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Association between muscle strength and metabolic syndrome in older Korean men and women: the Korean Longitudinal Study on Health and Aging

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ABSTRACT

The objective of the study was to investigate the association between metabolic syndrome (MS) and muscle strength in community-dwelling older men and women in Korea. Korean men and women 65 years and older living in a single, typical South Korean city (n = 647) were enrolled in the Korean Longitudinal Study on Health and Aging study. The diagnosis of MS was evaluated according to the definition of the National Cholesterol Education Program Adult Treatment Panel III. Isokinetic muscle strength of the knee extensors, as determined by peak torque per body weight (newton meter per kilogram) and hand-grip strength per body weight (newton per kilogram), was measured. Participants without MS had greater leg muscle strength and grip strength per weight. The effect of MS on muscle strength was more prominent in men than in women in our study population. Only men showed a significant interaction between MS and age for muscle strength (P = .014), and the effect was greater in men aged 65 to 74 years compared with those older than 75 years (119.2 ± 31.2 vs 134.5 ± 24.3 N m/kg). Participants with MS had weaker knee extensor strength after controlling the covariates (β = −90.80, P = .003), and the interaction term (age × MS × male sex) was significant (β = 1.00, P = .017). Metabolic syndrome is associated with muscle weakness, and this relationship is particularly pronounced in men. Age can modify the impact of MS on muscle strength. Men aged 65 to 74 years with MS need a thorough assessment of muscle strength to prevent disability.

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1. Introduction

Metabolic syndrome (MS), characterized by central (abdominal) obesity, dyslipidemia, hyperglycemia, and hypertension, is currently a major global public health challenge because it involves a risk of cardiovascular disease and type 2 diabetes mellitus [1]. Metabolic syndrome is based on insulin resistance, which is closely associated with the inflammatory process [2]. Several studies have shown that low-grade inflammation is linked with muscle weakness [3,4]. From this, MS may be associated with an exacerbation of age-related declines in muscle strength. Recent studies have shown a graded association between increased glucose levels and weaker muscle strength in those with diabetes mellitus [5]. This inverse association between impaired metabolic and muscle functions may extend to other important insulin-resistant, glucose-intolerant states, such as MS [6,7]. Several studies have been reported regarding the association between MS or its individual components and a decline in physical performance among the general population [8,9], but results in older subjects remain controversial.

Age-related decline in muscle strength manifests in an impaired mobility and fall-related injuries in older adults [10-14]. People older than 75 years have significantly higher rates of functional impairment. Insulin resistance has been considered as a contributing factor to age-related muscle mass loss [15,16], which is an essential variable underlying a decline in muscle strength [17,18]. Curiously, the peak prevalence of MS was noted in the sixth decade of life for men and in the seventh decade for women, although prevalence declined in the eighth decade of life [15]. Therefore, the relationship between MS and muscle strength may be different in younger old and older old adults.

Several studies have identified sex differences in physical performance and function in older adults [19-21]. Although men have greater muscle strength than women, men exhibit a greater age-related decline in absolute strength and strength in all muscle groups over time [22]. Metabolic syndrome shows several significant sex-associated differences that have been attributed to variations in endocrine profiles, and the sex hormones are of major importance [23,24]. Men with MS have significantly lower testosterone levels, which may be one explanation for muscle weakness [25,26] compared with age-matched healthy subjects [27]. Sex differences in sex hormones may explain the MS-related decline in muscle strength in older subjects [28].

The goal of the present study was to evaluate the association between MS and muscle strength in older Korean men and women aged 64 to 99 years. In addition, we assessed whether age and sex had an effect on this association in the older population. We hypothesized that MS would be related to the decline in muscle strength after adjusting for comorbidity and that sex and age differences in the MS-related muscle strength decline would be found in older population.

