Body Fat and Physical Activity Modulate the Association between Sarcopenia and Osteoporosis in Elderly Korean Women

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Abstract
This study examined whether modifiable lifestyle factors, such as body fatness and physical activity, modulate the association between sarcopenia and osteoporosis. In a cross-sectional design, 269 postmenopausal women, aged 65 years and older, underwent dual-energy X-ray absorptiometry (DEXA) scans to measure their body fat percentage, total fat mass, total fat-free mass, appendicular lean mass, bone mineral density (BMD) and bone mineral content. The participants wore a uniaxial accelerometer for seven consecutive days to quantify daily physical activity. The collected data were analyzed using descriptive statistics, Pearson correlation, and a binary logistic regression. Pearson correlation analyses showed that total neck/femur BMD was positively associated with weight-adjusted appendicular skeletal muscle mass (ASM) and objectively-measured physical activities. ASM was positively associated with body fatness. Binary logistic regression analyses showed that the odds ratio (OR) of sarcopenia for osteopenia and/or osteoporosis was substantially attenuated but remained marginally significant when adjusted for age and postmenopausal period (OR = 2.370 and p = 0.050). However, the OR was no longer significant when additionally adjusted for body fatness (OR = 2.218 and p = 0.117) and physical activity (OR = 1.240 and p = 0.448). The findings of the study showed that, in this sample of elderly Korean women, modifiable lifestyle risk factors such as body fatness and physical inactivity played an important role in determining the association between sarcopenia and osteopenia/osteoporosis.

Key words: Women, menopause, risk factors, sarcopenia, osteoporosis.

Introduction
Aging is associated with a number of structural and functional changes that are conducive to increased disability, frailty and falls (Baumgartner et al., 1998). Contributing factors for the physical impairments are a gradual deterioration of bone (osteoporosis) (WHO Scientific Group, 2003) and a progressive decline in muscle mass (sarcopenia) (Santilli et al., 2014).

Osteoporosis is a disease characterized by low bone mass and micro-architectural deterioration of bone tissue, leading to enhanced bone fragility and a consequent increase in fracture risk. Bone mineral density (BMD) is influenced by ethnicity, geographic factors, diet, exercise, family history, and other lifestyle factors. For example, BMD values in white females are lower than in black females (Kao et al., 1994), and values in Asian females are lower than in white females (Russell-Aulet et al., 1993).

Sarcopenia is characterized by an abnormal loss of muscle mass with qualitative changes to the muscle, resulting in a loss of strength (Santilli et al., 2014). The loss of muscle mass from sarcopenia is thought to affect functional ability as shown by the positive association between muscle mass and lower extremity function, and the negative association between muscle mass and use of a cane or walker (Visser et al., 2005), history of falling (Landi et al., 2012), and self-reported difficulty with gait and daily activities (Estrada et al., 2007).

The prevalence of osteoporosis and sarcopenia increases with age, in conjunction with physical inactivity (Ryu et al., 2013), malnutrition (Vandewoude et al., 2012) and body fatness (Hsu et al., 2006). Korea’s population is rapidly aging. In 2010, people 65 years and older comprised 11% of the population, and the number is projected to increase to 24.3% in 2030 and reach 37.4% in 2050 (Korean National Statistical Office, 2012). In a nationwide survey of Koreans 65 years and older, the prevalence of sarcopenia was estimated to be 9.7% for men and 11.8% for women (Kim et al., 2012). The prevalence of osteoporosis was 7.5% for men and 35.5% for women (Choi et al., 2012). Despite the high prevalence, few studies have investigated the potential association between sarcopenia and osteopenia/osteoporosis, especially in older Korean women. Further, the majority of existing studies on the association between sarcopenia and osteoporosis have been from Western societies.

Given the close association between sarcopenia and osteoporosis, physical activity should be encouraged throughout life as an efficient strategy to maintain bone and muscle health. For example, compelling data support the efficacy of physical activity, resistance exercise in particular, in maintaining muscle mass and muscle function in aging populations (Ryu et al., 2013; Fiatarone et al., 1994). In addition, physical activity regulates bone maintenance and stimulates bone formation, including the accumulation of mineral, strengthening of muscles, and improvement of balance, and thus reduces the overall risk of falls and fractures (Moayyeri, 2008). Together, the previous findings suggest physical activity as a mediator in the association between sarcopenia and osteoporosis in older adults. Further, in older women, sarcopenia and osteoporosis may act together. However, there is little information on exactly how modifiable risk factors such as body fatness and physical inactivity mediate the association between sarcopenia and osteoporosis.

