



## Research Article

## Lifestyle and Genetic Predictors of Stiffness Index in Community-dwelling Elderly Korean Men and Women



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## SUMMARY

**Purpose:** Differing lifestyle, nutritional, and genetic factors may lead to a differing stiffness index (SI) determined by quantitative ultrasound in elderly men and women. The purpose of this study was to determine SI and the gender-specific factors associated with low SI in a Korean elderly cohort.

**Methods:** This was a cross-sectional descriptive study identifying the gender-specific factors related to SI in 252 men and women aged 65 years and greater from local senior centers in Seoul, Korea between January and February 2009.

**Results:** The mean SI of elderly men was significantly higher than that of the women's. A multiple regression analysis reveals that age, nutritional status, and physical activity were predictive factors of lower SI in men, whereas age, alcohol consumption, educational level, and genetic polymorphism were predictive factors for elderly women.

**Conclusions:** Low SI was common in both elderly men and women. We found gender differences in factors linked to low SI. In multiple regression analysis, nutritional status and physical activity were more important factors in men, whereas alcohol consumption, educational level, and genetic polymorphism were significant factors predicting low SI in women. Gender-specific modifiable risk factors associated with low SI should be considered when developing osteoporosis prevention programs for the elderly.

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## Introduction

Osteoporosis is a metabolic bone disease characterized by low bone mass and microarchitectural deterioration of bony tissue leading to enhanced bone fragility and a consequent increase in fracture risk [1]. Osteoporosis is diagnosed when a person's bone mineral density obtained from dual-energy X-ray absorptiometry (DXA) is at 2.5 standard deviations below the World Health Organization (WHO)-defined threshold value or more. This value, called the T score, is a measurement derived from healthy young adults' bone mineral density [2]. Osteoporotic fractures account for more disability-adjusted life years than many other diseases, including hypertension, stomach cancer, and breast cancer [3].

Osteoporosis-related fractures can also lead to a huge economic burden on society worldwide [4–6], with a trend towards further increases [4,7] because of the direct (medical care costs, medical services, and nonmedical costs) and indirect (work loss) costs of osteoporosis [7,8].

The Fourth Korean National Health and Nutrition Examination Survey revealed that the elderly population (aged  $\geq 65$  years) is rapidly increasing in Korea [9], just as it is in most Western countries. Although elderly females are known to suffer more from osteoporosis-related fractures than males do, the risks of osteoporosis development and related fractures are also common in elderly men [10]. The residual lifetime probability of osteoporosis-related fractures in Korean male adults was reported to be 23.8% [10].

Although bone mineral density obtained from DXA is a standard diagnostic technique for osteoporosis, it is difficult to apply in community-based studies because of a lack of portability, high cost, and exposure to ionizing radiation. Quantitative ultrasound (QUS, Achilles Express ultrasonometer (GE Lunar Healthcare Corporation,

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Madison, WI, USA), however, is inexpensive and easy to carry, and also estimates the bone density of the calcaneus. Many studies have suggested that stiffness index (SI) obtained from QUS was correlated strongly with DXA measurements [11,12]. SI is the sum of the scaled and normalized speed of sound (SOS) and broad ultrasound attenuation (BUA) values, which is a measure of bone strength (bone density and bone quality) and is sensitive to bone structure used to predict the risk of bone fracture due to osteoporosis in both men and women [13–15]. Low SI can indicate and screen individuals with low bone mass [16], assisting medical personnel in the screening of osteoporosis. SI was reported to decrease with age and be higher for men than for women [17]. Heritability estimates of QUS parameters have ranges between 53% and 74% at the calcaneus [18,19].

Different lifestyle, nutritional status, nutrient intakes, and genetic factors may lead to a different SI of each gender group, but gender-specific factors associated with low bone mass have yet to be identified. Data correlating lifestyle/nutritional status and low SI in each gender are often inconsistent or insufficient. The level of education was found to be correlated with low SI on QUS in elderly women [20], whereas physical activity and body mass index (BMI) have been reported to be related to SI as measured by QUS in elderly men [21]. Some have reported that malnutrition, which is frequent in elderly is a risk factor for osteoporotic fractures (repetitive) [22] and correlations between nutritional markers and QUS parameter in Australian elderly care residents were found [23]. However, another study reported no correlation between nutritional status and SI measured by QUS in elderly women [23].