2. Methods

2.1. Study population

This analysis was based on data from the Korean Longitudinal Study on Health and Aging (KLoSHA) [29], a population-based cross-sectional study conducted from September 2005 to August 2006 in residents 65 years or older in Seongnam, Korea. In 2005, the total population of Seongnam was 931 019; and 6.6% (61,730) of the population was 65 years or older. A simple random sample (n = 1118) was drawn from the roster of 61 730 persons 65 years or older who were residents on August 1, 2005. Subjects were invited to participate in the study by letter and telephone. In total, 1000 subjects agreed to participate in the study; the baseline cohort included 439 men and 561 women. The subjects included 132 men and 155 women older than 85 years (Fig. 1). Each subject's medical history, including any medication, and social details such as alcohol intake, smoking status, and exercise habits were assessed by trained nurses who were certified for epidemiological studies and the assessment of elderly patients. Isokinetic muscle strength was assessed in 647 of the subjects. All assessments were performed at our hospital, located in Seongnam, from September 2005 through October 2006.

The study protocol was approved by the institutional review board of our hospital. All subjects were fully informed regarding study participation, and they or their legal guardians provided written informed consent.

2.2. Definition of metabolic syndrome

According to the National Cholesterol Education Program Adult Treatment Panel III [30], people with MS are operationally defined by having 3 or more of the following components: (1) abdominal obesity (waist circumference ≥90 cm in men and ≥80 cm in women) based on Asia-Pacific abdominal obesity criterion, (2) elevated triglycerides (≥150 mg/dL), (3) reduced high-density lipoprotein (HDL) cholesterol (<40 mg/dL in men and <50 mg/dL in women), (4) elevated blood pressure (≥130/85 mm Hg), and/or (5) elevated fasting glucose (≥110 mg/dL) or diabetes.

2.3. Muscle mass measurement by computed tomography

The midthigh areas (square centimeters) were quantified by a single scout scan using computed tomography (CT) (Somatom Sensation 16; Siemens, Erlangen, Germany). The range was 30 to 100 Hounsfield units. The CT scan was taken at the *midthigh*, defined as the midpoint from the inguinal crease to the proximal pole of the patella.

2.4. Isokinetic muscle strength measurements

The isokinetic strength of knee flexors and extensor muscles was measured using an isokinetic device at an angular velocity of 60°/s (Biodex Medical Systems, Shirley, NY) [31]. Subjects were asked to perform 2 sets of 5 repetitions, with a 30-second rest between sets, by exerting maximum pressure on the arm of the isokinetic device through the entire range of movement. The concentric peak torque values (newton meter) obtained from 5 torque-angle curves of each set were used to evaluate the flexion/extension muscle strengths of knee joints, and these were subsequently normalized with respect to body weight (newton meter per kilogram). Peak torque per body weight

