Original article

The effects of sarcopenia and obesity on femur neck bone mineral density in elderly Korean men and women

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Abstract

Objectives: We aimed to clarify the relationship between fat, muscle, and bone in elderly men and women.
Methods: We analyzed 1373 men and 1803 women who were older than 65 years from the 2008–2010 Korea National Health and Nutritional Examination Surveys. Body composition and femur neck bone mineral density (BMD) were measured by dual-energy X-ray absorptiometry. Sarcopenia was defined as an appendicular skeletal muscle index (SMI) below one standard deviation (SD). Obesity was classified by fat mass index (FMI). Osteoporosis was defined as a BMD of 2.5 SD below that of femur neck BMD.
Results: SMI and FMI were positively correlated with femur neck BMD. In multiple regression analysis, SMI ($\beta = 0.302$ in men, $\beta = 0.154$ in women; $p < 0.001$ each) and FMI ($\beta = 0.079$ in men, $\beta = 0.179$ in women; $p = 0.003$ and $p < 0.001$ respectively) had a positive relationship with femur neck BMD. Men with sarcopenia were 3.89 times more likely to develop osteoporosis. Women with sarcopenia were 1.87 times more likely to develop osteoporosis. Sarcopenia was more clinically significant in the development of osteoporosis in men with a fat deficit and women with excess fat.
Conclusions: Muscle mass and fat mass were identified as determinants of femur neck BMD in men and women. Among them, muscle mass of men and fat mass of women are the most important determinants of femur neck osteoporosis.
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Keywords: Obesity; Osteoporosis; Sarcopenia

1. Introduction

A two-component model of body composition is divided into a fat component and a fat-free component (lean body mass), which includes muscles, bones, and internal organs [1]. Advancing age in older adults is accompanied by body composition changes, which are characterized by the loss of lean body mass, especially bone and muscle [2].

Osteoporosis is a systemic skeletal disease, characterized by low bone mass and microarchitectural deterioration of bone tissue, with a consequential increase in bone fragility and susceptibility to fracture [3]. Sarcopenia is the loss of skeletal muscle mass and strength that occurs with advancing age [4]. Osteoporosis and sarcopenia are common diseases in older adults [5,6]. A common etiology may cause both osteoporosis and sarcopenia, and the two diseases may act together in the development of a disability [7]. Some studies reported that sarcopenia was significantly associated with both osteopenia and osteoporosis [8–12].

Extensive epidemiological data show that a higher body weight is associated with a higher bone mineral density (BMD) [13–15]. Body weight is a major determinant of BMD, and adipose tissue mass is regarded as a major contributor to this relationship [15,16]. Some studies suggest that higher levels of total body fat may be associated with a lower BMD in both men and women, after adjusting for

similar body size [13,17,18]. However, in a recent review article, Reid [16] pointed out that those studies that incorporate weight with lean and fat mass in statistical models would mislead the results. They may not show a true representation of the physiological relationship between fat and bone because these statistical models are confounded by substantial co-linearity between variables and yielding [16]. Several studies about regarding sarcopenia and osteoporosis incorporated weight with lean and fat mass in statistical models [9,12]. Therefore, the interrelationships between obesity, sarcopenia, and osteoporosis were not clear in clinical practice.

The aim of this study was to clarify the relationship between fat, muscle, and bone in elderly men and women. More specifically, we aimed to determine the association between sarcopenia and osteoporosis in terms of obesity in elderly Korean men and women using the Korea National Health and Nutrition Examination Survey (KNHANES), a nationally representative cross-sectional survey.

2. Material and methods

This study is based on data acquired from the KNHANES between 2008 and 2010. The KNHANES, initiated in 1998, was designed to assess the health and nutritional status of adults and children living in Korea. The Korea Center for Disease Control and Prevention administers this national representative survey. The KNHANES targets the civilian non-institutionalized Korean population and collects data from interviews, physical examinations, and medical tests every 3 years from approximately 30,000 people. The KNHANES (2008–2010) included dual-energy X-ray absorptiometry (DXA) measurements of the BMD of the spine and hip, and body composition. We analyzed the DXA data of 1373 men and 1803 women who were older than 65 years and had participated in the KNHANES from 2008 to 2010.

