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Research Article

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Age-Related Loss of Skeletal Muscle and Associated Risk Factors in Middle-Aged Men: A Comprehensive Study

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| Abstract |

PURPOSE: This study examined the specific clinical risk factors in middle-aged men with age-related loss of skeletal muscle mass (ALSMM).

METHODS: The present research analyzed the data from a cross-sectional study of 1,564 community-dwelling participants aged between 40 to 49 years old. The participants were screened for ALSMM. The study examined various risk factors, including age, height, weight, body mass index, waist circumference, skeletal muscle mass index, smoking and drinking status, systolic and diastolic blood pressure, fasting glucose levels, and triglyceride and cholesterol levels.

RESULTS: The risk factors of ALSMM were height, body mass index, waist circumference, skeletal muscle mass index, systolic blood pressure, diastolic blood pressure, drinking status, fasting glucose, and triglyceride levels ($p < .05$). The weight, triglyceride, and smoking status variables were non-significant ($p > .05$).

CONCLUSION: The risk factors for ALSMM among community-dwelling adults were determined. These results are expected to contribute to the existing literature on ALSMM and provide potential risk factors associated with the development of ALSMM in middle-aged males.

Key Words: Age, Muscle Loss, Odd ratios, Risk factor

Ⅰ. Introduction

Progressive age-related skeletal loss of muscle mass is a prevalent health issue [1]. Age-related loss of skeletal muscle mass (ALSMM) can lead to various adverse outcomes, including falls, fractures, physical disability, metabolic disorders, reduced quality of life, and even mortality. Critchley first described the concept of skeletal muscle loss and weakness in 1931. Since then, ALSMM has emerged as a significant health concern for older adults [2]

The aging population in Asia is growing rapidly, and Korea is one of the fastest aging countries in the world. In 2021, approximately 16.5% of the population in Korea was above the age of 65, which is projected to rise to 39.8% by 2050 [3]. Consequently, age-related conditions,

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such as ALSMM, will impact Korea and Asia more substantially than other nations.

Furthermore, age-related loss of skeletal muscle mass is more prevalent in men than women. Brown et al. [4] evaluated 4,425 adults in the US and found a higher prevalence in males (44.8%) compared to females (30.24%). Similarly, Liu et al. [5] examined 4,500 Chinese people in an urban community and reported that the prevalence was 22.1% in men and 17.8% in women. Hai et al. [6] assessed 834 community-dwelling Chinese individuals and reported that the incidence was 11.3% in men and 9.8% in women. Chan et al. [7] reported a prevalence of 9.30% in males and 5.30% in females among 3,957 people in Hong Kong. These studies suggested that ALSMM is more prevalent in males than females.

Despite the high number of older adults at risk for ALSMM and the significant proportion of males affected by this condition, there are still challenges in identifying risk factors and addressing ALSMM among this population, compared to well-researched ALSMM studies on females [8-11].

Although Silva et al. [12] examined ALSMM in 108 participants with a mean age of 43 years, they grouped males and females, which may have limited ability to identify gender-specific risk factors.

Most studies on ALSMM focused on individuals over 50 years of age [13-16]. Nevertheless, evidence suggests that age-related muscle loss may begin as early as the 40s [17-21]. Identifying the risk factors in middle-aged men between 40 and 49 years of age is crucial to developing early prevention strategies for age-related muscle loss. Therefore, this study examined specific clinical risk factors in middle-aged men between 40 and 49 years of age. This study hypothesized that middle-aged men have distinct risk factors associated with muscle loss.

Ⅱ. Methods

1. Study Participants

The present study used data from the Korea National Health and Nutrition Examination Survey, which is a survey conducted by the Centers for Disease Control and Prevention to monitor the health-risk behaviors of the population. The survey utilized a stratified, clustered, multistage probability sampling design. A total of 35,737 individuals participated in the survey during 2008–2011. Of the subjects, 32,325 individuals were excluded from the study because they were either below 40 or above 49 years of age, leaving 5,428 participants. Furthermore, 3,864 subjects were excluded because no data on their health surveys and DEXA measurement was available. Consequently, only data from 1,564 male participants between the ages of 40 and 49 years were included in the final analysis (Fig. 1). The inclusion criteria are individuals between 40 and 49 years of age. The exclusion criteria for this study were individuals with no DEXA measurements and health survey data and who were hospitalized for any reason. Of these, 84 middle-aged individuals were assigned to an ALSMM group based on their skeletal muscle mass index score, while the remaining 1480 individuals were assigned to the normal group. The study was approved by the institutional review board of the Center for Disease Control and Prevention (approval numbers 2008-04EXP-01-C, 2009-01CON-03-2C, 2010-02CON-21-C, and 2011-02CON-06-C), and informed