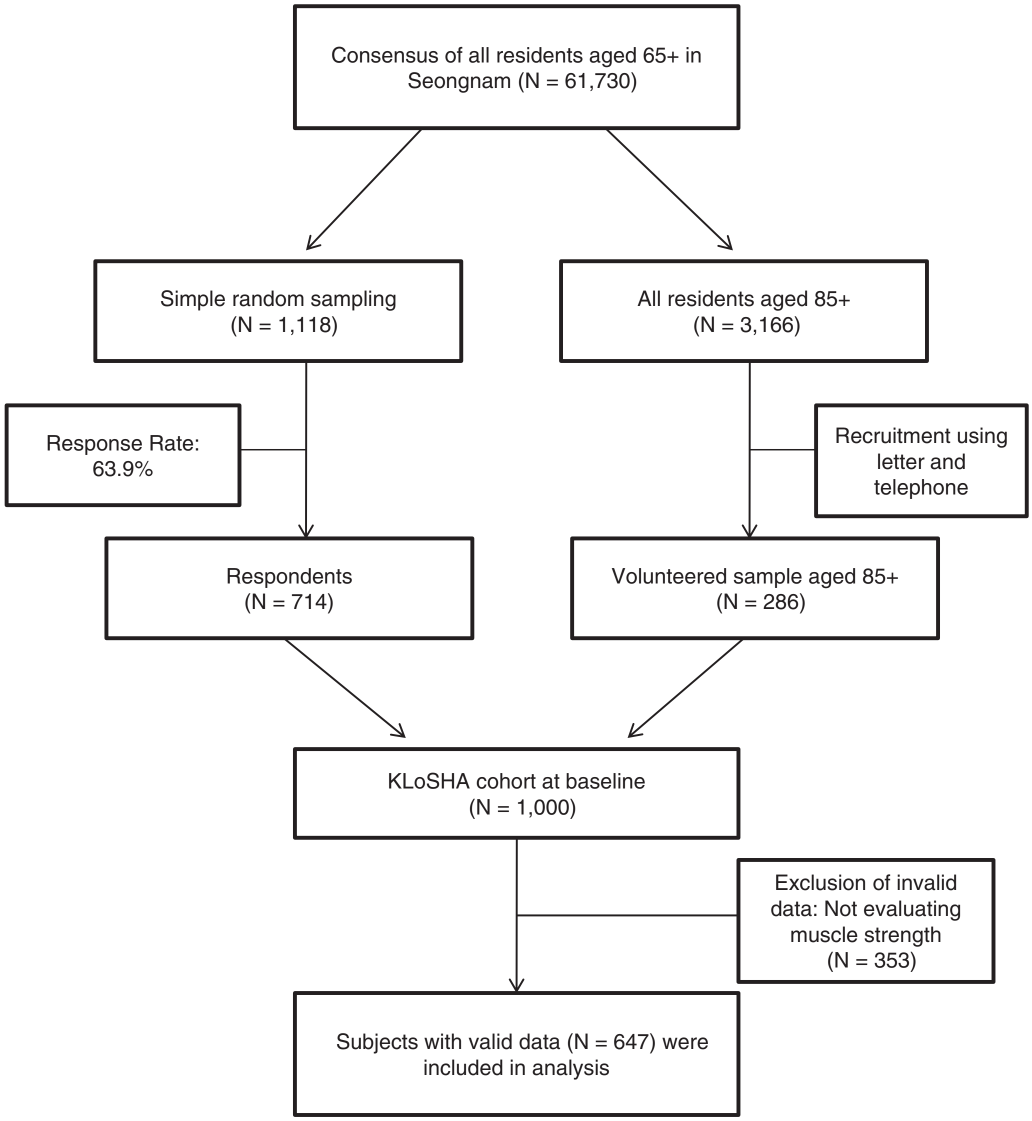

Fig. 1 – Flowchart of KLoSHA, a population-based, prospective cohort study on residents of one urban Korean city aged at least 65 years.

(newton meter per kilogram) of the right knee extensor muscle was used in the analysis.

2.5. *Grip strength*

Voluntary isometric muscle strength was measured using an electronic hand-grip dynamometer (JAMAR hydraulic hand dynamometer; Sammons Preston, Bolingbrook, IL) [32,33]. Before the measurement, the dynamometers were calibrated using a back-loading rig and were within ±0.5 kg error range. The evaluator gave verbal encouragement to elicit maximal performance from the participants during measurement. Forces were measured twice for each hand, and the greatest force was used for the analyses. These were subsequently normalized to body weight (newton per kilogram). The test-retest variability for maximal voluntary force on the part of the same subject was reported to be approximately ±9% [34].