2.1. Measurements of bone mineral density and body composition

In the KNHANES, BMD and body composition were measured by DXA methods with a QDR Discovery (formerly the QDR 4500A) fan beam densitometer (Hologic, Inc., Bedford, MA) according to the manufacturer's recommended procedure. All subjects were asked to wear light clothing and to remove any clothing that might interfere with the DXA examination. The DXA results were reviewed and analyzed using industry-standard techniques at The Korean Society of Osteoporosis (Seoul, Republic of Korea). Analysis was performed using Hologic Discovery software (version 12.1) with the default configuration. The KNHANES dataset contains regional (lumbar and femur) DXA measurements of bone mineral content (BMC, g), BMD (g/cm^2), z-score, and t-score, as well as whole-body DXA measurements of bone mineral content (BMC, g), BMD (g/cm^2), fat mass (g), lean mass including BMC (g), and percentage fat (fat mass/total mass $\times$ 100), along with demographic information on each subject. Of the DXA data, we used femur BMD, and femur t-

score. The derivative values were calculated as follows: fat mass index [FMI; fat mass (kg)/height^2 (cm^2)] and appendicular skeletal muscle mass (four limb fat-free soft tissue; four limb lean mass - four limb BMC; g), appendicular skeletal muscle mass/height^2 (skeletal mass index, SMI) from body composition data.

3. Sarcopenia, osteoporosis and obesity

Sarcopenia was defined as an SMI below one standard deviation (SD) from the sex-specific normal mean of the young reference group. The young reference group is defined as 20–39 year old men (n = 1800) and women (n = 2009). We excluded 1361 of 5170 participants because they had cancer, or liver, kidney, pulmonary, or metabolic disease [19]. The characteristics of the young reference group are shown in Supplement Table 1. The mean SMI was 7.90 ± 0.88 kg/m^2 in men and 5.74 ± 0.74 kg/m^2 in women. Sarcopenia is defined as <7.02 kg/m^2 in men and <5.00 kg/m^2 in women. Osteoporosis is defined as a BMD of 2.5 SD below the peak bone mass of a young, healthy, sex- and race-matched reference population, according to the World Health Organization (WHO) diagnostic classification [3]. In this study, the diagnosis of osteoporosis was established by a measurement of BMD by DXA of the proximal femur neck region. The World Health Organization (WHO) defined overweight and obesity as abnormal or excessive fat accumulation [20]. In this study, overweight and obesity were classified by fat mass index (fat mass/height^2, FMI), which matched classification thresholds of Body Mass Index (BMI) in young adults [21,22].

3.1. Osteoporosis or sarcopenia related factors

In the KNHANES, blood was collected after an 8-h fast. Blood samples were immediately processed, refrigerated, and transported in cold storage to the central testing institute (NeoDin Medical Institute, Seoul, South Korea), where they were analyzed within 24 h. Serum 25(OH) vitamin D concentration was measured with a radioimmunoassay kit (DiaSorin Inc., Stillwater, MN, USA) using a γ-counter (1470Wizard; PerkinElmer, Turku, Finland).

Trained interviewers collected data on demographic factors, health behaviors, and dietary intakes of the participants via personal interviews. Exercise was defined based on how many days per week the participants exercised for more than 30 min with moderate intensity (professional and athletic activities, such as swimming, doubles tennis, volleyball, badminton, and table tennis).

Dietary intake data were obtained by a dietary recall survey asking participants what food and what quantity of food had been consumed during the last 24 h. Consumed nutrients and electrolytes were assessed by the food composition table, which was created and validated by the Rural Development Administration. Dietary variables used in this study included total energy (kcal/day), carbohydrate (% energy), total fat (% energy), protein (% energy), calcium (mg/1000 kcal), and phosphate (mg/1000 kcal) intakes.

3.2. Statistical analysis

Data were expressed as mean ± SD or percentage (%). Pearson linear correlation was used to investigate a possible association. If any association was found between BMD and the independent variables, it was selected for analysis by multiple linear regression in the model "stepwise" to compare muscle mass to femur neck BMD. We divided the subjects between age-adjusted quartiles of the SMI for each of the FMI classifications (deficit, normal and excess-obesity). A one-way ANOVA was used to compare femur neck BMD across quartiles of SMI in the classification of FMI. We conducted the multiple logistic regression in the model "stepwise" to investigate the relationship between sarcopenia and obesity, and osteoporosis, adjusting for age, exercise habits, alcohol consumption, smoking habits, vitamin D levels, and nutritional factors. We conducted the multiple logistic regression in the model "stepwise" to investigate the relationship between sarcopenia and osteoporosis per classification of FMI adjusting for age, exercise habits, alcohol consumption, smoking habits, vitamin D levels, and nutritional factors. Results were considered significant when $p < 0.05$. The statistic program, SPSS for Windows (version 18.0 SPSS Inc., an IBM Company, Chicago, Illinois) was used for all the analyses.

