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Original article

Lean mass and peak bone mineral density

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abstract

Objectives: The association between body composition parameters and peak bone mineral density is not well documented. The aim of this study is to assess the relative contributions of lean mass and fat mass on peak bone mineral density (BMD).
Methods: The study involved 416 women and 334 men aged between 20 and 30 years who were participants in the population-based Vietnam Osteoporosis Study. Whole body composition parameters (eg, fat mass and lean mass) and BMD at the lumbar spine and femoral neck were measured by dual-energy X-ray absorptiometry. The association between lean mass and fat mass and BMD was analyzed by the linear regression model using the Least Absolute Shrinkage and Selection Operator (LASSO).
Results: Peak BMD in men was higher than women, and the difference was more pronounced at the femoral neck (average difference: 0.123 g/cm^2; 95% confidence interval [CI] 0.105–0.141 g/cm^2) than at the lumbar spine (average difference 0.019 g/cm^2; 95% CI, 0.005–0.036 g/cm^2). Results of LASSO regression indicated that lean mass was the only predictor of BMD for either men or women. Each kilogram increase in lean mass was associated with ~0.01 g/cm^2 increase in BMD. Lean mass alone explained 16% and 36% of variation in lumbar spine and femoral neck BMD, respectively.
Conclusions: Lean mass, not fat mass, is the main determinant of peak bone mineral density. This finding implies that good physical activity during adulthood can contribute to the maximization of peak bone mass during adulthood.
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1. Introduction

In humans, bone mass reaches its peak value (ie, peak bone mass) between the age of 20 and 30 years, and occurs earlier in women than in men [1–3]. However, men tend to have higher peak bone mass than women [2]. Individuals with low peak bone mass have higher risk of osteoporosis in later life, and the risk is accelerated with greater age-related bone loss at advanced ages. Therefore, a study of factors that are associated with peak bone mass is of clinical and public health significance.

Peak bone mass is determined by multiple factors, including genetic, hormonal, nutritional, physical activity, and lifestyle factors. Twin studies have consistently estimated that genetic factors account for up to 90% of the variance in peak bone mass [4–6]. Among hormonal factors that contribute to the accrual of bone mass, estrogen is the most important factor in both men [7] and women [8]. Estrogen deficiency in the undernutrition setting is an important risk factor for osteopenia [9]. Moreover, previous studies have shown that nutritional factors (eg, calcium, vitamin D, salt intakes) and physical activity contribute to the acquisition of bone mass during adulthood [10]. These factors – estrogen, nutrition, physical activity – are also strongly associated with body composition parameters (eg, lean mass and fat mass).

Body composition parameters are known to be associated with bone mineral density (BMD). Indeed, in postmenopausal women and old men, lean mass is a stronger than fat mass as a determinant of BMD [11,12]. However, the relative contributions of lean mass and fat mass to peak bone mass in younger individuals have not been well documented. Studies in Caucasian populations suggested that lean mass was an important predictor of peak bone mineral

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density in women [13], as well as in men [14]. Given that peak bone mass is related to both estrogen and physical activity, we hypothesize that peak bone mass is positively associated with both lean mass and fat mass. The present study seeks to test the hypothesis by evaluating the relative contributions of lean mass and fat mass to the variation in BMD among individuals aged 20–30 years.

2. Methods

2.1. Study design

This cross-sectional study was initiated in 2015–2016, with the setting being Ho Chi Minh City, Vietnam [15]. Participants were sampled from the general population by 2 approaches. In the first approach, we contacted temples, churches, and community organizations to obtain a list of members, and we used a computer program to randomly select individuals aged 18 years and above. They were then sent a letter of invitation to participate in the study. In the second approach, we ran a campaign in television, newspapers, and internet with a flyer. The flyer, written in Vietnamese, described the study's aim, procedures, benefit and potential risks. Individuals agreed to participate in the study were then transported to the Bone and Muscle Research Laboratory at the Ton Duc Thang University for clinical assessment and evaluation. The study's procedure and protocol were approved by the research and ethics committee of the People's Hospital 115. The study was conducted according to the ethical principles of the Declaration of Helsinki, and all participants gave written informed consent. There was no financial incentive involved, but participants were entitled to a free health check-up and lipid analyses.

