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Research paper

Association between appendicular skeletal muscle mass and depressive symptoms: Review of the cardiovascular and metabolic diseases etiology research center cohort

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ABSTRACT

Background: The effects of skeletal muscle mass on depressive symptoms remain poorly understood, especially in the middle-aged population. We examined the relationship between skeletal muscle mass and depressive symptoms according to sex and menopausal status in the middle-aged Korean population.

Methods: Herein, 1,151 men and 2,176 women aged 30–64 years completed questionnaires and underwent health examinations in the Cardiovascular and Metabolic Disease Etiology Research Center study. Appendicular skeletal muscle mass (ASM) was measured via bioelectrical impedance analysis and adjusted for height squared (ASM/Ht^2). Both continuous values and tertile groups of ASM/Ht^2 were used for analysis. Depressive symptoms were assessed using the Beck Depressive Inventory-II (BDI), and the prevalence of depressive symptoms was determined as a BDI score ≥ 20.

Results: Multiple logistic regression analysis using a fully adjusted model showed that depressive symptoms were more frequently observed among men in the lower ASM/Ht^2 tertile and middle ASM/Ht^2 tertile than among those in the higher ASM/Ht^2 tertile. Each 1-kg/m^2 decrease in ASM/Ht^2 was significantly associated with the presence of depressive symptoms in men. Such significant association was not observed among premenopausal and postmenopausal women.

Limitations: The cross-sectional nature of the study design, measurement of skeletal muscle mass and depressive symptoms only once, estimation of skeletal muscle mass using bioelectrical impedance analysis, assessing depressive symptoms by self-reported questionnaire, and potential unknown confounding variables constitute the limitations of our study.

Conclusions: The independent association between low skeletal muscle mass and depressive symptoms was observed in men but not in women.

1. Introduction

Depression is one of the most common mental health problems worldwide, with a lifetime prevalence ranging 10–15% (Lepine and Briley, 2011). Studies have shown that sarcopenia, which is the decline in skeletal muscle mass or muscle strength with age, leads to metabolic and vascular abnormalities (Rolland et al., 2008; Rosenberg, 2011). Moreover, several population studies that have mainly included older participants have reported a relationship between skeletal muscle mass and depressive symptoms. However, these studies have often generated conflicting results. For example, some studies found an inverse association between skeletal muscle mass and depressive symptoms (Gariballa and Alessa, 2017; Hamer et al., 2015; Hsu et al., 2014; Kim et al., 2011; Rantanen et al., 2000; Wu et al., 2017), whereas others failed to find a significant association (Ishii et al., 2016).

Previous studies have reported that both skeletal muscle mass

Abbreviations: CMERC, Cardiovascular and Metabolic Disease Etiology Research Center; ASM, appendicular skeletal muscle mass; Ht^2, height squared; BDI, Beck Depressive Inventory-II; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressures; HbA1c, hemoglobin A1c; BIA, bioelectrical impedance analysis; OR, odds ratio; CI, confidence interval

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decline and depressive symptoms are related with aging (Gallagher et al., 1997; Maurya et al., 2016). Although the absolute age-related reduction in muscle mass has been found to be greater in men than in women (Kim et al., 2016), the prevalence of depression is more dominant in women than in men (Schuch et al., 2014). In addition, previous studies confirmed that perimenopausal as well as postmenopausal women are at increased risk for the development of depressive symptoms and/or depression (Humeniuk et al., 2011; Wang et al., 2013). However, the impact of sex and menopausal status on the association between skeletal muscle mass and depressive symptoms has not been appropriately assessed. Moreover, only a few studies have examined this association in middle-aged populations (Byeon et al., 2016; Cho et al., 2015). Therefore, we investigated the association between skeletal muscle mass and depressive symptoms according to sex and menopausal status in a middle-aged Korean population.

2. Methods

2.1. Study population

The present study used data from the Cardiovascular and Metabolic Disease Etiology Research Center (CMERC) cohort study. The CMERC study initially enrolled 3,332 participants aged 30–64 years between 2013 and 2016. All participants completed health questionnaires and examinations according to a predefined protocol. The sampling and measurement procedures have been described in detail previously (Shim et al., 2017). Five participants were excluded owing to missing key variables, such as appendicular skeletal muscle mass (ASM, $n = 4$) and the Beck Depression Inventory-II (BDI; Korean version; $n = 1$) score. Finally, a cross-sectional analysis of the remaining 1,151 men and 2,176 women was conducted. All participants provided written informed consent, and the study protocol was approved by the Institutional Review Board of Severance Hospital at Yonsei University College of Medicine.