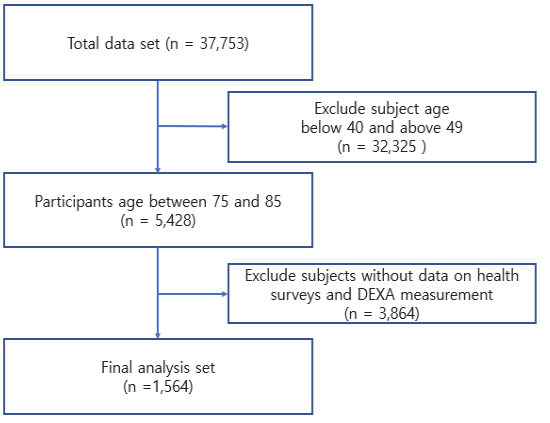

Fig. 1. Flowchart for recruiting the participants.

Table 1. General characteristics of the participants

	ALSMM group (N = 84)	Normal group (*n* = 1480)	p
Age (years)	44.76 ± 2.97	44.21 ± 2.92	.097
Height (cm)	162.98 ± 5.10	171.04 ± 5.45	.000**
Weight (kg)	69.97 ± 10.19	71.37 ± 10.08	.214

ALSMM, age-related loss of skeletal muscle mass
Values are expressed as the mean ± standard deviation. The independent *t*-test was significant at p < .01 **.

written consent was obtained from all participants. Further details are listed in Table 1.

2. Research Variables

The study incorporated various variables in the analysis, including age, height measured in centimeters, weight measured in kilograms, body mass index (BMI), waist circumference (WC), skeletal muscle index (SMI), smoking and drinking status, fasting glucose, triglycerides, total cholesterol (TC), systolic blood pressure, and diastolic blood pressure. The WC was measured by determining the circumference at the mid-point between the bottom of the ribcage and the top of the iliac crest during full expiration. The blood test was conducted after an eight-hour fast, and the systolic and diastolic blood pressures were measured using a mercury sphygmomanometer after a ten-minute rest in a chair. The smoking and drinking statuses were categorized as non-users, ex-users, or current users.

3. Criteria for ALSMM

The diagnosis of ALSMM, a condition with an ICD-10-CM code of M62.84, involves measuring the amount of skeletal muscle mass in the limbs. Dual X-ray absorptiometry (DXA, using QDR4500A equipment from Hologic, Inc. in Bedford, MA) was used to determine the amount of skeletal muscle mass in the limbs. The ASM (in kg) to BMI (in kg/m^2) ratio, also known as the skeletal muscle mass index (SMI), was calculated to assess the muscle mass. ALSMM was diagnosed when the SMI value was less than .789 for men and below .521 for women, according to the criteria established by the Foundation for the National Institutes of Health ALSMM Project [22]. The methodology used in this study accurately diagnosed ALSMM among the study participants.

4. Data Analysis

SPSS version 22.0 was used for the statistical analyses. Weights were utilized during the analysis to account for the complex sampling design of KNHANES. The data utilized a stratified, clustered, multistage probability sampling design. Independent t-tests and chi-square analyses were conducted to compare the chemical parameters between the participants with ALSMM and without ALSMM. Multiple logistic regression was used to determine the odds ratio of ALSMM. The statistical significance level was set at p = .05.

Ⅲ. Results

1. Clinical Risk Factors

The height, BMI, WC, SMI, fasting glucose, triglyceride, systolic blood pressure, diastolic blood pressure, and drinking status were statistically significant (p < .05). By contrast, the weight, TC, and smoking status variables were non-significant (p > .05) (Table 2).

