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ORIGINAL ARTICLE

Association between Fractures and Low Muscle Mass in Korean Menopausal Women: Data from Korean National Health and Nutrition Survey (2010–2011)

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Objectives: This study used the Korean National Health and Nutrition Examination Survey (KNHANES) to determine the association between fractures and low muscle mass.

Methods: This cross-sectional study used the 2010–2011 KNHANES data. Low muscle mass was defined as (appendicular skeletal muscle mass [kg]/Height^2 [m^2]) < 5.45 kg/m^2, which is < 2 SD below the sex-specific mean of a young reference group. Patients with T-scores between –1.0 and –2.5 indicated osteopenia, whereas those with T-scores lower than –2.5 indicated osteoporosis.

Results: Out of 1,306 women enrolled in the study, 330 were diagnosed with low muscle mass according to the abovementioned diagnostic criterion. The prevalence of fractures at various sites was significantly higher in postmenopausal women with low muscle mass than in those without low muscle mass (relative risk [RR], 1.64; odds ratio [OR], 1.62; 95% confidence interval [CI], 1.06–2.48; P = 0.027). Furthermore, the prevalence of fractures was increased by the presence of osteopenia or osteoporosis in addition to low muscle mass (RR, 1.59; OR, 1.60; 95% CI, 1.02–2.49; P = 0.039) and by osteoporosis only (RR, 2.12; OR, 2.29; 95% CI, 1.11–4.70; P = 0.025).

Conclusions: Fracture was more prevalent in postmenopausal women with low muscle mass than in those without low muscle mass. This finding is consistent in a subgroup analysis that included women who had osteoporosis or osteopenia. Moreover, the risk of fractures increased as low muscle mass worsened.

Key Words: Osteoporosis, Postmenopause, Sarcopenia

INTRODUCTION

Sarcopenia is considered an important cause of the decrease in sex hormones due to aging, and an increase in inflammatory cytokines is known to promote muscle catabolism and worsen sarcopenia. In addition, menopausal women are expected to have a high prevalence of sarcopenia due to decrease in muscle strength caused by a decrease in sex hormones. Previously Sarcopenia was defined as low muscle mass only [1], but there was recently an agreement that low muscle mass and low muscle function should go together to fully define Sarcopenia [2]. Asian Working Group for Sarcopenia 2019 also defined sarcopenia as low appendicular skeletal muscle mass and low muscle strength or low physical performance [3]. In this paper, we defined the low muscle mass and wanted to find out its influence. Most studies on low muscle mass have been conducted on the elderly, so the prevalence rate in menopausal women and the relationship with other diseases are still unknown.

The World Health Organization has defined osteopo-

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rosis as a metabolic bone disease that increases the risk of fractures as bones become fragile due to low bone mass and microscopic structural deterioration of bone tissue [4]. In women, bone density is highest at the age of 25–35 and begins to decrease after the age of 40, resulting in a 1%–2% annual decrease in spongy bone. Immediately after menopause, the density of the spinal spongy bone decreases by an average of 4.4% to 8.5% per year, and menopause is an important factor in the reduction of bone density.

The probability of fractures due to osteoporosis over a lifetime is estimated to be about 40% [5], and the increased incidence of osteoporosis and resulting fractures due to the extension of life expectancy and the increase in the elderly population is now a global health issue. One in five patients with femoral fractures that result from osteoporosis dies within a year, and the risk of death in osteoporosis patients is 3.5 times that in the general public; for women, the risk of dying from femoral fractures is the same as that of breast cancer and four times higher than that of endometrial cancer.

Although menopause reduces muscle strength, increases body fat, and decreases bone density, only a few studies investigated the relationship between low muscle mass and fractures. In particular, research on this topic is still insufficient in Korea. Interventions to prevent and treat low muscle mass are effective when they are based on increasing muscle mass, strength, and physical performance, although they have not been proven to decrease the prevalence of fractures [6]. The aim of this study was to evaluate whether Korean menopausal women with low muscle mass have a higher risk of fractures than those without low muscle mass.

MATERIALS AND METHODS

Study design and setting

This was a nationwide cross-sectional observational study that used data from Korean National Health and Nutrition Survey (KNHANES) conducted from 2010 to 2011. KNHANES is a national, population-based cross-sectional survey and health examination that collects data on the health and nutrition status of Koreans by selecting representative noninstitutionalized Korean civilians. Approximately 10,000 individuals are selected each year. The survey is collecting information by health interviews, physical examinations, and nutrition surveys. All the components of the survey were conducted either at a mobile screening center or at participants' home by trained medical staff, dieticians, health interviewers, and medical technicians.