2.2. Measurements

Data collection was conducted using a structured questionnaire and electronic equipments. Detailed information pertaining to lifestyle factors and clinical history were obtained by questionnaire which is written in Vietnamese. Current and past smoking habits as well as intakes were ascertained. Current and past alcohol consumption were also ascertained by the questionnaire. Height and weight were measured by an electronic portable, wall-mounted stadiometer (Seca Model 769; Seca Corp, Chino, CA, USA) without shoes, ornaments, hats or heavy layers of clothing. Body mass index (BMI) was derived as the weight in kilograms divided by the square of the height in meters (kg/m^2), and categorized into 4 groups: underweight (< 18.5); normal (18.5 to < 23.0); overweight (23.0 to < 27.5) and obese (≥ 27.5) [16].

BMD at the hip and lumbar spine was measured by a Hologic Horizon (Hologic Corp., Bedford, MA, USA). Fat mass (FM) and lean mass (LM) tissue were derived from the whole body scan. In addition, we derived the fat mass index (FMi) and lean mass index (LMi) by the following formulae: $FMi = FM/(height)^2$ and $LMi = LM/(height)^2$, where height is expressed in meters [17]. The densitometer was standardized before each measurement with a phantom. The measurement was conducted by a qualified radiology technologist.

2.3. Data analysis

The present analysis was limited to individuals aged between 20 and 30 which are widely considered ages of peak bone mass [1,2]. The association between body composition parameters and BMD was primarily analyzed by the multiple linear regression model. In this model, the dependent variable was BMD; predictor variables were LM and FM; and covariates were gender, current smoking (yes/no), and current alcohol use (yes/no). The magnitude of association between each predictor variable and BMD was assessed by the regression coefficient and its associated standard error. The model goodness-of-fit was evaluated by the coefficient of determination (ie, R-squared value), Akaike Information Criterion (AIC), and mean squared error (MSE).

It is expected that LM would be positively correlated with FM, and this correlation poses a challenge in the regression modeling. To alleviate this collinearity, we applied the Least Absolute Shrinkage and Selection Operator (LASSO) method [18] to search for the most robust predictor variables that contribute to the variation in BMD. LASSO is a method of parameter estimation that imposes a constraint on the model parameters that causes regression coefficients to shrink toward 0. Consequently, predictor variables with non-zero coefficients are retained in the model. All analyses were conducted using the R statistical environment [19].

3. Results

The study included 416 women and 334 men, whose average age (standard deviation [SD]) was 24 (3.5) years. Based on the criteria of BMI ≥ 30 kg/m^2, 2.1% (n = 16) individuals were classified as obese, and 13% (n = 100) overweight, and 22% (n = 73) of men and none of the women reported to be current smokers. Almost one-third (n = 104) of men and 4% (n = 18) of women reported to have regularly used alcohol.

As expected, mean percent body fat was higher in women than in men (39.2% vs 29.5%; P < 0.0001), and mean whole body lean mass was higher in men than in women (44.9 vs 30.4 kg; P < 0.0001). After adjusting for stature, fat mass index was still greater in women than men, and lean mass index was greater in men than women (Table 1).

3.1. Peak bone mineral density

Lumbar spine mean BMD in men (0.975 g/cm^2) was significantly higher than in women (0.956 g/cm^2; P < 0.01). The 95% confidence interval of difference in lumbar spine BMD between the 2 genders ranged between 0.005 and 0.036 g/cm^2 (Table 2).

However, the gender-related difference in femoral neck BMD was greater than that in lumbar spine BMD. Femoral neck mean BMD in men (0.868 g/cm^2) was approximately 1 standard deviation (0.123 g/cm^2) higher than women (0.745 g/cm^2; P < 0.01). The 95% confidence interval of difference in femoral neck BMD between the

Table 1
Basic characteristics of 416 women and 334 men aged between 20 and 30 years.

