclear. This study was conducted to examine the association of different body compartments in order to find out the major determinant of bone mass. We used both size-dependent and size-adjusted bone mass measures in the analysis.

Methods: A group of 128 healthy pre-menopausal females, aged 25-50 years was selected randomly from the local community, stratified according to their BMI. Lean mass (LM), fat mass (FM), total body bone mineral density (TBBMD) and total body bone mineral content (TBBMC) were measured using a DXA scan. TBBMD was divided by the standing height to estimate height-adjusted total body BMD (TBBMD-ht). Furthermore, TBBMD was divided by the bone area and height to estimate bone mineral apparent density (BMAD).

Results: Both FM and LM showed significant and positive correlations with TBBMC and corresponding r values were 0.33 and 0.73, respectively ($P < 0.001$ for both). LM ($r = 0.43$, $P < 0.001$), but not the FM ($r = 0.16$, $P = 0.064$) showed a significant correlation with TBBMD. When TBBMD was adjusted for height, the correlation with LM became less strong ($r = 0.26$, $P<0.004$). When TBBMD was further adjusted to be representative of volumetric BMD (i.e. BMAD), the association with LM became negative ($r = -0.31$, $p<0.001$). In regression analysis a unit (1kg) change in LM was associated with a greater regression coefficient than a unit (1kg) change in FM for all size-dependent and size-adjusted bone mass measurements.

Conclusions: Among these premenopausal women LM predicted bone mass stronger than FM. Magnitude and directions of the correlations between bone mass and LM were different when BMC was adjusted for bone size and height of subjects. These results support the idea that lean mass has dual effects on bone tissue where it influences both linear measurements and mineral content to different extents.

Key words: premenopausal, bone mineral density, bone mineral content, bone mineral apparent density

Introduction

According to previous studies three main body compartments; fat, lean and bone have clear inter-relationships and their combined or coordinated actions help maintain normal health or contribute to disease state.[1-3] While an isolated abnormality in a given body compartment has defined clinical implications, co-existence of an abnormality in another body compartment may lead to an interaction between them and could possibly modify the expected clinical outcome. While reduced BMC/BMD increases the fracture risk, co-existent sarcopenia may enhance the tendency for recurrent falls resulting in greater fracture risk.[4] Similarly, if low BMD/BMC is co-existent with high fat content, fat tissue can, to some extent, off-set the fracture risk following a fall as fat tissue would absorb the excess energy generated at the site of impact.[5]

Different methods are used to measure body composition and Dual-Energy X-ray Absorptiometry (DXA) is a safe and non-invasive method with a high measurement precision.[6,7] Other methods available to measure body composition include CT and MRI technologies.

There is an uncertainity regarding the relative contribution made by lean and fat tissues to the variation of BMD. Previous studies have shown conflicting results where some studies found lean mass to be the main determinent of BMD[8,10] while others found fat mass to be more predictive of BMD than lean mass.[11,12] The exact mechanisms that explain the association between different body compartments

---

[1] *Departments of Medicine,*

[2] *Pharmacology, and*

[3] *Nuclear Medicine Unit, Faculty of Medicine, University of Ruhuna, Sri Lanka.*

are not well known. While physical activity is the most plausible explanation,[13] other possibilities such as vitamin D[14] and simultaneous programming of different body compartments during the early period of life[15] have also been postulated.

Most of the previous studies on this subject have been done in Western countries and are based on white Caucasian populations. The direct applicability of such results to Asians is questionable as the factors that are relevant to body composition; genetic background, dietary habits and physical activity, have an ethnic variation.[16] Furthermore, most of the previous studies have used either a real BMD or BMC as surrogate markers of bone mass. BMC and a real BMD are not adjusted for body size (body size-dependent variables) hence body measurements such as height and weight could have influenced the previous data and may have led to spurious associations. Recent studies have made an attempt to adjust BMD and BMC to accommodate body size to make these indices more representative of volumetric BMD.[17] However, not many studies have used these body size-adjusted bone measurements in analyzing the associations between bone mass and other body tissue compartments.

This study examined the association of different body compartments in order to find out the major determinant of bone mass and used both size-dependent and size-adjusted bone mass measures in the analysis.