A written informed consent from participants were approved by KNHANES. For this study, we used the patients' data from 2010 to 2011, and this study was approved by the Institutional Review Board of the Korea Centers for Disease Control and Prevention (No. 2010-02CON-21-C, 2011-02CON-06C).

Participants

All participants were postmenopausal women, and 3,474 of them who answered a question about their osteoporotic fractures were enrolled. We selected only those who answered all questions about their menopausal status, medical history, hypertension (HTN) and diabetes mellitus (DM) medication, lifestyle (smoking, alcohol consumption), and hormone therapy. We checked physical examination results for body mass index (BMI, kg/m^2), waist circumference (cm), and dual-energy x-ray absorptiometry (DXA). We excluded 2,168 patients using the following exclusion criteria: age < 60 years or > 80 years (n = 811), thyroid disease, end-stage renal disease, or malignancy (n = 308), and missing DXA data (n = 1,049) (Fig. 1).

Finally, this study included 1,306 women who answered that they had the history of fractures. They were divided into two groups, those diagnosed with low muscle mass and normal controls.

Definition of low muscle mass and osteoporosis

The definition of the low muscle mass group was based on the appendicular skeletal muscle (ASM) calculated from the results of the systemic bone density test and body mass. ASM was defined as the total muscle mass of the four limbs determined using DXA according to the European Working Group for Sarcopenia guidelines [7]. A standardized diagnostic criterion to define sarcopenia does not exist [8]. Referring to previous data, we used the ASM index (%), which is calculated by dividing ASM to the square of the body weight and multiplying by 100. We designated low muscle mass group when 2 × SD was lower than the sex-specific mean of a young reference group.

DXA is a standard test that commonly measures lumbar and femur and diagnoses osteoporosis on the basis of the lowest levels. According to the guidelines of the World Health Organization, a T-score of −1.0 to −2.5 standard deviation indicates osteopenia, and a T-score of −2.5 standard deviation or less indicates osteoporosis

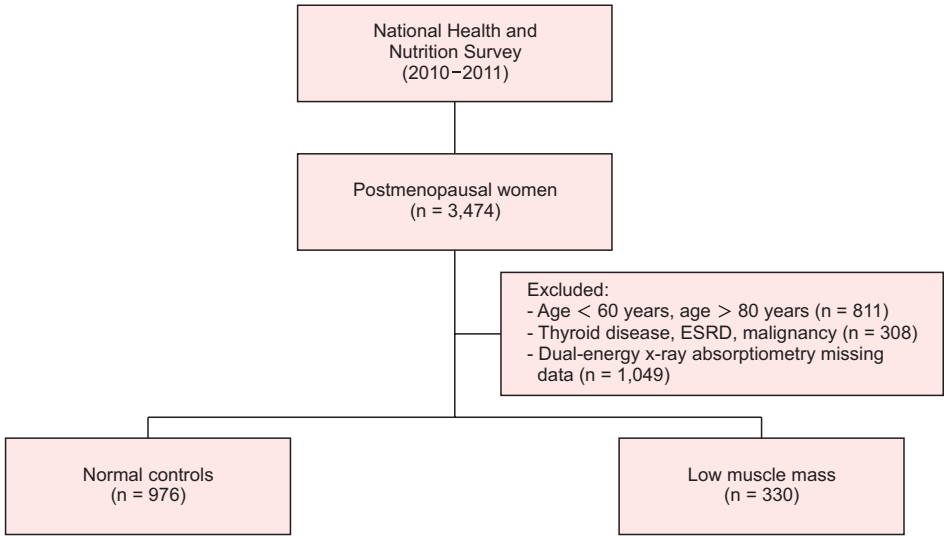

Fig. 1. Study flowchart. ESRD: end-stage renal disease.

[4]. Osteoporotic fracture diagnosis was based on the questionnaire included in KNHANES.

Measurements of variables

Age, menopause age, height, body weight, BMI, waist circumference, use of hormones, total number of pregnancies carried to a viable gestational age (parity), history of smoking, the amount of alcohol consumed and medical history of HTN, DM, bone density and fractures were considered as confounding variables.