4. Results

The characteristics of the 3176 participants (men: 1373, women: 1803) included in the study are shown in Table 1. The mean age was 71.7 ± 5.0 years old in men and 71.9 ± 5.1 years old in women. The prevalence of sarcopenia was 43.7% in men and 7.38% in women. The prevalence of osteoporosis was 6.25% in men and 37.1% in women.

The correlations between muscle, bone, and related variables are listed in Table 2. Age showed a significant, negative correlation with SMI and femur neck BMD in men and women. Femur neck BMD had a positive correlation with BMI, FMI, and SMI in both men and women. Vitamin D had a positive correlation with SMI of men and women, and femur neck BMD of women. Only women had a positive correlation between exercise, and femur neck BMD and SMI. Current smoking habits had a negative correlation with SMI of women, and femur neck BMD of men and women. Alcohol consumption had a positive correlation with femur neck BMD of men and women, and SMI of men. Total calorie, protein, fat, calcium, and phosphate intake had a significant positive correlation with femur neck BMD of men. Total calorie, protein, and fat intake had a significant positive correlation with femur neck BMD in women. Total calorie, protein, fat, and phosphate intake had a significant positive correlation with SMI of men, whereas only total calorie intake in women had a positive association with SMI of women.

We compared the means of the femur neck BMD across age-adjusted quartiles of SMI for each of the FMI classifications (Fig. 1). Femur neck BMD increased as SMI increased in fat deficit (p for trend < 0.001), fat normal (p for trend < 0.001), and fat excess-obesity (p for trend < 0.001) of men, and in fat normal (p for trend < 0.001) and fat excess-obesity (p for trend < 0.001) of women. Multiple regression analysis was performed on femur neck BMD using age, BMI, and related factors (vitamin D levels, exercise habits, alcohol consumption, smoking habits, and nutritional factors) as independent variables. This revealed that age, BMI, alcohol intake, current smoking, and phosphate intake in men and women, and vitamin D in men were significant (Table 3). Body mass is crudely composed of fat, muscle and bone.

Table 1
Population characteristics.

	Men		Women	
	Mean ± or %	Standard deviation	Mean ± or %	Standard deviation
Age (y)	71.7	5.0	71.9	5.1
Height (cm)	165	6	151	6
Weight (kg)	62.8	9.4	55.0	9.1
Waist circumference (cm)	84.5	9.0	83.2	9.8
Body mass index (kg/m^2)	23.1	2.9	24.1	3.4
Skeletal mass index (kg/m^2)	7.16	0.80	5.91	0.66
Residuals appendicular lean mass (kg)	−1.67	2.08	0.09	1.48
Fat mass index (kg/m^2)	5.12	1.71	8.16	2.32
Sarcopenia (below 1SD of SMI, %)	43.7		7.38	
Femoral neck bone mineral density (g/cm^2)	0.700	0.114	0.563	0.090
Femur Osteoporosis (%)	6.25		37.11	
Exercise (more than 5 days per week, %)	14		13	
Current smoking (%)	61		9	
Alcohol intake(more than 2 times per month)	51		12	
25(OH) Vitamin D (ng/mL)	22.2	7.7	19.2	7.5
Calories intake (kcal)	1900	673	1426	527
Protein intake (%energy)	13.3	3.7	12.5	3.5
Fat intake (%energy)	71.5	12.1	77.6	8.8
Carbohydrate intake (%energy)	12.3	7.1	10.6	6.4
Calcium intake (mg/1000 kcal)	257	169	259	263
Phosphate intake (mg/1000 kcal)	604	145	591	134

Table 2
Correlations between muscle, bone and related variables.