Variable	Women	Men	P-value
Age, yr	24.2 ± 3.5	23.9 ± 3.5	0.325
Height, cm	156.0 ± 5.5	167.0 ± 5.8	< 0.001
Weight, kg	50.1 ± 7.9	63.9 ± 10.5	< 0.001
Body mass index, kg/m^2	20.7 ± 3.0	22.8 ± 3.4	< 0.001
Weight classification			< 0.001
Underweight	88 (21.2)	28 (8.4)	
Normal	289 (69.5)	228 (68.3)	
Overweight	33 (7.9)	67 (20.1)	
Obese	5 (1.2)	11 (3.3)	
Whole body lean mass, kg	30.4 ± 3.6	44.9 ± 5.1	< 0.001
Whole body fat mass, kg	20.0 ± 5.1	19.4 ± 6.6	0.179
Body fat, %	39.2 ± 4.6	29.5 ± 5.8	< 0.001
Lean mass index, kg/m^2	12.5 ± 1.2	16.0 ± 1.6	< 0.001
Fat mass index, kg/m^2	8.3 ± 2.1	6.9 ± 2.3	< 0.001
Current smoking	0 (0)	73 (21.9)	< 0.001
Current use of alcohol	18 (4.3)	104 (31.1)	< 0.001

Values are presented as mean ± standard deviation or number (%). P-values were derived from tests of significance for difference between 2 genders was t-test (for continuous variables) and Chi-squared test (for categorical variables).

Table 2
Peak bone mineral density in women and men.

Variable	Women	Men	Difference and 95% confidence interval
Number of individuals	416	334	
Lumbar spine BMD, g/cm^2	0.956 ± 0.105	0.975 ± 0.107	0.019 (0.005, 0.036)
Femoral neck BMD, g/cm^2	0.745 ± 0.093	0.868 ± 0.133	0.123 (0.105, 0.141)
Total hip BMD, g/cm^2	0.838 ± 0.105	0.948 ± 0.127	0.110 (0.093, 0.127)

Values are presented as mean ± standard deviation. The 95% confidence intervals of difference between genders were derived t-test.

2 genders ranged between 0.105 and 0.141 g/cm^2. Total hip mean BMD in men (0.948 g/cm^2) was also significantly greater than in women (0.838 g/cm^2; P < 0.01). The 95% confidence interval of difference in total hip BMD between the 2 genders ranged between 0.093 and 0.127 g/cm^2.

3.2. Determinants of peak bone mineral density

In univariate correlation analysis, LM or FM significantly correlated with BMD (Fig. 1). The correlation between LM and BMD ranged between 0.28 (for lumbar spine BMD) to 0.59 (for femoral neck BMD). Furthermore, the correlation between FM and BMD ranged between 0.16 (femoral neck BMD) and 0.19 (lumbar spine BMD).

The LASSO analysis identified lean mass as the only one significant predictor for BMD. Moreover, when the model with LM as a predictor was compared to the model with LM and FM as predictors, the model with LM was found to be the most 'optimal'; adding FM into the model did not improve the model's goodness-of-fit (Table 3). When LM and FM were replaced by LMI and FMI, respectively, only LMI was the significant predictor.

The magnitude of association between LM and BMD is shown in Table 4. In all 3 BMD sites, the magnitude of association in men was slightly higher than in women, but the difference was not statistically significant (P = 0.10 for lumbar spine, P = 0.15 for femoral neck, and P = 0.75 for total hip BMD; data not shown). In all BMD sites, each kilogram increase in LM was equivalent to an increase of 0.01 g/cm^2 in BMD.

We found no statistically significant association between smoking, alcohol, and BMD.

4. Discussion

Peak bone mass is an important parameter of osteoporosis. Individuals with low peak bone mass have a greater risk of develop osteoporosis in later years of life. Although it has been known that most of the variation in peak bone mass between individuals is genetically determined [6], environmental factors or non-genetic factors do play important roles. Parameters of body composition (eg, lean mass and fat mass) have been shown to contribute to the variation in bone mass in the elderly, but their contributions to peak bone mass have not been well documented. In this study, we have shown that in young individuals, lean mass, and not fat mass, was the key determinant of peak bone mass. This finding deserves