In this study we examined: 1) the association between sarcopenia and osteopenia and/or osteoporosis in community-dwelling women 65 years and older and 2)
whether covariates such as body fatness and physical activity modulate the association between sarcopenia and osteopenia and/or osteoporosis in this study population.

Methods

Study participants
Initially, 280 study participants were recruited via advertisements (i.e., local newspapers and flyers) from local community centers in the Northwestern Gyeonggi Province of South Korea between December 2014 and December 2015. Eligibility criteria included: women aged 65 years or older; self-report of no difficulty walking; no difficulty performing basic activities of daily living; no reported use of cane, walker, crutches or other special equipment to get around; no history of active treatment for cancer in the prior 3 years; and no enrollment in a lifestyle intervention trial.

After receiving information describing the study, potential participants were screened for the eligibility criteria described above. Of the 280 participants, 7 were excluded due to mobility limitations and/or use of cane, walker, and crutches. An additional 4 participants refused to participate in body composition and/or physical activity assessments due to personal reason(s). Consequently, a total of 269 participants were available for analysis.

Procedures
Data was collected during three separate visits. During the first visit, the participants’ demographic characteristics and general health statuses were assessed with a standardized self-administered questionnaire modified from ACSM’s Guidelines for Exercise Testing and Prescription (American College of Sports Medicine, 2014) and interviews were conducted by geriatric nurses. One week after the first visit, each participant’s body composition was analyzed using dual-energy X-ray absorptiometry (DEXA). Finally, daily physical activity was monitored and analyzed using self-administered questionnaire modified from the American College of Sports Medicine, 2014 and International Diabetes Federation, 2009. Participants were asked to wear the device from the time they woke up in the morning until they went to bed at night, except while bathing, for the full 7-day data collection period. The Sungkyunkwan University Institutional Review Board, in accordance with the Declaration of Helsinki of the World Medical Association, approved the study protocol. All participants provided written informed consent to participate in the study.

Instrumentation
Total body composition and bone densitometry by DEXA was performed at Yongin University on equipment branded QDR 4500A (Hologic, Waltham, MA, USA). The DEXA measurement methods and validation have been tested and reported by Visser et al. (1997) and Salamone et al. (2000). The performance of the densitometries of the whole body, lumbar spine, femoral neck, and total hip was performed by the same operator. The results of the bone densitometry were expressed in g/cm² and T-score, calculated by the device itself, and analyzed according to the criteria of the World Health Organization (WHO Scientific Group, 2003). In brief, osteopenia was defined as a BMD more than 1.0 but less than 2.5 standard deviations (SD) below the young adult mean (T-score –1 and –2.5), and osteoporosis was defined as a BMD of 2.5 or more SDs below the young adult mean (T-score –2.5). The BMDs were measured from DEXA of the lumbar spine (L2–L4) and the total hip.

From the whole-body composition data obtained using DEXA, appendicular skeletal muscle mass (ASM) was calculated as the sum of muscle mass in arms and legs, assuming that all nonfat and nonbone tissue is skeletal muscle (Baumgartner et al., 1990; Delmonico et al., 2007). Sarcopenia was defined as weight-adjusted ASM below -2 SD (Kim et al., 2012).

Physical activity (PA) was assessed using the Kenz Lifecorder EX, a uniaxial accelerometer (LC; Suzuken Co. Ltd, Nagoya, Japan). The activity levels were categorized into nine activity classes from light (activity level of 1.0) to vigorous (activity level of 9). The nine activity levels were further classified low (<3.0 MET; activity level of 1-3), moderate (3.0-6.0 MET; activity level of 4-6), and vigorous (>6.0 MET; activity level of 7-9) based on PA energy expenditure as described previously (Kumahara et al., 2004).

Statistical analyses
All variables were checked for normality and if necessary, subjected to a log10 transformation before statistical analyses. Descriptive statistics for raw variables across BMD categories are presented as the mean±SD. Tests for linear trends were performed with the linear contrast analysis of one-way ANOVA for each category (normal, osteopenia, and osteoporosis) of BMD. Pearson correlation and binary logistic regression analyses were conducted to evaluate the impact of sarcopenia on BMD-based osteoporosis and/or osteopenia while controlling for the measured covariates such as age, postmenopausal period, body fatness, and daily physical activity. Values of p ≤ 0.05 were considered statistically significant.