Methods

This cross-sectional study included 128 healthy pre-menopausal females aged 25 to 50 years selected randomly from four PHM areas of the Bope Poddala MOH division (32 subjects from each area). Consenting subjects were stratified into four groups (32 in each) according to their body mass index (BMI) (BMI=18-22.5, 22.6-25, 25.1-30, >30kg/m^2). Subjects who were postmenopausal (period of amenorrhoea >6 months without being pregnant or other valid reason), pregnant or breast feeding were not included. Futhermore, subjects who were on long-term medications such as oral hypoglycaemics, anti hypertensives, lipid lowering medications, gluco-corticoids, thyroxine, hormonal contraceptives or hormone-replacement therapy were excluded. Subjects with the history of hypertension, diabetes, hyperlipidaema, ischemic heart disease, heart failure, liver diseases, renal diseases, endocrine diseases, metabolic bone diseases or epilepsy were not included in the study.

Body weight and height were measured while wearing light indoor clothes and without shoes (Weigh Master International; Japan, model BW-110 H). The waist and hip circumferences were measured according to the standard protocols.

Lean mass (LM), fat mass (FM), total body bone mineral density (TBBMD) and total body bone mineral content (TBBMC) were measured using DXA (Hologic Discovery QDR 4500 A, Hologic, Bedford,MA). The area of the bone image was also obtained from the Region of Interest in DXA results. All analyses were performed adhering to the instructions given by the manufacturer and the same technician performed all scans. The in-vitro precision of the machine was checked on each scanning day by scanning the two phantoms provided by the manufacturer. In-vivo precision of the machine has been published previously.[18]

Statistical analysis; TBBMD was divided by the standing height to estimate height-adjusted total body BMD (TBBMD-ht). Furthermore, TBBMD was divided by the area and height to estimate bone mineral apparent density (BMAD).[17] Absolute FM and LM measured in kg were divided by body weight to estimate percentage fat and lean masses. Correlations of lean and fat contents with TBBMC, TBBMD, TBBMD-ht and BMAD were examined by Pearson correlations. Linear regression analyses were done for TBBMD and TBBMC (as dependent variables) to detect the predictive value of lean and fat contents.

Bone mineral content; BMC (g) = bone mineral content

Bone mineral density; BMD (g/cm^2) = BMC/ area

Height adjusted bone mineral density; BMD-ht (g/cm^3) = BMD/height

Bone mineral apparent density; BMAD (g/cm^3) = BMD/ ht/area

Results

Descriptive data related to body composition and anthropometry of the selected 128 women are given in Table 1. None of them had ever smoked or taken alcohol.

Height, weight and BMI showed positive correlations with BMD/BMC, fat and lean masses (Table 2). Both fat and lean masses showed significant positive correlations with TBBMC and bone area. LM, but not the FM showed a significant correlation with TBBMD. When TBBMD was adjusted for height, the correlation with LM became less strong but still remained statistically significant. When TBBMD was further adjusted to BMAD, the correlation with LM became negative (Table 3).

Regression analysis supported our observations described above. A unit (1kg) change in LM was

Table 1. Descriptive data of 128 premenopausal women included in the analysis

Measurement (unit)	*Mean (SD)*
Age (years)	40.5 (6.1)
Height (m)	1.51 (0.56)
Weight (kg)	59.3 (11.4)
BMI (kg/m^2)	25.8 (4.3)
Total fat content (kg)	21.97 (7.41)
Abdominal fat content (kg)	8.97 (3.28)
Lean mass (kg)	34.67 (5.83)
Total BMC (g)	1745.3 (274.1)
Total BMD (g/cm^2)	1.042 (0.098)

associated with greater regression coefficients than a unit (1kg) change in FM for all size-dependent and size-adjusted bone mass measurements. Similar to the observations made in correlation analysis, adjusting BMD for height nullified the association with LM and further adjusting reversed the direction of association (Table 4).

When the regression models were fitted with LM, FM and percentages of lean and fat masses as independent variables and either TBBMC or TBBMD as the dependent variable and weaker variables were excluded in forward stepwise manner, LM remained the strongest predictor of both BMD and BMC (data not shown).