2.6. *Covariates*

Age, sex, activity level, and educational level were determined by 3 research nurses using standardized questionnaires. Activity levels were estimated by summing times spent walking, gardening, woodworking, lifting, or shoveling over a 24-hour period. Global cognition was assessed using the validated Korean version of the Mini-Mental State Examination (MMSE) of the Consortium to Establish a Registry for Alzheimer's Disease assessment packet [35]. The Korean version of the MMSE consists of 30 questions that evaluate orientation, attention, immediate- and short-term recall, language function, and the ability to follow simple verbal and written commands. Scores range from 0 to 30 (worst to best). Incidence and severity of depression were evaluated using the Korean version of the Geriatric Depression Scale (GDS). Comorbidity index was determined by

Table 1 – Characteristics of men and women in relation to the presence or absence of MS

	Men (n = 327)			Women (n = 320)		
	MS (n = 133)	Non-MS (n = 194)	P value	MS (n = 190)	Non-MS (n = 130)	P value
Age (y)	75.6 ± 8.4	75.1 ± 8.3	.64	74.6 ± 7.8	73.3 ± 7.1	.12
Education (y)	10.9 ± 4.7	10.7 ± 5.0	.77	5.1 ± 4.9	6.4 ± 5.1	.03 †
Smoking						
None	33 (24.8%)	57 (29.4%)	.59	177(93.2%)	119 (91.5%)	.81
Ex	75 (56.4%)	99 (51.0%)		8 (4.2%)	6 (4.7%)	
Current	25 (18.8%)	38 (19.6%)		5 (2.6%)	5 (3.8%)	
Weight (kg)	70.4 ± 8.6	61.5 ± 8.8	.00 §	57.3 ± 8.2	52.7 ± 9.3	.00 §
BMI (kg/m^2)	25.7 ± 2.8	22.8 ± 2.8	.00 §	25.1 ± 2.9	23.2 ± 3.3	.00 §
Comorbidity index	1.4 ± 1.1	1.2 ± 1.0	.20	1.9 ± 1.1	1.5 ± 1.2	.00 ‡
Physical activity score	17.1 ± 7.7	17.8 ± 7.9	.45	16.0 ± 5.3	16.5 ± 5.3	.40
MMSE	25.7 ± 2.8	25.1 ± 3.7	.12	22.2 ± 4.6	23.1 ± 4.6	.09 *
GDS	8.3 ± 6.0	9.8 ± 7.1	.06 *	12.6 ± 7.2	11.7 ± 7.3	.25
Muscle mass (cm^2)	81.9 ± 14.1	82.2 ± 14.5	.85	55.5 ± 11.2	52.7 ± 12.0	.20

Data are presented as mean ± SD or number (percentage). BMI indicates body mass index.
* $P < .1$.
† $P < .05$.
‡ $P < .01$.
§ $P < .001$.

summation of self-reported illnesses including hypertension, heart disease, diabetes, cancer, arthritis, fracture, and respiratory disease.

2.7. *Statistical analyses*

The data are presented as means ± standard deviation or numbers (percentages), separately, for men and women. Student *t* test and the χ^2 test were used to assess differences in demographic characteristics and measures of physical functioning between the subjects with and without MS. The analyses were stratified by sex because the interaction terms of MS with sex were significant. The sample size (n = 647) gives to a linear model greater than 90% power to detect a coefficient of determination greater than 6% with 10 parameters. The interaction between MS and age on muscle strength was verified, and then we further divided men into younger old (65-74 years) and older old (≥75 years) age groups according to the previous studies [36]. We used a generalized linear mixed (GLM) model approach to fit the models assessing the relationship between MS and muscle strength after adjusting for possible covariates. Both unadjusted and covariate adjusted models were fitted in a sequential fashion. The final models were fit to test the main effects of sex, age, and MS with interaction effects of age × sex, MS × sex, and age × MS × sex after controlling for possible covariates. Covariates were built by choosing clinically relevant variables and variables identified from prior published studies and included MMSE, GDS, physical activity score, and comorbidity index. Before conducting multiple regression analysis, the assumptions of normality and homoscedasticity of the criterion, predictor variables, and multicollinearity were checked. Statistical analyses were conducted using the SPSS Version 17.0 Software (SPSS, Chicago, IL). Bonferroni correction for multiple comparisons was calculated for 2 dependent variables leading to a corrected *P* value of .025.