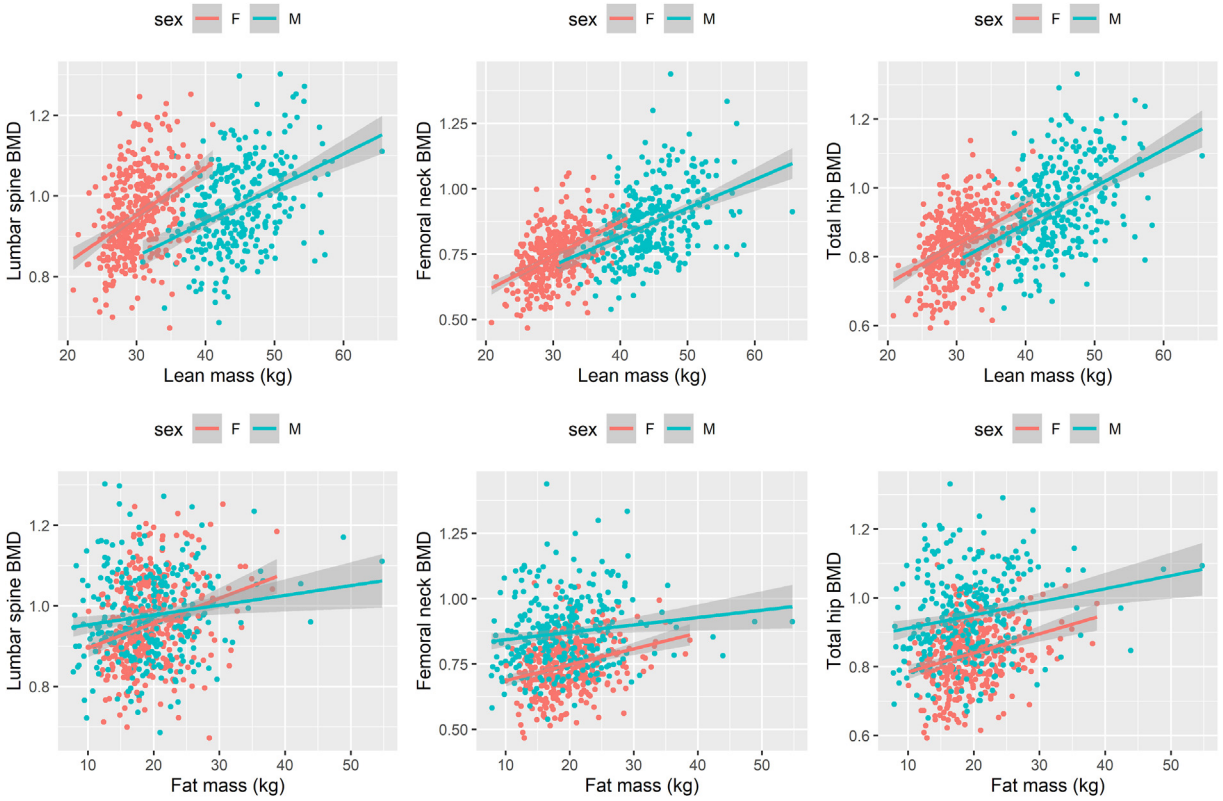

Fig. 1. Association between lean mass and bone mineral density (BMD) (upper panel) and between fat mass and BMD (lower panel) for men (blue dots) and women (red dots).

Table 3
Comparison of model-fittings in the prediction of peak bone mineral density.

Dependent variable and indices of fit	Model 1: LM	Model 2: LM + FM	Model 3: LMI	Model 4: LMI + FMI
Lumbar spine BMD				
R^2	0.155	0.156	0.117	0.119
AIC	−1356.3	−1355.4	−1323.6	−1323.3
MSE	0.009	0.009	0.010	0.010
Femoral neck BMD				
R^2	0.364	0.368	0.348	0.355
AIC	−1231.8	−1234.7	−1213.8	−1219.8
MSE	0.011	0.011	0.011	0.011
Total hip BMD				
R^2	0.350	0.351	0.366	0.369
AIC	−1325.4	−1324.2	−1343.6	−1345.7
MSE	0.010	0.010	0.010	0.010

All models included sex as a covariate. LM, lean mass; FM, fat mass; LMI, lean mass index; FMI, fat mass index. BMD, bone mineral density; AIC, Akaike Information Criterion; MSE, mean squared error.

Table 4
Association between gender and lean mass and peak bone mineral density.