Results
With respect to demographic measures, there was a significant positive, linear trend in mean age (p < 0.001) across the incremental severity of BMD from normal to osteoporosis. With respect to body composition and BMD, there were significant negative linear trends in BMI (p = 0.039), lean mass (p = 0.032), ASM index (p = 0.007), femur total BMD (p < 0.001), femur total T-score (p < 0.001), femur neck BMD (p < 0.001), and femur neck T-score (p < 0.001) across the incremental severity of bone health status. With respect to daily activity, there were also significant negative, linear trends in low (p < 0.001) and moderate (p = 0.002) physical activity across the incremental severity of bone health status (Table 1).

The bivariate Pearson correlation was used to test the relationships between measured variables. Age was significantly, positively associated with waist circumference (r = 0.272) and postmenopausal period (r = 0.836) and negatively with femur total BMD (r = -0.324), femur total
T-score (r = -0.290), femur neck BMD (r = -0.392), femur neck T-score (r = -0.389, p < 0.001), low (r = 0.446), moderate (r = 0.403), and vigorous physical activity (r = -0.354). Similarly, postmenopausal period was significantly, negatively associated with femur total BMD (r = -0.320), femur total T-score (r = -0.298), femur neck BMD (r = -0.036), femur neck T-score (r = -0.329), low (r = 0.372), moderate (r = 0.293), and vigorous physical activity (r = -0.402) (Table 2).

With respect to body composition parameters, waist circumference was significantly, positively associated with postmenopausal period (r = 0.224) and ASM (r = 0.317) and negatively with moderate (r = -0.267) and vigorous (r = -0.261) physical activity. BMI was negatively associated with moderate (r = -0.198) and vigorous (r = -0.324) physical activity. Lean mass was significantly, positively associated with ASM (r = 0.646). In addition, ASM was positively associated with femur total BMD (r = 0.204) and femur total T-score (r = 0.189). Femur total BMD and T-score were significantly, positively associated with low (r = 0.411 and r = 0.413, respectively), moderate (r = 0.249 and r = 0.254, respectively), and vigorous (r = 0.248 and r = 0.228, respectively) physical activity. Femur neck BMD and T-score were significantly, positively associated with low (r = 0.413 and r = 0.399, respectively), moderate (r = 0.254 and r = 0.241, respectively), and vigorous (r = 0.228 and r = 0.212, respectively) physical activity (Table 2).

A binary logistic regression analysis was used to determine the odds ratio (OR) of sarcopenia for osteoporosis and/or osteopenia. Compared to women without sarcopenia (reference group, OR = 1), women with sarcopenia had an OR of 2.488 (95% CI of 1.048 ~ 5.904, p = 0.039) for having osteopenia/osteoporosis. When adjusted

Table 1. Comparison of body composition variables between normal, osteopenia and osteoporosis. Values are means (±SD).

<table>
<thead>
<tr>
<th>Variables</th>
<th>Normal (n = 85)</th>
<th>Osteopenia (n = 120)</th>
<th>Osteoporosis (n = 64)</th>
<th>P for linear trends</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td>71.7 (5.3)</td>
<td>72.4 (4.5)</td>
<td>80.3 (6.0)</td>
<td>.001</td>
</tr>
<tr>
<td>Menopause period (yrs)</td>
<td>50.7 (3.9)</td>
<td>49.0 (4.8)</td>
<td>49.0 (3.0)</td>
<td>.180</td>
</tr>
<tr>
<td>BMI (kg·m⁻²)</td>
<td>25.3 (3.1)</td>
<td>25.1 (3.4)</td>
<td>22.7 (3.3)</td>
<td>.039</td>
</tr>
<tr>
<td>Body fat (%)</td>
<td>36.7 (6.2)</td>
<td>36.3 (6.1)</td>
<td>33.6 (7.7)</td>
<td>.264</td>
</tr>
<tr>
<td>Lean mass (kg)</td>
<td>35.3 (3.0)</td>
<td>34.9 (3.4)</td>
<td>32.6 (3.3)</td>
<td>.032</td>
</tr>
<tr>
<td>WC (cm)</td>
<td>83.6 (9.3)</td>
<td>84.3 (8.3)</td>
<td>83.8 (8.8)</td>
<td>.934</td>
</tr>
<tr>
<td>ASM index (kg·m⁻²)</td>
<td>6.1 (4)</td>
<td>5.9 (6)</td>
<td>5.5 (5)</td>
<td>.007</td>
</tr>
<tr>
<td>Femur total BMD (g·cm⁻²)</td>
<td>.937 (.076)</td>
<td>.783 (.048)</td>
<td>.655 (.107)</td>
<td>.001</td>
</tr>
<tr>
<td>Femur total T-score</td>
<td>-2.22 (.67)</td>
<td>-1.61 (.42)</td>
<td>-2.89 (.73)</td>
<td>.001</td>
</tr>
<tr>
<td>Femur neck BMD (g·cm⁻²)</td>
<td>.814 (.073)</td>
<td>.704 (.058)</td>
<td>.588 (.132)</td>
<td>.001</td>
</tr>
<tr>
<td>Femur neck T-score</td>
<td>-1.06 (.61)</td>
<td>-1.99 (.50)</td>
<td>-2.94 (1.09)</td>
<td>.001</td>
</tr>
</tbody>
</table>