3. Results

The mean age was 74.9 ± 8.7 years (range, 65-98 years). Men accounted for 50.9% of the total population. Mean waist circumference and fasting glucose were higher and HDL cholesterol was lower in men as compared with women. A total of 323 participants (49.9%) had MS, including 133 (40.7%)

Table 2 – Muscle strength in MS by sex

	All (n = 647)			Men (n = 327)			Women (n = 320)		
	MS (n = 323)	Non-MS (n = 324)	[a]P value	MS (n = 133)	Non-MS (n = 194)	[b]P value	MS (n = 190)	Non-MS 1(n = 130)	[b]P value
Knee extensor strength per weight (%)	93.2 ± 36.6	106.9 ± 39.8	.037 *	109.1 ± 40.6	118.7 ± 42.6	.021 *	80.2 ± 30.0	89.2 ± 32.3	.059
Grip strength per weight (%)	69.2 ± 34.3	77.4 ± 31.2	.048 *	75.9 ± 24.4	83.1 ± 29.7	.042 *	47.1 ± 21.2	49.7 ± 25.3	.307

Data are presented as mean ± SD.
[a] Adjusted for age, sex, and comorbidity index.
[b] Adjusted for age and comorbidity index.
* $P < .05$.

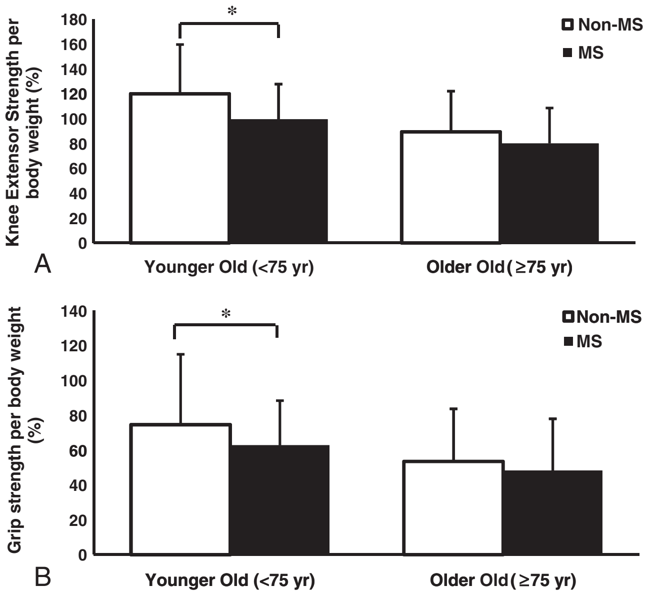

Fig. 2 – Knee extensor strength per body weight (A) and grip strength per body weight (B) according to MS and age group. Results are presented as means, and bars above the columns represent standard error. *P < .01 for comparison of non-MS (open columns) and MS (filled columns).

men and 190 (59.4%) women. Metabolic syndrome was more common in women (59.4%) than in men (40.7%, $P < .001$). When the individual components of MS were analyzed, abdominal obesity was detected in 73.1% of women and 41.1% of men ($P < .001$). Hypertriglyceridemia was found in 28.1% of women and 25.8% of men ($P = .290$); low HDL cholesterol in 19.9% of women and 4.6% of men ($P < .001$); high blood pressure in 77.0% of women and 75.1% of men ($P = .311$); and high fasting blood glucose in 40.6% women and 48.9% of men ($P = .020$).

Table 1 shows subject characteristics according to the presence of MS and sex. Regarding anthropometric values, men and women with MS showed significantly greater body mass index values and body weight as compared with non-MS subjects. Compared with those without MS, participants with MS were more likely to have high blood pressure (men: 54.1% vs 33.0%, women: 54.7% vs 33.8%, $P < .001$) and diabetes (men: 25.6% vs 9.8%, women: 20.0% vs 4.6%, $P < .001$) (Table 1). Men with MS had a lower GDS than men without MS ($P = .06$). Women with MS had a lower educational level ($P = .03$), higher comorbidity index ($P = .003$), and lower MMSE ($P = .09$) than women without MS.