All participants completed physical and blood tests at a mobile screening center or at home. They wore simple clothing without shoes and measured their height, weight, and blood pressure. BMI was calculated from the measured height and weight. Blood was sampled after fasting for at least 8 hours overnight and analyzed on the same day. All participants filled out standardized questionnaires about their medical history and lifestyles. Questions were asked about previously diagnosed HTN and DM. The participants were asked to report all previous drinking and smoking history (including recent smoking amounts). Excessive drinking was defined as consumption of more than 30 g of alcohol a day. About smoking also asked about all previous smoking experiences and recent of smoking.

Statistical analysis

Statistical analysis software was used for all statistical analyses and the KNHANES data were analyzed according to the KNHANES data analysis guidelines. All analyses were two tailed, and a P value of < 0.05 was considered significant.

RESULTS

Demographic characteristics of participants

Participant characteristics are presented in Table 1.

Low muscle mass was diagnosed in 25.27% (n = 330) of postmenopausal women. The mean age was 69.48 (± 0.28) years in normal group and 71.18 (± 0.49) years in low muscle mass group ($P = 0.003$).

As obesity-related characteristics such as weight, waist circumference, and BMI are lower in low muscle group, one could assume thought that the prevalence of low muscle mass is higher in people with low obesity (all $P < 0.001$). The prevalence of HTN and DM did not differ among the groups ($P = 0.392$ and $P = 0.912$, respectively). Smoking was significantly higher in low muscle mass group ($P = 0.002$), but alcohol consumption was not significantly different ($P = 0.174$). The use of hormone therapy was also not significantly different among the patients ($P = 0.987$).

Low muscle mass and fractures

Tables 2–4 show the P values of multiple groupwise comparisons between normal and low muscle mass group. The incidence of fractures at various sites (spine + femur + wrist) was significantly higher in women with low muscle mass (risk ratio [RR] = 1.64, odds ratio [OR] = 1.62; 95% confidence interval [CI], 1.06–2.48; $P = 0.027$; Table 2). The incidence of fractures was increased in low muscle mass group by the presence of osteopenia or osteoporosis (RR = 1.59, OR = 1.6, $P = 0.039$; Table 3) or osteoporosis only (RR = 2.12, OR = 2.29, $P = 0.025$; Table 4). Among postmenopausal women with low muscle mass, the prob-

Table 1. Baseline characteristics of study participants

	Low muscle mass		
	Normal (n = 976)	Low muscle mass (n = 330)	*P* value
Age (y)	69.48 ± 0.28	71.18 ± 0.49	0.003
Age of menopause (y)	55.04 ± 3	53.15 ± 3.37	0.677
Height (cm)	151.97 ± 0.22	150.92 ± 0.48	0.045
Weight (kg)	58.16 ± 0.4	49.83 ± 0.42	< 0.001
Waist circumference (cm)	85.46 ± 0.37	78.48 ± 0.53	< 0.001
BMI (kg/m^2)	25.13 ± 0.15	21.85 ± 0.15	< 0.001
Fasting glucose (mg/dL)	103.17 ± 1.06	101.39 ± 1.60	0.362
HbA1c	6.45 ± 0.08	6.36 ± 0.13	0.549
Triglycerides	145.64 ± 3.40	138.56 ± 5.62	0.253
HDL cholesterol	47.3 ± 0.45	48.46 ± 0.87	0.235
LDL cholesterol	122.76 ± 2.59	128.61 ± 4.67	0.270
GOT	23.91 ± 0.47	21.53 ± 0.37	< 0.001
GPT	20.38 ± 0.45	16.63 ± 0.44	< 0.001
Alkaline phosphatase (IU/L)	260.65 ± 2.81	265.13 ± 4.75	0.405
Parathyroid hormone (pg/mL)	70.83 ± 1.37	74.38 ± 2.36	0.183
HTN medication (%)	53.38 (2.03)	51.05 (3.49)	0.552
DM medication (%)	15.14 (1.33)	16.34 (2.46)	0.646
DM (%)			0.912
Normal	58.16 (1.94)	58.99 (4.00)	
Insulin resistance	22.24 (1.70)	20.83 (3.16)	
DM	19.6 (1.48)	20.18 (2.99)	
Alcohol (%)			0.174
None	72.17 (2.82)	75.77 (4.55)	
Less than once a month	18.63 (2.47)	11.22 (3.17)	
Once a month	5.47 (1.37)	6.87 (3.08)	
Once a week	3.34 (1.21)	3.58 (1.78)	
Every day	0.39 (0.29)	2.56 (1.91)	
Smoking (%)	3.31 (0.59)	8.38 (2.06)	0.002
Parity (%)	98.6 (0.37)	98.58 (0.62)	0.980
COCP (%)	25.69 (1.68)	22.54 (2.70)	0.310
Use of hormones (%)	11.06 (1.21)	11.1 (1.89)	0.987
HTN stage (%)			0.397
Normal	10.72 (1.11)	13.49 (2.31)	
Pre-HTN	20.65 (1.46)	21.89 (2.65)	
HTN	68.62 (1.74)	64.61 (3.17)	