Table 2. Bivariate correlations among the measured variables (n = 269).

| Age (yrs)   | 1                  |                      |                      |                      |
| BMI (2)     | .039               |                      |                      |                      |
| BF (3)      | .003               | .821**               | 1                    |                      |
| LM (4)      | -.055              | .470**               | .112                 | 1                    |
| WC (5)      | .272*              | .743**               | .675**               | .402**               | 1                    |
| PM-period (6)| .836**             | .048                 | .016                 | -.064                | .224*                | 1                    |
| ASM (7)     | -.036              | .529**               | .120                 | .646**               | .317**               | -.044                | 1                    |
| FT BMD (8)  | -.324**            | .163                 | .142                 | .140                 | .030                 | -.320**              | .204*                |                      |
| FT T-score (9)| -.290*             | .160                 | .147                 | .145                 | .025                 | -.298**              | .189*                 | .945**               | 1                    |
| FN BMD (10) | -.392**            | .086                 | .075                 | .164                 | -.030                | -.336**              | .132                   | .889**               | .842**               | 1                    |
| FN T-score (11)| -.389**            | .080                 | .082                 | .139                 | -.036                | -.329**              | .111                   | .881**               | .835**               | .996**               | 1                    |
| LPA (12)    | -.446**            | -.049                | -.037                | -.028                | -.178                | -.372**              | -.057                  | .375**               | .411**               | .413**               | .399**               | 1                    |
| MPA (13)    | -.403**            | -.115                | -.198*               | .047                 | -.267*               | -.293**              | -.047                  | .221*                 | .249*                 | .254*                 | .241*                 | .441*                 | 1                    |
| VPA (14)    | -.354**            | -.177                | -.241*               | -.013                | -.261*               | -.402**              | .089                   | .240*                 | .248*                 | .228*                 | .212*                 | .274*                 | .408**               | 1                    |

* p < 0.05, ** p < 0.001; BMI: body mass index; WC: waist circumference; PM: postmenopausal; ASM: appendicular skeletal muscle; FT: femur total; BMD: bone mineral density; FN: femur neck; LPA: low intensity physical activity; MPA: moderate intensity physical activity; VPA: vigorous intensity physical activity.
for age and postmenopausal period, the OR of sarcopenia for osteopenia and/or osteoporosis was substantially attenuated but remained marginally significant (OR = 2.370, CI of 0.969 ~ 5.830, p = 0.050). However, the OR was no longer significant when additionally adjusted for body fatness (OR = 2.218, CI of 0.820 ~ 6.000, p = 0.117) and for physical activity (OR = 0.1240, CI of 0.583 ~ 3.210, p = 0.448) (Table 3).

**Discussion**

Osteoporosis and sarcopenia are major health conditions responsible for an increased risk of bone fractures and reduced functional capacity, respectively, in older adults. Body fatness (Hsu et al., 2006) and physical inactivity (Ryu et al., 2013) are established risk factors for sarcopenia and osteoporosis. Asians have relatively lower muscle mass but higher body fat than Caucasians (Rush et al., 2007), suggesting that Asians have a greater risk of sarcopenia than Caucasians. Yet, the majority of the previous studies on the association between sarcopenia and osteoporosis have looked at Caucasians rather than Asians. Consequently, little information is available regarding whether lifestyle risk factors modulate the association between the two health conditions, especially in elderly Korean women.