Discussion

This study shows the strengths and directions of associations between lean, fat and bone tissue among healthy premenopausal women in our study sample. While both FM and LM showed positive correlations TBBMC, LM showed stronger associations with TBBMD, TBBMD-ht and BMAD indicating that LM has more influence than FM on bone tissue of these young healthy women. LM showed stronger correlations with both bone area and TBBMC but the correlation between LM and TBBMD was comparatively less. The correlation reduced further when TBBMD was adjusted for height indicating that as the association between LM on TBBMD is partly explained by its effect on

Table 2. Correlations between anthropometric measures and body composition of 128 premenopausal women

Variable	*TBBMC*	*TBBMD*	*Fat mass*	*Lean mass*
Height	0.59 (<0.001)	0.23 (0.009)	0.24 (0.006)	0.46 (<0.001)
Weight	0.61 (<0.001)	0.37 (<0.001)	0.76 (<0.001)	0.77 (<0.001)
BMI	0.46 (<0.001)	0.34 (<0.001)	0.74 (<0.001)	0.67 (<0.001)

Given values in cells are Pearson correlation coefficients and p values (within brackets), TBBMD= total body bone mineral density, TBBMC= total body bone mineral content.

Table 3. Correlatons of lean and fat measurements with size-dependent and size-adjusted bone mineral density measurements among 128 women included in the analysis

Measurements	*TBBMC*	*TBBMD*	*TBBMD-ht*	*BAMD*	*Bone area*
Total fat content	0.33 (<0.001)	0.16 (0.064)	0.07 (0.41)	-0.41 (<0.001)	0.47 (<0.001)
Total lean mass	0.73 (<0.001)	0.43 (<0.001)	0.26 (0.004)	-0.31 (<0.001)	0.71 (<0.001)
Percentage of fat mass	0.01 (0.88)	-0.01 (0.88)	-0.03 (0.75)	-0.26 (0.003)	0.17 (0.067)
Percentage of lean mass	0.08 (0.394)	0.11 (0.24)	0.10 (0.24)	0.23 (0.009)	-0.07 (0.41)

Given values in cells are Pearson correlation coefficients and p values (within brackets)

TBBMC; total body bone mineral content, TMBMD; total body bone mineral density, BMD-ht; height adjusted bone mineral density, BMAD; bone mineral apparent density

Table 4. Regression coefficients (SE) between TBBMC, TBBMD, bone area, lean mass and fat masses

Measurement	*Total fat mass (kg)*	*Total lean mass (kg)*
TBBMC (g)	9.85 (3.19)*	28.23 (2.79)**
TBBMD (g/cm^2)	0.002 (0.001)	0.007 (0.001)**
Bone area (cm^2)	8.94 (1.75)**	14.97 (1.73)**
BMD-Ht (g/cm^3)	44 x 10-7 (76 x 10-7)	28 x 10-6 (8 x 10-6)
BMAD (g/cm^3)	-23 x 10-6 (52 x 10-7)**	-16 x 10-6 (62 x 10-7)*

*$p<0.05$, **$p<0.001$

height. In support of this, we observed a correlation of 0.46 ($p<0.001$) between LM and height among our subjects (Table 2). Interestingly, when TBBMD was adjusted for height and bone area, correlation became inversed but remained significant.

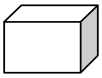
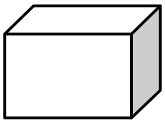
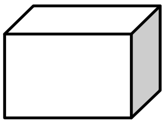
Our observations are keeping with the previous analysis involving a group of healthy young female volunteers from Southern part of Sri Lanka in whom LM showed stronger associations than FM with both BMD and BMC in different skeletal sites.[10] However, only the size-dependent BMD measurements were used in that study, hence the mechanism of the associations witnessed was not clear. Our data are comparable with those observed by Zagarins *et al* in a similar analysis where they used both size-dependent and size-adjusted BMD variables.[17] In this analysis, LM showed positive correlations, stronger than FM with BMC, BMD and BMD-ht. Similar to our data LM showed a negative correlation with BMAD in this study.

Our results possibly explain the influence of LM on different aspects of the bone tissue. It is well known that LM has a positive influence on BMC due to its tensile strains on the skeleton. Blain *et al* in 2001 found that 30% variation of femoral neck BMD is related to the strength of quadriceps muscles in healthy elderly women.[19] Similarly, Calbet *et al* in 2001 found higher BMC, BMD and muscle mass among pre-pubertal football players when compared with matching controls.[20] Furthermore, skeletal tissue increases cross-sectional bone area both in the growing and adult skeleton.[21,22] Janz *et al* in 2007 reported a positive association between femoral neck cross-sectional area and moderate/vigorous physical activities in children and part of this association was attributable to the variation in lean mass content.[21] Similar observations were made by Daly and others who observed most measurements of muscle functions to correlate, positively, with BMD, BMC and bone geometry of prepubertal subjects.[22] These studies indicate that LM influences many facets of human bone tissue such as bone length, bone width and the amount of bone material.