Values are presented as mean ± SD or number (%).
BMI: body mass index, HbA1c: glycated hemoglobin, HDL: high-density lipoprotein, LDL: low-density lipoprotein, GOT: glutamic oxaloacetic transaminase, GPT: glutamlc pyruvic transamlnase, HTN: hypertension, DM: diabetes mellitus, COCP: combined oral contraceptive pill.

Table 2. Incidence rates and odds ratios of fractures at various sites in postmenopausal women with low muscle mass

Fracture sites	Normal		Low muscle mass		Unadjusted		Adjusted	
	Total (n)	Event (n [%])	Total (n)	Event (n [%])	OR (95% CI)	*P* value	OR (95% CI)	*P* value
Spine + femur + wrist combined	976	8.35 (1.01)	330	13.73 (2.27)	1.75 (1.12–2.72)	0.013	1.61 (1.05–2.46)	0.0282
Femur	976	0.47 (0.26)	330	1.10 (0.85)	2.34 (0.36–15.26)	0.375	2.16 (0.29–15.79)	0.4489
Wrist	976	6.22 (0.83)	330	10.08 (2.09)	1.69 (1.01–2.83)	0.046	1.57 (0.98–2.51)	0.0604

Adjusted by age, age of menopause, use of hormones, and smoking, height.
OR: odds ratio, CI: confidence interval.

Table 3. Incidence rates and odds ratios of fractures at various sites in postmenopausal women with low muscle mass and osteopenia or osteoporosis

Fracture sites	Normal		Low muscle mass		Unadjusted		Adjusted	
	Total (n)	Event (n [%])	Total (n)	Event (n [%])	OR (95% CI)	*P* value	OR (95% CI)	*P* value
Spine + femur + wrist combined	815	8.99 (1.14)	301	14.28 (2.44)	1.69 (1.06–2.68)	0.028	1.59 (1.02–2.47)	0.0402
Femur	815	0.42 (0.27)	301	1.19 (0.92)	2.85 (0.39–20.93)	0.304	2.95 (0.38–22.86)	0.2997
Wrist	815	6.61 (0.96)	301	10.32 (2.26)	1.63 (0.93–2.84)	0.088	1.52 (0.91–2.52)	0.1084

Adjusted by age, age of menopause, use of hormones, and smoking, height.
OR: odds ratio, CI: confidence interval.

Table 4. Incidence rates and odds ratios of fractures at various sites in postmenopausal women with low muscle mass and osteoporosis

Normal			Low muscle mass		Unadjusted		Adjusted	
Fracture sites	Total (n)	Event (n [%])	Total (n)	Event (n [%])	OR (95% CI)	*P* value	OR (95% CI)	*P* value
Spine + femur + wrist	249	9.58 (2.29)	135	20.34 (4.61)	2.41 (1.11–5.22)	0.025	2.33 (1.13–4.79)	0.0220
Femur	249	0.84 (0.71)	135	2.18 (1.87)	2.65 (0.23–30.34)	0.433	4.47 (0.65–30.89)	0.1291
Wrist	249	6.54 (1.88)	135	16.49 (4.63)	2.82 (1.15–6.94)	0.024	2.59 (1.12–6.00)	0.0261

Adjusted by age, age of menopause, use of hormones, and smoking, height.
OR: odds ratio, CI: confidence interval.

ability of fractures was significantly higher in the case of osteoporosis alone than in the case of osteoporosis or osteopenia. All these tables show that the relationship between low muscle mass and fractures at various sites remained strong in the adjusted models.

The lower the low muscle mass level (ASM/height^2 < 5.45, which is the diagnostic criterion for low muscle mass), the higher was the odds ratio (Fig. 2), indicating that patients with lower muscle mass have greater risk of fractures.