Table 2 shows the main effect of MS on knee extensor strength and grip strength per weight after controlling for age and sex. In the overall population, MS was significantly associated with muscle strength. Further analysis by sex revealed a relationship between MS and muscle strength in men but not in women after adjusting for age and covariates (Table 2).

Given that muscle strength was only significant in men, we examined the interaction between the MS and age for muscle strength in men. We found a significant interaction of age with muscle strength ($P = .014$) in men. The association between MS and muscle strength was more pronounced in the younger old (65-74 years) men group than in the older old (≥75 years) men group (Fig. 2). The mean difference of muscle strength between men with MS and without MS was 33.7 (%) and 23.8 (%), respectively. Results from the GLM models indicated that older participants ($\beta = -2.79$, $P < .001$) and women ($\beta = -97.12$, $P = .006$) had weaker muscle strength (Table 3). Participants with MS had weaker knee extensor strength ($\beta = -82.25$, $P = .010$), and the interaction term (age × MS × male sex) was significant ($\beta = 1.00$, $P = .017$). After adjusting for MMSE, GDS, physical activity score, and comorbidity index, participants with MS had weaker knee extensor strength than participants without MS ($\beta = -90.80$, $P = .003$); and the interaction term (age × MS × male sex) was significant ($\beta = 1.10$, $P = .007$) (Table 3).

4. Discussion

In this population-based cohort, men in the younger old group (65-74 years) with MS were at higher risk for muscle weakness

Table 3 – Factors associated with knee extensor strength and grip strength per weight

	Knee extensor strength per body weight (%)						Grip strength per body weight (%)					
	Unadjusted			Adjusted[a]			Unadjusted			Adjusted[a]		
	R^2	b (SE)	P value	R^2	b (SE)	P value	R^2	b (SE)	P value	R^2	b (SE)	P value
Main effects	0.372			0.385			0.555			0.573		
Age		−2.79 (0.27)	<.001*		−2.55 (0.27)	<.001*		−1.43 (0.12)	<.001*		−1.31 (0.12)	<.001*
Sex		−97.12 (34.91)	.006*		−128.56 (34.65)	<.001*		−60.07 (14.90)	<.001*		−76.19 (15.01)	<.001*
MS		−82.25 (31.78)	.010*		−90.80 (30.91)	.003*		−20.88 (14.06)	.138		−24.26 (13.79)	.079
Interactions												
Age × sex		0.85 (0.47)	.071		0.37 (0.47)	.003*		0.45 (0.20)	.024*		0.69 (0.20)	.001*
MS × sex		58.22 (47.86)	.224		84.63 (46.92)	.071		14.36 (20.49)	.483		23.16 (20.28)	.253
Age × MS × sex		1.00 (0.42)	.017*		1.10 (0.41)	.007*		0.31 (0.19)	.097		0.35 (0.18)	.056

The GLM model was applied to analyze factors affecting the muscle strength.
[a] Adjusted by MMSE, GDS, physical activity score, and comorbidity index.
* $P < .025$.

than were their counterparts without MS. However, men with MS in the older old group (>75 years) were not at a higher risk for muscle weakness than were those without MS. This may be explained by the increasing rate of muscle weakness in the older old men without MS. These results indicate that having MS may be a strong risk factor for a decline in muscle strength between the ages of 65 and 74 years in men. We found no relationship between MS and muscle strength in women in our elderly cohort.

Several studies have described the loss of muscle mass and strength with age. In contrast, few studies have investigated the loss of muscle strength in concordance with insulin resistance. In 20- to 80-year-old North American men, muscle strength (1-repetition maximal measures) for leg and bench press adjusted for body weight was inversely associated with the incidence of MS, independent of age and body size [37]. Another study suggested that impaired grip strength was associated with the presence of MS in both men and women aged 59 to 73 years [6]. However, little data are available regarding muscle strength in individuals 65 years or older with or without MS.