The diverse associations witnessed between LM and different expressions of bone tissue need an explanation. This could partly be a technical phenomenon as described in the following model which incorporates amount of bone material and bone dimensions; two measurements we found related to LM (Table 5). As illustrated in model 1 in column 2, if a bone cube of 1cmx1cmx1cm contains 1g of bone mineral, all measurements such as BMC, BMD, BMD-ht and BMAD will be equal to 1. If LM has an effect only confined to bone area, we would consider the example illustrated in model 2 where bone linear measurements have increased but the amount of material has remained the same. Here, BMC would increase by 8 fold, but BMD would only double. However, BMD-ht would remain same as in model 1 but BMAD would decline. Our data would not fit this model as we observed a positive, relatively small but statistically significant correlation between LM and BMD-ht. If LM has a dual effect both on linear measurements and material content of bone tissue, we could consider the illustration shown in the model 3 where in addition to linear measurements, the amount of bone material also has increased. Here, BMC and bone area have the greatest increase followed by BMD with a relatively less increase. BMD-ht will also increase marginally but BMAD will decline from the original value. This appears the most likely explanation for the associations observed between LM and different expressions of the bone mass in this analysis.

The knowledge that LM has a dual action on bone tissue has clinical relevance, as higher lean mass will associate with more bone material as well as wider and longer bones. While BMD and BMC are proven indices of bone strength, cross-sectional area and bone width are also known to influence bone strength.[23] Wider bones have a wider width and a higher cross-sectional area (cortical bone equivalent of the cross-section of

Table 5. The hypothetical model based on linear measurements and material properties of bone tissue used to explain the association between lean mass and different measurements of bone tissue

	Model 1	*Model 2*	*Model 3*
			
Measurements	1cm x 1cm x 1cm	2cm x 2cm x 2cm	2cm x 2cm x 2cm
Ca content	1gm/cm^3	1gm/cm^3	1.5gm/cm^3
BMC (g)	1.0	8.0	12.0
BMD (g/cm^2)	1.0	2.0	3.0
BMD-ht (g/cm^3)	1.0	1.0	1.5
BMAD (g/cm^3)	1.0	0.25	0.375

bone), therefore, less vulnerable to buckling. Furthermore, this could explain the lower incidence of fractures seen among women of Afro-Caribbean descent and anti-fracture benefits seen in interventions based on physical activities.

As a limitation of the study, we did not measure the volumetric BMD directly but estimated BMAD as a surrogate. However we selected our subjects from the community on random basis and all DXA analyses were done by a single technician. These would enhance the validity of our findings.

In summary, we demonstrate significant relationships between the three major body components; lean, fat and bone mass in this group of healthy premenopausal women. Although both FM and LM showed positive correlations with measurements of bone mass, the association between LM and bone mass was stronger than that between FM and bone mass. The strength and directions of associations were different when BMC was adjusted for bone size and the height of subjects. We also illustrated the possibility that LM has dual effects on bone tissue where it influences both linear measurements and bone mineral content to different extents.

References

1. Arabi A, Tamim H, Nabulsi M, Maalouf J, Khalife H, Choucair M, Vieth R, El-Hajj Fuleihan G. Sex differences in the effect of body-composition variables on bone mass in healthy children and adolescents. *Am J Clin Nutr* 2004; **80**: 1428-35.
2. Barondess DA, Nelson DA, Schlaen SE . Whole body bone, fat, and lean mass in black and white men. *J Bone Miner Res* 1997; **12**: 967-71.
3. Bonnet E, Delpierre C, Sommet A, Marion-Latard F, Herve R, Aquilina C, Labau E, Obadia M, Marchou B, Massip P, Perret B, Bernard J. Total body composition by DXA of 241 HIV-negative men and 162 HIV-infected men: proposal of reference values for defining lipodystrophy. *J Clin Densitom* 2005; **8**: 287-92.
4. Baumgartner RN. Body composition in healthy aging. *Ann N Y Acad Sci* 2000; **904**: 437-48.
5. Ensrud KE, Lipschutz RC, Cauley JA, Seeley D, Nevitt MC, Scott J, Orwoll ES, Genant HK, Cummings SR. Body size and hip fracture risk in older women: a prospective study. Study of Osteoporotic Fractures Research Group. *Am J Med* 1997; **103**: 274-80.
6. Bolanowski M, Nilsson BE. Assessment of human body composition using dual-energy x-ray absorptiometry and bioelectrical impedance analysis. *Med Sci Monit* 2001; **7**: 1029-33.
7. Black A, Tilmont EM, Baer DJ, Rumpler WV, Ingram DK, Roth, GS Lane, MA. Accuracy and precision of dual-energy X-ray absorptiometry for body composition measurements in rhesus monkeys. *J Med Primatol* 2001; **30**: 94-9.
8. Blain H, Vuillemin A, Teissier A, Hanesse B, Guillemin F, Jeandel C. Influence of muscle strength and body weight and composition on regional bone mineral density in healthy women aged 60 years and over. *Gerontology* 2001; **47**: 207-12.
9. Capozza RF, Cointry GR, Cure-Ramirez P, Ferretti JL, Cure-Cure C. A DXA study of muscle-bone relationships in the whole body and limbs of 2512 normal men and pre- and post-menopausal women. *Bone* 2004; **35**: 283-95.
10. Lekamwasam S, Weerarathna T, Rodrigo M, Arachchi WK, Munidasa D. Association between bone mineral density, lean mass, and fat mass among healthy middle-aged premeno-