DISCUSSION

In our study, fracture risk was increased in menopausal women with low muscle mass, especially in the presence of osteoporosis rather than osteopenia. In particular, consistent results were obtained from the subgroup analysis of women with osteopenia or osteoporosis, which confirmed that the risk of multiple fractures increased as the degree of muscle mass decreased. Femur fractures appeared not to be associated with low muscle mass, but it was difficult to obtain significant

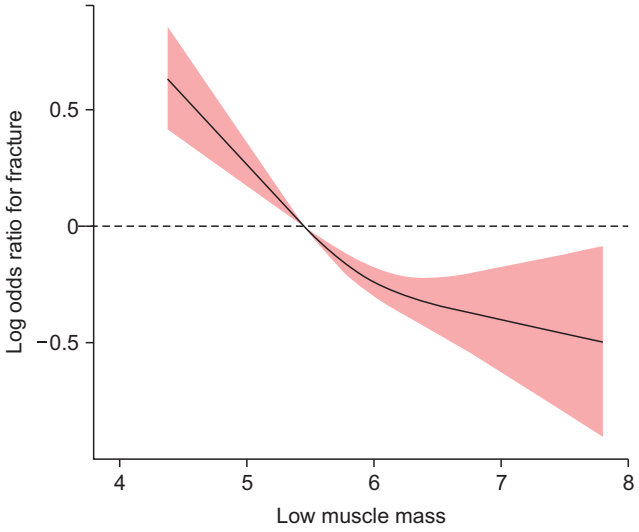

Fig. 2. Spline curve for patients with low muscle mass.

results due to the low femur fracture incidence among the participants.

Low muscle mass is one of the geriatric syndromes [9]. It reduces muscle mass and functions and is related to fractures in the elderly, but the reason for the increased risk of fractures in the elderly with low muscle mass is unclear. Possible mechanisms include sarcopenia-associated deterioration of bone quality or microstructural changes that increase fracture risk [10]. Harris et al. [11] revealed that elderly men with components of sarcopenia and slow gait speed were at greater risk of experiencing any fractures, hip or major osteoporotic fractures than normal subjects; our study investigated the prevalence of low muscle mass and its association with fractures by limiting the scope to postmenopausal women.

Menopause is a time when hormones change rapidly, and it is known to have a great influence on bone mass density and body fat distribution due to a decrease in sex hormones [12]. The decrease in bone mass density increases the incidence of osteoporosis, which reduces bone strength due to damage to the microstructure of bone tissue and causes fractures to occur easily [4]. Fragility fractures are a major side effect of osteoporosis and cause physical disability, inability to care for oneself, and even death [13]. Severe fractures are estimated to lead to an additional 30% risk of death [14]. Previous studies have shown that postmenopausal women with sarcopenia are more likely to have fractures. França et al. [15] reported that postmenopausal women with sarcopenia (or women with low muscle mass or strength) are very vulnerable to hip fractures because they have a high risk of falling, low bone mineral density, and impaired bone geometry. Frisoli et al. [16] revealed that co-existence of sarcopenia and osteoporosis in postmenopausal patients have consequences such as falls, poor balance, fractures, and frailty.

In this study, we tried to find out the prevalence of fractures due to low muscle mass in postmenopausal women with or without osteoporosis. To the best of our knowledge, the relationship between low muscle mass and osteoporosis and the prevalence of fractures in Korean postmenopausal women has not been reported.

Our findings showed that among menopausal women, patients diagnosed with low muscle mass were more likely to have fractures, and patients with low muscle mass and osteoporosis were even more likely to experience fractures. This indicates that treating low muscle mass is important for reducing the risk of osteoporosis-related fractures. From this point of view, continuous management of women with low muscle mass, which account for about 25% of menopausal women, may help prevent fractures and will further help solve global health problems.

This study has several strengths. First, it used nationally standardized data collected from numerous participants. Second, the results were divided to find out the effects of osteoporosis and osteopenia while investigating the relationship between sarcopenia and fracture. Third, this is the first study conducted in Korea to demonstrate the relationship between sarcopenia and fractures in postmenopausal women.

However, this study has some limitations. First, variables obtained from self-questionnaires have either information bias or recall bias. Second, in this study, we analyzed by defining the patient group only in terms of low muscle mass. Currently, sarcopenia is also judged on the basis of various functional values such as grip strength and physical performance. The reason why other diagnostic criteria' were not used is that the study was planned before comprehensive diagnostic criteria for sarcopenia were established, and KNHANES included only data on low muscle mass. Therefore, future studies should use better diagnostic criteria based on functional values in addition to muscle mass.

In conclusion, this study found that the prevalence of fractures increases in postmenopausal women with low muscle mass, and these results were also consistent with subgroup analysis of women with osteoporosis or osteopenia. We confirmed that the risk of fractures in-

creases with the worsening of low muscle mass.

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CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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