In our study, the association of MS with reduced muscle strength remained significant even after controlling for comorbid conditions, such as depression, cancer, fracture history, and physical inactivity, in men with MS aged 65 to 74 years. This finding suggests that muscle weakness in MS cannot be explained solely by comorbidity status or physical inactivity but, rather, may have a specific pathophysiological pathway. Other study results support this by showing an inverse association between muscle strength and the presence of MS, independent of subjects' aerobic fitness and other confounding factors [9,38-40], such as indicators of obesity [8].

It has previously been reported that hand-grip muscle strength in nondiabetic populations is significantly associated with fasting insulin level or insulin resistance, as evaluated by homeostasis model assessment [41,42]. Skeletal muscle plays a key role in glucose disposal, and lipid content in skeletal muscle is inversely correlated with insulin sensitivity [43]. Therefore, low muscle strength may be a marker for impaired glucose disposal by skeletal muscle, which is closely associated with whole-body insulin resistance. Conversely, insulin resistance may lead to deficits in muscle strength. Insulin-resistant glucose-intolerant states, such as MS, may have adverse effect on muscle contractile function and force generation [44,45]. Glucose modifies myosin function, the molecular motor protein in skeletal muscle; and glycation has been suggested to contribute to deficits in skeletal muscle function in a dose-dependent manner during aging and diabetes [46].

The association between muscle strength and MS in aging women was not significant in the present study. Various studies on aging have reported that there are differences in physical functioning between sexes [21]. The Baltimore Longitudinal Study on Aging reported that men had greater rates of decline in muscle strength than did women, even after accounting for greater initial strength, and that increased age was associated with a greater loss of strength [39,47,48]. Sex differences in the skeletal-muscle energy metabolism may explain this phenomenon. In men, the prevalence of MS was associated with lower androgen levels [49,50]. The levels of androgens in men with MS are lower than those in men without MS, and testosterone levels decrease as the number of MS indicators increases [51]. Testosterone retains nitrogen, an action essential for the development and maintenance of muscle mass [25], and improves physical strength and performance [26]. Therefore, decreased testosterone in men with MS may be a possible explanation for muscle weakness in this population. In men, testosterone levels decline gradually with age from middle age [24]. In contrast, testosterone levels decrease rapidly after menopause in women [28]. It remains unclear whether testosterone levels are significantly lower in older women with MS.

Few studies have investigated the association between muscular strength and MS in elderly women. One study [8] showed that muscular strength was inversely related to MS in women aged 18 to 75 years. However, the sample included only healthy adults; and the women appeared to be generally weaker and have a more homogenous level of function compared with the men. Because sex hormone levels were not evaluated in our cohort, further studies are needed to elucidate this hypothesis. Overall, our findings suggest that sex and age differences should be considered when evaluating the association between MS and muscle strength in older adults.

The present study had several advantages over previous studies. First, the subjects were recruited from a community-based elderly population, represented a single ethnic group, and were all 65 years or older. Second, our use of an isokinetic dynamometer to evaluate muscle strength provided higher-accuracy measurements than the methods used in previous studies. Furthermore, we assessed hand-grip strength and leg muscle strength.

Limitations of the study include the fact that our study was a cross-sectional study and, consequently, no conclusion can be drawn regarding the causality or direct relationship between MS and muscle strength. Longitudinal or interventional studies are required to demonstrate this association further. Because the KLoSHA is an ongoing survey, further explorations of related issues may be undertaken in the future.

In conclusion, men with MS aged 65 to 74 years were at higher risk for muscle weakness than were their counterparts without MS, whereas women in this elderly cohort did not show MS-related muscle weakness. Lifestyle modification, such as nutritional support and weight-bearing exercises, should be implemented to improve muscle weakness and reduce metabolic impairment.

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Conflict of Interest

We have no financial or other relationships that might pose a conflict of interest in connection with the submitted article.

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