		Femur neck BMD	Age	BMI	SMI	FMI	Vitamin D	Exercise	Current smoking	Alcohol drinking	Calories intake	Protein intake	Fat intake	Carbohydrate intake	Calcium intake	Phosphate intake
Men	Femur neck BMD (g/cm^2)	1	−0.282***	0.372***	0.392***	0.187***	0.042	0.044	−0.060*	0.090**	0.155***	0.125***	0.104***	−0.080**	0.120***	0.135***
	SMI (kg/m^2)	0.392***	−0.293***	0.714***	1	0.288***	0.082**	0.037	−0.001	0.084***	0.201***	0.076***	0.070*	−0.061*	0.041	0.057*
Women	Femur neck BMD (g/cm^2)	1	−0.393***	0.331***	0.285***	0.263***	0.071**	0.090***	−0.083***	0.063***	0.142***	0.054*	0.073***	−0.045	0.045	0.040
	SMI (kg/m^2)	0.285***	−0.158***	0.653***	1	0.358***	0.057*	0.092***	−0.060*	0.007	0.155***	−0.009	−0.030	0.045	0.007	−0.026

***p < 0.001.
**p < 0.01.
*p < 0.05.
BMD, bone mineral density; BMI, body mass index; FMI, fat mass index; SMI, skeletal muscle index.

Therefore, we replaced BMI with SMI and FMI and repeated the multiple regression analysis. In these multiple regression analyses, SMI and FMI also had a positive relationship with femur neck BMD, as independent variables. Standardized coefficients (β) of SMI (β = 0.302) were greater than FMI (β = 0.079) in men, but FMI standardized coefficients (β = 0.179) were greater than SMI (β = 0.154) in women (Table 3). After adjusting for various potential confounders, we analyzed the odds ratios (ORs) of sarcopenia and obesity classification by FMI for femur neck osteoporosis with multiple logistic regression analysis (Table 4). Men with sarcopenia had a 3.890 (95% confidence interval (95CI): 2.265−6.781) times higher likelihood of femur neck osteoporosis than men without sarcopenia, but this was not the case for obese men. Women with a fat deficit and normal levels of fat had a 3.362 (95CI: 2.207−5.122) and 1.512 (95CI: 1.187−1.927) respectively, times higher likelihood for femur neck osteoporosis than that of obese women. Women with sarcopenia had 1.868 (95CI: 1.227−2.844) times higher odds for femur neck osteoporosis than that of women without sarcopenia (Table 4). We analyzed the ORs of femur neck osteoporosis by sarcopenia in subgroups of FMI classification. In men, the odds of developing femur neck osteoporosis in the presence of sarcopenia decreased as FMI classification increased (deficit, normal, excess-obesity), OR = 4.873 (95CI: 1.056−22.496), OR = 4.719 (95CI: 2.137−10.421), and OR = 2.558 (95CI: 0.972−6.730) respectively. However, in women, OR of femur neck osteoporosis for sarcopenia increased as FMI classification increased (deficit, normal, excess-obesity), OR = 1.755 (95CI: 0.547−5.629), OR = 1.796 (95CI: 1.066−3.025), and OR = 2.896 (95CI: 1.142−7.345) respectively. Therefore, sarcopenia was clinically significant in the development of osteoporosis in fat deficit men, and excess-obesity women (see Table 5).

5. Discussion

In this cross-sectional study, the association of muscle mass and fat mass with femur neck BMD differed depending on sex. In men, muscle mass was more strongly associated with femur neck BMD than fat mass. Sarcopenia, but not obesity, predicted femur neck osteoporosis. In women, muscle mass and fat mass was similarly associated with femur neck BMD, and sarcopenia and obesity predicted femur neck osteoporosis. In the prediction of osteoporosis, sarcopenia was more significant in men with low fat mass and in women with high fat mass.

Several studies have suggested that muscle mass is significantly associated with BMD. Similarly, in an elderly Korean population from the 2008−2010 KNHANE, men and women with sarcopenia identified using SMI measured via DXA have a significantly higher risk of osteoporosis [23]. In a study of 590 Finnish post-menopausal women, the lowest quartile of SMI had a 11.7 times higher odds of having femur neck osteoporosis [8]. Naohisa Miyakoshi et al. [24] reported that among 2400 Japanese women aged 40−88 years, SMI had a significant positive correlation with lumbar spine BMD and total hip BMD. Prevalence of sarcopenia defined by SMI was
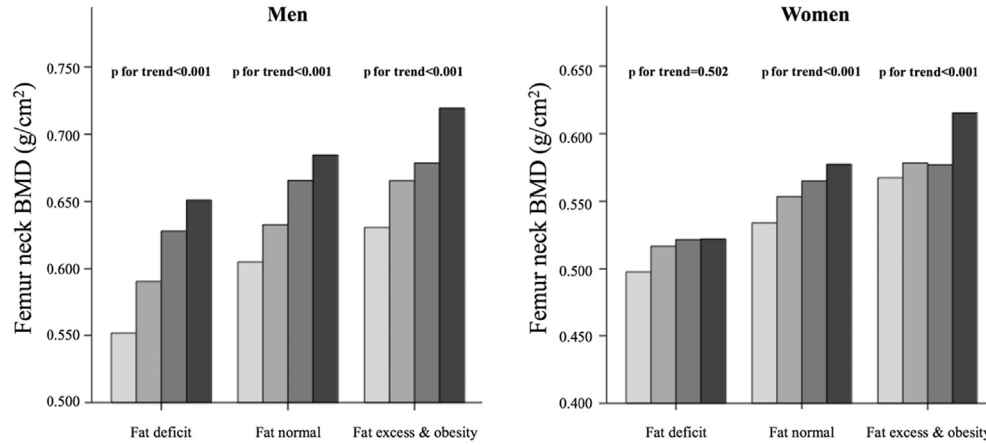
Fig. 1. Means of the femur neck bone mineral density, across age-adjusted quartiles of the skeletal mass index in deficit, normal and excess-obesity of the classification of fat mass index. The bars from left to right are age adjusted quartiles 1, 2, 3, and 4 of skeletal mass index in each fat mass index stratum.