pausal women: a cross-sectional study in southern Sri Lanka. *J Bone Miner Metab* 2009; **27**: 83-8.

11. Compston JE, Bhambhani M, Laskey MA, Murphy S, Khaw KT. Body composition and bone mass in post-menopausal women. *Clin Endocrinol* (Oxf) 1992; **37**: 426-31.

12. Cui LH, Shin MH, Kweon SS, Park KS, Lee YH, Chung EK, Nam HS, Choi JS. Relative contribution of body composition to bone mineral density at different sites in men and women of South Korea. *J Bone Miner Metab* 2007; **25**: 165-71.

13. Reid IR, Legge M, Stapleton JP, Evans MC, Grey AB. Regular exercise dissociates fat mass and bone density in premenopausal women. *J Clin Endocrinol Metab* 1995; **80**:1764-68.

14. Grundberg E, Brandstrom H, Ribom EL, Ljunggren O, Mallmin H, Kindmark A. Genetic variation in the human vitamin D receptor is associated with muscle strength, fat mass and body weight in Swedish women. *Eur J Endocrinol* 2004; **150**: 323-8.

15. Gale CR, Martyn CN, Kellingray S, Eastell R, Cooper C. Intrauterine programming of adult body composition. *J Clin Endocrinol Metab* 2001; **86**: 267-72.

16. Mackelvie KJ, McKay HA, Khan KM, Crocker PR. Lifestyle risk factors for osteoporosis in Asian and Caucasian girls. *Med Sci Sports Exerc* 2001; **33**:1818-24.

17. Zagarins SE, Ronnenberg AG, Gehlbach SH, Lin R, Bertone-Johnson ER. The association of lean mass and fat mass with peak bone mass in young premenopausal women. *J Clin Densitom* 2010; **13**(4): 392-8.

18. Lekamwasam S, Rodrigo M, Arachchi WK, Munidasa D. Measurement of spinal bone mineral density on a Hologic Discovery DXA scanner with and without leg elevation. *J Clin Densitom* 2007; **10**(2): 170-3.

19. Blain H, Vuillemin A, Teissier A, Hanesse B, Guillemin F, Jeandel C. Influence of muscle strength and body weight and composition on regional bone mineral density in healthy women aged 60 years or more. *Gerontology* 2001; **47**(4): 207-12.

20. Calbet JA, Dorado C, Diaz-Herrera P, Rodriguez LP. High femoral bone mineral density in male football (soccer) players. *Med Sci Sports Exerc* 2001; **33**(10): 1682-7.

21. Janz KF, Gilmore JM, Levy SM, Letuchy EM, Burns TL, Beck TJ. Physical activity and femoral neck bone strength during childhood: the Lowa Bone Development Study. *Bone* 2007; **41**(2): 216-22.

22. Daly RM, Dunstan DW, Owen N, Jolley D, Shaw JE, Zimmet PZ. Does high-intensity resistance training maintain bone mass during moderate weight loss in older overweight adults with type 2 diabetes? *Osteoporos Int* 2005; **16**(12): 1703-12.

23. Nelson DA, Barondess DA, Hendrix SL, Beck TJ. Cross-sectional geometry, bone strength, and bone mass in the proximal femur in black and white postmenopausal women. *J Bone Miner Res* 2000; **15**(10) 1992-7.