BMD and predictors	Women		Men	
	Regression coefficient ± SE	P-value	Regression coefficient ± SE	P-value
Lumbar spine BMD				
Intercept	0.615 ± 0.041	< 0.01	0.602 ± 0.048	< 0.01
Lean mass	0.011 ± 0.001	< 0.01	0.008 ± 0.001	< 0.01
Femoral neck BMD				
Intercept	0.328 ± 0.038	< 0.01	0.373 ± 0.060	< 0.01
Lean mass	0.014 ± 0.001	< 0.01	0.011 ± 0.001	< 0.01
Total hip BMD				
Intercept	0.482 ± 0.036	< 0.01	0.446 ± 0.055	< 0.01
Lean mass	0.012 ± 0.001	< 0.01	0.011 ± 0.001	< 0.01

Values are presented as regression coefficients mean ± standard error derived from the linear regression analysis. BMD, bone mineral density; SE, standard error.

some elaborations.

Our finding of lean mass as an important predictor of BMD is actually consistent with previous studies in pre-menopausal women [20] and young women [21]. For instance, a study in Caucasian women found that lean mass, not fat mass, was the key determinant of BMD at the hip and spine [21]. The Healthy Twin Study on individuals of Korean background found that the association between lean mass and BMD was greater than between fat mass and BMD [22] which was also found in a previous meta-analysis [11]. Taken together, our present data and previous studies suggest that lean mass is an important determinant of peak bone mass in both Caucasian and Asian populations.

The above finding does not mean that fat mass is not biologically related to BMD. Biologically, fat mass positively affects bone mass via the increased estrogen synthesis by adipose tissue [23]. Some previous studies found that fat mass was more important as a determinant of BMD [24]. However, statistically, in the presence of lean mass, fat mass was no longer statistically significant, because fat mass and lean mass are highly correlated, and the correlation between lean mass and BMD is greater than that between fat mass and BMD.

The correlation between lean mass and fat mass poses a challenge in the delineation of the separate effects of lean mass and fat mass on BMD. When the 2 correlated variables are considered in a linear model, the parameter estimates are biased or is even a wrong sign. Stepwise regression method cannot resolve the issue of collinearity. In this study we used the LASSO method which alleviates the problem of collinearity, and it was clear that for the purposing of predicting BMD, lean mass was the only important predictor.

The finding that lean mass is a key predictor of BMD has important public health implications. Lean mass is highly correlated with, or is a marker for, muscle strength and physical activity. Physically active individuals have higher muscle strength and higher lean mass than those less physically active. In this study, we found that lean mass alone may explain more than one-third of variation in BMD which is fairly substantial. Moreover, we note that the magnitude of association between lean mass and BMD was quite consistent across 3 BMD sites (lumbar spine, femoral neck, and total hip) and the 2 genders. Therefore, the fact of a strong association between lean mass and BMD implies that physical activity is an important component for young individuals to achieve their peak bone mass, and hence reduce the risk of having osteoporosis in later years of life.

The findings of this study should be considered in relation to its strengths and weaknesses. The participants of this study were randomly sampled from the community which may be representative of the City's general population. The sample size was also large enough to ensure the reliability and reproducibility of the findings. Bone mineral density and body composition considered in the study were measured by the state-of-the art equipment which is considered the 'gold standard' method, and this is very important because it ensures the internal validity of the findings. However, the study was designed as a cross-sectional investigation, and the associations observed here cannot be interpreted as causal relationships. The participants of this study were primarily urban residents whose lifestyle and living standards are different from those living in rural areas.

5. Conclusions

These data suggest that of the 2 key components of body weight, lean mass is the main determinant of peak bone mineral density in individuals of Vietnamese background. This finding implies that

maintaining good physical activity levels during adulthood is an important factor contributing to the maximization of peak bone mass during adulthood and reduction of osteoporosis risk in later years of life.

CRediT author statement

Huy G. Nguyen: Conceptualization, formal analysis, writing - original draft. **Minh TD. Pham**: Investigation, data curation. **Lan T. Ho-Pham**: Conceptualization, methodology, investigation, validation, formal analysis, data curation, writing - review & editing. **Tuan V. Nguyen**: Conceptualization, methodology, supervision, writing - review & editing.

Conflicts of interest

The authors declare no competing interests.

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