Table 3
Association between body mass index, lean and fat mass, osteoporosis related variables and femur neck BMD: multivariable model.

		Standardized coefficients	p		Standardized coefficients	p
Men	Age	−0.206	<0.001	Age	−0.173	<0.001
	BMI	0.328	<0.001	SMI	0.302	<0.001
				FMI	0.079	0.003
	Alcohol intake	0.064	0.012	Alcohol intake	0.061	0.016
	Current smoking	−0.051	0.044	Current smoking	−0.055	0.031
	Vitamin D	0.074	0.004	Vitamin D	−	−
	Phosphate intake	0.094	<0.001	Phosphate intake	0.102	<0.001
Women	Age	−0.345	<0.001	Age	−0.340	<0.001
	BMI	0.288	<0.001	SMI	0.154	<0.001
				FMI	0.179	<0.001
	Alcohol intake	0.051	0.017	Alcohol intake	0.047	0.027
	Exercise	0.050	0.019	Exercise	0.046	0.034
	Vitamin D	0.079	<0.001	Vitamin D	0.070	0.001

BMD, bone mineral density; BMI, body mass index; FMI, fat mass index; SMI, skeletal muscle index.

highest in people with osteoporosis, followed by people with osteopenia, and lowest in people with normal BMD. Walsh et al. [25] investigated the prevalence of sarcopenia, defined using SMI, in 213 healthy women in the United States. They reported that the prevalence of sarcopenia was 11.7% in all

women, 12.5% in pre-menopausal osteopenic women, 25% in post-menopausal women with osteopenia, and 50% in post-menopausal women with osteoporosis. However, SMI was not significantly correlated to BMD after adjusting for

Table 4
Odds ratios for femur neck osteoporosis by sarcopenia and obesity: multivariable logistic model with age, vitamin D, exercise, current smoking, alcohol intakes, and nutritional factors.

			Odds ratio	95% CI	p
Men	Sarcopenia	No	1 (ref)		
		Yes	3.890	2.265−6.781	<0.001
	Obesity classification by fat mass index	Deficit	1.485	0.696−3.170	0.306
		Normal	1.011	0.565−1.809	0.970
		Excess & obesity	1 (ref)		
Women	Sarcopenia	No	1 (ref)		
		Yes	1.868	1.227−2.844	0.004
	Obesity classification by fat mass index	Deficit	3.362	2.207−5.122	<0.001
		Normal	1.512	1.187−1.927	0.001
		Excess & obesity	1 (ref)		

Table 5
Odds ratios for femur neck osteoporosis by sarcopenia in deficit, normal and excess-obesity of the classification of fat mass index: multivariable logistic model with age, vitamin D, exercise, current smoking, alcohol intakes, and nutritional factors.