Among a large number of osteoporosis risk candidate genes, the estrogen receptor (ER) gene (X03635, X99101) and vitamin D receptor (VDR) gene (J03258) have been most widely studied. ER and VDR genotype polymorphisms may act differently on elderly men and elderly women [24–26]. Moreover, the difference may present in different ethnic groups [27]. Many studies have reported a positive relationship between the ER gene/VDR gene and low bone mass based on QUS in postmenopausal women [28–30], whereas an association between genetic polymorphism and low SI in elderly males has been far less studied, except for one study. This study has suggested a relationship between ER and low bone mass in Korean men [14]. Therefore, no conclusion has yet been reached as to whether ER and VDR genotype polymorphisms are associated with SI in elderly men and women.

In the present study, therefore, we assessed the calcaneal SI measured by QUS and investigated the relationship of the SI with a comprehensive set of factors including lifestyle factors, nutritional status, nutrient intakes, and genetic factors in a cohort of Korean elderly men and women.

## Methods

### Study design

This study was a secondary data analysis identifying the gender-specific factors related to SI. Briefly, between 2009 and 2011, consecutive elderly from two senior centers were participated in our study. We first investigated the effects of lifestyle factors, nutritional status and nutrient intakes on SI. We also investigated the relationship of the SI with gene polymorphisms.

### Setting and sample

The participants were recruited from two nearby local senior centers in Seoul, Korea who wished to participate in the study on a voluntary basis, between January and February in 2009. Out of the 381 participants who attended the center on a regular basis, 307

participants (164 elderly men and 143 elderly women) were enrolled after seeing the advertisement posted at the centers.

The inclusion criteria were age 65 years or more and the absence of dementia. The participants were excluded if they had dementia severe enough to preclude a reliable interview, which was determined by the modified Korean version of the Mini Mental State Examination (K-MMSE). The K-MMSE had been developed regarding age, educational attainment and gender [31,32] due to their generational characteristics, which is that age and gender differences exist in educational levels in Korean elderly [33]. We also excluded older adults with involvement in any osteoporosis treatments or drugs, and presence of diseases affecting bone metabolism in order to rule out any effects of those on SI. Of the initial 307 participants who wished to participate, 28 (22 men and 6 women) were excluded due to dementia, and 27 (15 men and 12 women) were excluded due to incomplete data, history of fracture, or taking osteoporosis medication. Thus, in the end, 252 participants were included in the study.

### Ethical consideration

This study was a secondary data analysis. The institutional review board at Seoul National University approved the study (2011–50). Researchers explained the purpose and the procedures of the study and obtained written informed consent before the data collection procedure. Participants were informed that they were not obliged to participate in the study and incentives were provided after the study.

### Calcaneal QUS measurement

We measured bone mass with QUS, which has been used as a screening tool for osteoporosis and low bone mass in elderly men and women [12,34]. QUS measurements were performed with an Achilles Express ultrasonometer (GE Lunar Healthcare Corporation, Madison, WI, USA) at the right calcaneus. Quality control was performed according to the manufacturer's instructions before the first measurement of each survey day. The measurement was taken with a single ultrasonometer by the same trained nurse. All measurements were performed at room temperature. This ultrasonometer provides parameters in less than 1 minute, providing real-time imaging of the calcaneus. Two main parameters, SOS and BUA can be measured by QUS devices, derived from the velocity or attenuation of the ultrasound waves through the bone tissue. SI, introduced by the manufacturer to measure bone fragility, was defined as a combination of normalized SOS and BUA [35]. SI was calculated using the following equation [36]:

$$SI = (0.67 \times BUA) + (0.28 \times SOS) - 420$$

### Sociodemographic and lifestyle data

The participants were interviewed using a structured questionnaire to obtain sociodemographic data, including age, gender, years of formal education, income, and family structure (living alone/living with spouse/living with others). The lifestyle data were assessed. When the participants reported being current smokers/alcohol drinkers, information on the amounts of alcohol/tobacco they consumed were also obtained. The level of physical activity was assessed using the International Physical Activity Questionnaire (IPAQ). IPAQ levels were grouped into three categories: > 2,500 MET/min/week, 500–2,500 MET/min/week, and < 500 MET/min/week and classified as “vigorous”, “moderate”, and “low” physical activity, respectively [37]. Reasonable reliability of Korean version of IPAQ was reported in Korean female adult [38]. Recently

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