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Muscle strength and quality are associated with severity of menopausal symptoms in peri- and post-menopausal women

Jee-Yon Lee, Duk-Chul Lee*

Department of Family Medicine, Severance Hospital, Yonsei University, College of Medicine, 250 Seongsanno, Seodaemun-gu 120-752, Republic of Korea

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ABSTRACT

Objectives: Menopausal symptoms are common and affect the quality of life of menopausal women. Menopausal symptoms are associated with age-related conditions. Sarcopenia, loss of muscle mass and/or function, is also associated with several age-related conditions, suggesting that the severity of menopausal symptoms may be associated with sarcopenia. Therefore, we investigated the relationship between Kupperman index scores, a measure of menopausal symptom severity, and muscle strength and quality in peri- and post-menopausal women.
Study design: Cross-sectional study.
Main outcome measures: A total of 148 women participated. Biomarkers of metabolic risk factors were assessed along with muscle mass as measured with Dual-energy X-ray Absorptiometry. Handgrip strength was measured with isometric dynamometry. Muscle quality was calculated as the ratio of strength to muscle mass in upper extremities.
Results: Kupperman index scores correlated with the depression scale, handgrip strength, and specific force after adjusting for age and body mass index. Mean handgrip strength and specific force decreased gradually according to menopausal symptom severity. Multivariate logistic regression analysis showed that the fourth handgrip strength and specific force quartiles were associated with the prevalence of severe menopausal symptoms with adjusted odds ratios of 0.14 (95% confidence interval 0.03–0.68) and 0.09 (95% confidence interval 0.03–0.47), respectively.
Conclusions: Lower handgrip strength was associated with severe menopausal symptoms. Although we could not determine causality, muscle strength and quality during menopause may be related to the severity of menopausal symptoms. Further interventional and experimental studies are required to understand the clinical and pathophysiological significance of our findings.

1. Introduction

Menopause is the transitional phase of life, from a reproductive to a non-reproductive state, in women. Women may suffer from a variety of symptoms including hot flashes, night sweats, vaginal dryness, dizziness, and palpitations during menopause [1]. Although more than 80% of menopausal women in the US complain about menopausal symptoms [2], the severity of symptoms is very diverse among women. The quality of life and psychological well-being of women during the menopausal period depends on the severity of menopausal symptoms [3]. Although published data have shown mixed results, some studies have demonstrated an association between specific menopausal symptoms and the risk of cardio-metabolic diseases. Perez et al. have reported that Kupperman index scores are associated with an increased risk of cardiovascular disease and osteoporosis [4]. The prevalence of the metabolic syndrome was also related with the severity of the vasomotor symptoms in postmenopausal women [5]. Therefore, identification of predictive factors that determine the severity of menopausal symptoms is important in maintaining mental and physical health during menopause. Although several lifestyle factors [6] are associated with menopausal symptoms, little is known about the mechanisms determining menopausal symptom severity.

Sarcopenia is the loss of muscle mass and function associated with aging. Sarcopenia is one of the most common age-related conditions and is affected by hormonal changes and nutritional status [7]. Sarcopenia increases the risks of functional disability, falls, and overall mortality in the elderly [8]. Although maintenance of both muscle strength and mass is important, muscle strength is considered a better indicator of mortality [9] and cardiopulmonary function [10] than muscle mass. In addition, previous studies have suggested that muscle quality, as well as muscle quantity, should be considered when measuring sarcopenia because

* Corresponding author. Tel.: +82 2 2228 2330; fax: +82 2 362 2473.
E-mail address: faith@yuhs.ac (D.-C. Lee).

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muscle quality is more useful for estimating functional status [11]. In women, sarcopenia develops earlier than in men, around the menopausal period [12]. However, the precise role of maintaining muscle quality and quantity during the menopausal period has not been elucidated.

The incidence of sarcopenia increases rapidly during the menopausal period [12]; thus, the severity of menopausal symptoms may be associated with sarcopenia in women during the menopausal transition. However, no current studies have evaluated this relationship. Therefore, we investigated the relationship between menopausal symptoms and muscle strength and quality in 148 peri- and post-menopausal Korean women.

2. Methods

2.1. Study participants

This study was conducted as a Yonsei Menopause Study designed to identify factors related to the health of peri- and post-menopausal women in Korea. We enrolled peri-menopausal and post-menopausal women between the ages of 45 and 65 years who were apparently in good health. The peri-menopausal period was defined by changes in the length of menstrual cycles or no menstrual period for at least 3 months, but less than 12 months. Menopause was defined by amenorrhea for 12 consecutive months, in the absence of a clear biological or physiological cause. We excluded women with the following medical conditions: history of chronic renal disease, chronic liver disease, coronary artery disease, cerebrovascular diseases, or cancer. Women with a history of hysterectomy, oophorectomy, or hormonal therapy were also excluded. Participants were recruited by advertisements posted in the outpatient clinic of Family Medicine at Severance Hospital. All women participated in the study voluntarily, and written informed consent was obtained from each participant. The study complied with the Declaration of Helsinki, and the institutional review board of Severance Hospital approved this study (IRB number: 4-2011-0695). Among 162 women who initially participated, 148 women met all inclusion criteria and were included in the final study analysis.