	Obesity classification by fat mass index	Sarcopenia	Odds ratio	95% CI	p
Men	Deficit	No	1 (ref)		
		Yes	4.873	1.056−22.496	0.042
	Normal	No	1 (ref)		
		Yes	4.719	2.137−10.421	<0.001
	Excess & obesity	No	1 (ref)		
		Yes	2.558	0.972−6.730	0.057
Women	Deficit	No	1 (ref)		
		Yes	1.755	0.547−5.629	0.345
	Normal	No	1 (ref)		
		Yes	1.796	1.066−3.025	0.028
	Excess & obesity	No	1 (ref)		
		Yes	2.896	1.142−7.345	0.025

physical activity. Verschueren et al. [11] reported that skeletal muscle mass was strongly correlated with total hip and lumbar spine BMD in this analysis of middle-aged and elderly European men, after adjustment for potential confounders. However, some studies [8,11,24,25] incorporate weight or BMI with lean and fat mass in statistical models, which skews the results due to confounding by substantial co-linearity between the variables and yielding [16]. In our study, we separated body weight in to muscle and fat mass. We used SMI to represent muscle mass, and FMI to represent fat mass, and these were independent contributors to BMD.

In this study, the associations between muscle, fat, and BMD differed slightly between men and women. In men, sarcopenia, but not obesity, is associated with femur neck osteoporosis. In women, both sarcopenia and obesity are associated with femur neck osteoporosis. Sex-specific effects of sex hormones explain the difference between men and women in the relationship between bone, fat and muscle. In men, testosterone and insulin-like growth factor-1 results in a higher bone mass, muscle mass, and strength. In women, a higher level of estrogen results in a higher bone mass and muscle mass, but the large decrease in estrogen level after menopause appears to decrease the skeleton's responsiveness to exercise [26]. After menopause, estrogen levels decrease and extra-gonadal estrogen is synthesized in fat tissue, mediated by aromatase, and becomes the dominant estrogen source [27]. This may lead to the beneficial effects of a higher fat mass on bone density in women. In our study, in women, FMI was a more significant determinant of femur neck BMD than SMI, but this was not the case in men. Femur neck osteoporosis in women, but not in men, was influenced by obesity classification by FMI. Exercise had a positive relationship with femur neck BMD in women, but this relationship was not present in men. Sarcopenia, as a predictor of osteoporosis, was more important in men with low fat mass and in women with high fat mass. This may be due to a decrease in muscle response to exercise in women.

In addition, smoking had a negative effect on femur neck BMD based on our multiple regression model. Similarly, Pluijm et al. [28] stated that smoking was the strongest determinant of total hip BMD in men. This association was not observed in women, but this might be due to a low incidence of smoking in women (9% vs. 61% in men). Alcohol consumption had a positive effect on femur neck BMD based on the multiple regression model in our study. Rapuri et al. [29] reported that moderate alcohol intake was associated with a higher BMD in post-menopausal elderly women. This may be caused by a decrease in bone remodeling due to reduced parathyroid hormone concentrations, or an increase in estrogen concentrations, which both accompany a moderate alcohol intake.

Our study had several limitations. Firstly, this was a cross-sectional study without any prospective data, so it was not possible to determine a causal relationship. Secondly, Baumgartner et al. [19] suggested the definition of sarcopenia to be more than two SD below the mean of a young reference population. We defined sarcopenia as a SMI below one SD of the sex-specific normal mean of a younger reference group, because when defined below two SD, there were only five women with sarcopenia among 1803 women. Newman et al. [30] offered an alternative definition of sarcopenia using appendicular lean mass adjusted for height and body fat mass (residuals), defined below the sex-specific 20th percentile. The prevalence of sarcopenia was 43.7% in men and 16.5% in women. Residual appendicular lean mass was positively correlated with femur neck BMD (men, r = 0.292, p < 0.001; women, r = 0.058, p = 0.014) in a bivariate correlation model. Residual appendicular lean mass also had a positive relationship with femur neck BMD (men, B = 0.269, p < 0.001; women, B = 0.120, p < 0.001) in a multiple regression model adjusting for confounding factors. A similar result was observed whether sarcopenia was defined by the residual method or using SMI measurements. Thirdly, the European Working Group on Sarcopenia in Older People (EWGSOP) defined sarcopenia as not only low muscle mass, but also low muscle function (strength or performance) [31]. However, the KNHANES did not measure muscle function (strength or performance).

In conclusion, muscle mass and fat mass were identified as determinants of femur neck BMD in men and women. Smoking in men, alcohol consumption in both sexes, and vitamin D levels in women were also identified as determinants of femur neck BMD. In terms of body composition, muscle mass in men and fat mass in women are stronger determinants of femur neck BMD. Therefore, the diagnosis of sarcopenia is important to inform a diagnosis of osteoporosis in all men, and in women with obesity.

Conflicts of interest

No other potential conflict of interest relevant to this article.

Appendix A. Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.afos.2016.04.002.

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