In this study, we found that in a sample of elderly Korean women, sarcopenia was significantly associated with osteopenia/osteoporosis based on T scores of total femur and neck BMDs. Further, binary logistic regression analyses showed that women with sarcopenia had a greater risk of having osteopenia/osteoporosis (OR = 2.5) than women without sarcopenia (OR = 1.0). However, the OR of sarcopenia for osteopenia/osteoporosis was substantially attenuated when adjusted for age and postmenopausal period, and was no longer significant when additionally adjusted for body fatness and physical activity. Together, the current findings suggest that measured lifestyle risk factors, such as body fatness and physical inactivity, may modulate the association between sarcopenia and osteopenia/osteoporosis in this study of elderly Korean women.

The current findings support previous findings. In the 2008-2009 Korean National Health and Nutrition Examination (KNHNE) data, for example, Ryu et al. (2013) showed that physical activity was inversely associated with sarcopenia and sarcopenic obesity in the elderly Korean population. In that study, women with high physical activity had a significantly lower risk of sarcopenic obesity than their counterparts with low physical activity. The inverse relationship between physical activity and sarcopenia has also been reported from the epidemiologic studies of Chinese (Lee et al., 2007), Japanese (Park et al., 2010), Mexican (Baumgartner et al., 1998), and French (Szulc et al., 2004) elderly populations.

The current findings also support the hypothesis that higher fat mass may be an independent risk factor for osteoporosis and for osteoporotic fractures, at least in women. For example, Wyshak (2010) found a significant association between body fat percentage, estimated from anthropometrics measures, and wrist and vertebral fractures in female college alumnae 39 years and older. In a community-based, cross-sectional study of Chinese men and premenopausal women aged 25 to 64 years old, Hsu et al. (2006) found that fat mass was significantly inversely associated with bone mineral content in the whole body and total hip. Further, they found significant positive linear trends for higher risks of osteoporosis, osteopenia, and non-spine fractures across incremental percentage fat mass. Bredella et al. (2013) found that obese people with higher levels of fat in their liver, muscle tissue, and blood also have higher levels of fat in their bone marrow, putting them at risk for osteoporosis. Together, the current findings suggest that further increases in medical expenditures may be associated with sarcopenia and osteoporosis, given the relevant costs from frailty-related fractures, which the data suggest to be more common among women with sarcopenia and/or osteoporosis than among women without sarcopenia and/or osteoporosis.

Due to the cross-sectional nature of the study, we could not speculate the potential mechanism(s) by which body fatness and physical inactivity modulate the association between sarcopenia and osteopenia/osteoporosis. However, the observed association between sarcopenia and osteopenia/osteoporosis was consistent with previous studies that reported a reduction in the osteogenic effect resulting from minor mechanical stimulation imposed on the bone structure by reducing the muscle mass and muscle function (Ahedi et al., 2014) due to physical inactivity (Salminen et al., 2006). That is, physical inactivity leads to a decrease in the number and the size of muscle fibers due to muscle cell apoptosis and reduced mechanical stimuli (D’Antona et al., 2007). Studies from life-long athletes have shown that intense aerobic and resistance exercise may prevent and/or reverse the loss of muscle mass associated with aging (Ogawa et al., 2010).

This study has some limitations. First, due to the nature of the cross-sectional study, our study could not infer a cause-and-effect relationship between sarcopenia and osteopenia/osteoporosis. Therefore, a large, population-based study, consisting of both men and women, would be necessary to confirm the current study’s find-
lings with respect to a cause-and-effect relationship. Second, the current study also suggests menopause may be another mediator in the association between osteoporosis and sarcopenia. Menopause is linked to a reduction in lean mass and BMD (Ho-Pham et al., 2010), both of which are directly related to the reduced production of ovarian hormones, a result of menopause that is differentiated from the aging process.

Conclusion

The results of the present study suggest that abnormal BMD phenotype is significantly associated with sarcopenia in a sample of elderly Korean women. Further, physical activity in conjunction with body fatness modulates the association between abnormal BMD phenotype and sarcopenia in this study population. These findings highlight the importance of increased body fatness and physical inactivity as modifiable risk factors for osteoporosis and sarcopenia and provide a rationale for further exploration of the underlying mechanisms.

Acknowledgments

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References


Key points

- Osteoporosis and sarcopenia are major health conditions responsible for an increased risk of bone fractures and reduced functional capacity, respectively, in older adults.
- We investigated whether lifestyle-related risk factors modulate the association between sarcopenia and osteoporosis in older Korean adults.
- The current findings of the study suggest that physical activity and body fatness modulates the association between abnormal BMD phenotype and sarcopenia in this study population.

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