2.2. Questionnaire data

All participants were individually interviewed by trained interviewers using standardized questionnaires according to a pre-determined protocol. Socio-demographic variables included age, education (< 12 or ≥ 12 years), marital status, and household income. Participants were divided according to marital status into three groups: married, unmarried (never married, divorced, separated, or widowed) or unknown. The study population was also classified into three groups according to household income level: lower, middle, or upper ($<$ 30,000,000, 30,000,000–50,000,000, or $\geq$ 50,000,000 Won/year, respectively). Health behaviors included smoking status (current smoker, former smoker, or non-smoker), alcohol intake (current drinker, former drinker, or non-drinker), physical activity, and sleep duration. Physical activity was assessed using the International Physical Activity Questionnaire-Short Form. Regular exercise was defined as moderate-to-high-intensity physical activity performed at least three times per week. Sleep duration was calculated in hours per day as the average duration during the past year. Past history of physician-diagnosed diseases (chronic kidney disease, osteoporosis, and cancer) and medication use (antihypertensives, antidiabetics, and antidepressants) were self-reported.

2.3. Physical examination

Standing height was measured to the nearest 0.1 cm using a stadiometer (DS-102, JENIX, Seoul, Korea), and body weight was measured to the nearest 0.1 kg on a digital scale (DB-150, CAS, Seongnam, Korea) according to the predetermined protocol. Body mass index (BMI, kg/m^2) was calculated as the body weight divided by the standing height squared. Participants rested for five minutes before the blood pressure measurement, and systolic blood pressure (SBP) and diastolic blood pressures (DBP) were repeatedly measured three times at two-minute intervals. The average of second and third measurements was used in the analyses.

2.4. Laboratory assays

Blood samples were collected from the antecubital vein after the patients fasted for at least eight hours. Total cholesterol was measured via enzymatic methods (ADVIA 1800 Auto Analyzer, Siemens Medical Solutions, Deerfield, IL, USA). Fasting blood glucose concentrations were measured using a colorimetry method (ADVIA 1800 Auto Analyzer, Siemens Medical Solutions, Deerfield, IL, USA). Hemoglobin A1c (HbA1c) concentrations were assessed via high-performance liquid chromatography (Variant II TURBO, Bio-Rad, Berkeley, CA, USA). C-reactive protein concentrations were determined using a turbidimetric immunoassay (ADVIA 1800 Auto Analyzer, Siemens Medical Solutions, Deerfield, IL, USA).

2.5. Measurement of skeletal muscle mass

ASM was measured via bioelectrical impedance analysis (BIA) using Inbody370 (Biospace, Seoul, Korea) according to the instructions provided by the manufacturer. ASM was determined as the sum of the muscle masses of both arms and both legs. Skeletal muscle mass strongly correlates with body size, indicating that participants with a larger body size may have larger muscle mass. Therefore, the ASM was adjusted for height squared (ASM/Ht^2, kg/m^2). Participants were divided into three groups based on sex and menopausal-specific ASM/Ht^2 tertiles: $<$ 7.73, 7.73–8.29, and $\geq$ 8.30 for men; $<$ 6.11, 6.11–6.59, and $\geq$ 6.60 for premenopausal women; and $<$ 6.14, 6.14–6.60, and $\geq$ 6.61 for postmenopausal women.

2.6. Assessment of depressive symptoms

Depressive symptoms were assessed using the BDI questionnaire. The BDI consists of 21 questions targeted at evaluating emotional, cognitive, motivational, physiological, and other symptoms. Each item contains four statements describing the intensity of depressive symptoms. Each item is rated on a scale from 0 to 3, reflecting how participants have felt over the past two weeks. Thus, the total BDI scores ranged from 0 to 63, with higher scores representing greater disability. This index has demonstrated acceptable sensitivity and specificity in distinguishing between participants with and those without depressive symptoms and is considered a valid and reliable measure of depressive symptoms (Dere et al., 2015; Lim et al., 2011; Whisman et al., 2013). For the purpose of this study, the prevalence of depressive symptoms was defined as a BDI score $\geq$ 20, and participants were classified into four groups according to the severity of symptoms: normal (0–13), mild (14–19), moderate (20–28), and severe (29–63).

2.7. Definitions of comorbidities

Hypertension was defined as a SBP $\geq$ 140 mmHg, DBP $\geq$ 90 mmHg, or self-reported current use of antihypertensive medications. Diabetes mellitus was defined as a fasting blood glucose level $\geq$ 126 mg/dL or HbA1c $\geq$ 6.5% according to the American Diabetes Association criteria or the current use of oral antidiabetic agents or insulin.

2.8. Statistical analysis

All analyses were performed separately for men, premenopausal women, and postmenopausal women because both skeletal muscle mass and depressive symptoms differed significantly by sex and menopausal status in women (Supplemental Table 1). We evaluated differences in demographic characteristics among the three groups on the basis of the