2.2. Measurements of clinical parameters

All participants completed a questionnaire about lifestyle factors including cigarette smoking, alcohol consumption, and regular exercise. Smoking was defined as current or past smoking. Alcohol consumption was defined as drinking alcohol more than once per week or more than 70 g per week. Regular exercise was defined as physical exercise or physical work performed more than three times per week for 30 min or more. Symptoms of depression were assessed with the Korean version of short-form Geriatric Depression Scale (SF-GDS-15) consisting of 15 questions [13].

Anthropometric measurements were performed on all participants by a well-trained medical doctor. Blood pressure was measured in the sitting position after a 10-min resting period. The hypertension group was defined as women with a systolic blood pressure $\geq$140 mm Hg, diastolic blood pressure $\geq$90 mm Hg, or those using anti-hypertensive medications. Body mass index (BMI) was calculated as weight divided by height squared. Waist circumference was measured at the umbilicus level while the woman was standing.

Blood samples were collected after an overnight fast of at least 12 h. Fasting glucose, high sensitive C-reactive protein (hs-CRP), total cholesterol, triglycerides, and high-density lipoprotein (HDL)-cholesterol levels were measured using an ADVIA 1650 chemistry system (Siemens Medical Solution, Tarrytown, NY, USA). The inter-assay coefficients of variance for glucose, hs-CRP, total cholesterol, triglycerides, and HDL-cholesterol were $1.58 \pm 4.90\%$, $3.76 \pm 0.39\%$, $0.9 \pm 0.94\%$, $1.01 \pm 0.92\%$, and $1.37 \pm 0.47\%$, respectively. Low-density lipoprotein (LDL)-cholesterol levels were calculated using the Friedewald equation. Insulin levels were measured with an electrochemiluminescence immunoassay using an Elecsys 2010 (Roche, Indianapolis, IN, USA). Insulin resistance was estimated by the homeostasis model assessment of insulin resistance (HOMA-IR) index: (insulin [μIU/mL] $\times$ fasting blood glucose [mg/dL]/18)/22.5). The diabetes group was defined as women with a fasting blood glucose $\geq$126 mg/dL or the use of insulin or other hypoglycemic medication. The dyslipidemia group was defined as women with a total cholesterol >240 mg/dL, triglyceride >200 mg/dL, HDL-cholesterol <40 mg/dL, or those taking lipid-lowering agents.

2.3. Assessment of severity of menopausal symptoms

The Kupperman index scores [14] were used to measure the severity of menopausal symptoms. The Kupperman index consists of 11 questions about hot flashes, paresthesia, insomnia, nervousness, melancholia, vertigo, weakness, arthralgia, headaches, palpitations, and formication. The scores range from 0 to 3 (0 = no symptoms and 3 = severe) and were weighted as follows: hot flashes were multiplied by 4, and nervousness, insomnia, and paresthesia by 2. The sum of the scores represents an overall severity of menopausal symptoms (0–14 points, none; 15–20, mild; 21–34, moderate; >34, severe).

2.4. Assessment of muscle mass, strength, and quality

The lean mass of the upper extremities was measured using Dual-energy X-ray Absorptiometry (DXA) (Lunar Corporation, Madison, WI, USA). We assumed that all non-fat and non-bone tissues were skeletal muscle tissues. The in vivo inter-assay coefficient of variation (CV) was reported as 0.3–0.6%.

Handgrip strength was measured using a strain-gauged dynamometer (Takeii TKK 501, Scientific Instruments, Co. Ltd., Tokyo, Japan) as previously described [15]. The participants performed the test twice in both hands, allowing a 3-min rest period between measurements. The mean values were calculated as: [(maximum scores of right side + maximum scores of left side)/2] kg. The inter-assay coefficient of variance, which was calculated by repeated measurements of handgrip strength with more than 1-week intervals in 20 women, was 3.5%.

We used the ratio of muscle strength per muscle mass of upper extremities (handgrip strength (kg)/DXA arm lean mass) as a marker of muscle quality [16]. Because the strength was measured in kilogram of force, the term “specific force” was used.

2.5. Statistical analysis

Data are reported as the mean $\pm$ standard deviation for normally distributed data and as the median and interquartile range for non-normally distributed data. Fasting glucose, insulin, HOMA-IR, triglycerides, hs-CRP, and arm lean mass were logarithmically transformed to eliminate the skewness of the distribution. Pearson correlation analysis was performed to evaluate relationships between Kupperman index scores and other clinical variables. Mean handgrip strength and specific force according to the grade of severity in the Kupperman index were calculated by analysis of covariance (ANCOVA). Multiple linear regression analysis was used to identify factors contributing to Kupperman index scores. For this analysis, variables with $p < 0.1$ from univariate analysis and clinically important variables including age, BMI, alcohol, smoking,