2. Multiple Logistic Regression for Odd Ratio

Table 3 lists the odds ratio with a 95% of confidence interval (CI) for SO in males, performed multiple logistic regression analysis. The following were significant (p < .05): height 2.777 (.040–173.866), BMI 10.693 (.070–167.786), WC 2.680 (1.732–4.146), SMI 36.367 (30.608–43.209), SBP 1.995 (1.542–2.582), DBP .596 (.459–.775), FG .852 (.728–.998). The triglyceride 1.001 (.989–1.013) was not significant (p > .05) (Table 3).

Table 2. Clinical risk factors related to age-related loss of skeletal muscle mass (ALSMM)

	ALSMM group (N = 84)	Normal group (*n* = 1480)	p
Proportion (%)	5.37	94.63	
Age (years)	44.76 ± 2.97	44.21 ± 2.92	.097
Height (cm)	162.98 ± 5.10	171.04 ± 5.45	.000**
Weight (kg)	69.97 ± 10.19	71.37 ± 10.08	.214
BMI (kg/m^2)	26.27 ± 3.06	24.35 ± 2.96	.000**
WC (cm)	89.08 ± 8.61	84.68 ± 8.40	.000**
SMI (kg/m^2)	0.74 ± 0.04	0.95 ± 0.09	.000**
SBP (mmHg)	123.44 ± 16.73	119.26 ± 14.5	.011*
DBP (mmHg)	84.83 ± 12.95	82.04 ± 10.92	025*
Drinking status (%) (current-/ex-/non-drinker)	80.16 / 12.31 / 7.51	89.69 / 7.04 / 3.26	.033*
Smoking status (%) (current-/ex-/non-smoker)	70.58 / 14.38 / 15.03	59.47 / 24.95 / 15.57	.079
FG (mg/dL)	107.61 ± 33.22	99.50 ± 22.47	.002**
Triglyceride (mg/dL)	231.74 ± 172.01	178.14 ± 155.05	.003**
TC (mg/dL)	201.89 ± 47.859	195.063 ± 34.739	.091

ALSMM, age-related loss of skeletal muscle mass; BMI, body mass index; WC, waist circumference; SMI, skeletal muscle mass index SBP, systolic blood pressure; DBP, diastolic blood pressure; FG, fasting glucose; TC, total cholesterol.
Values are expressed as the mean ± standard deviation. The independent *t*-test and chi-square test were significant at $p < .05$ *, $p < .01$ **.

Table 3. Odds ratio for age-related loss of skeletal muscle mass

Variables	OR (95% CI)	p
Height	2.777 (.040 – 173.866)	.000**
BMI	10.693 (.070 – 167.786)	.000**
WC	2.680 (1.732 – 4.146)	.000**
SMI	36.367 (30.608 – 43.209)	.000**
SBP	1.995 (1.542 – 2.582)	.000**
DBP	.596 (.459 – .775)	.000**
FG	.852 (.728 – .998)	.046*
Triglyceride	1.001 (.989 – 1.013)	.878

ALSMM, age-related loss of skeletal muscle mass; BMI, body mass index; WC, waist circumference; SMI, skeletal muscle mass index SBP, systolic blood pressure; DBP, diastolic blood pressure; FG, fasting glucose.
Odd ratio (OR) values are present as the 95% confidence interval (CI)
Multiple logistic regression in complex sampling performed (*$p < .05$, **$p < .01$)

Ⅳ. Discussion

This study examined the prevalence and risk factors of community-dwelling middle-aged male individuals aged between 40 and 49 years. In addition, the WC, SBP, DBP, drinking status, fasting glucose, and triglyceride are risk factors for muscle loss.

The WC is the risk factor for age related to muscle loss. Numerous studies also show that the WC is associated with an increased risk of ALSMM in men [23,4,24]. Brown et al. examined a US cohort that reported the WC as a risk factor for ALSMM and identified odds ratios were 1.39 (1.05–1.84) in men [4]. Similarly, a cohort study among individuals with ALSMM in Brazil found an odds ratio of 17.90 (95% CI: 1.48–201.16) for the waist circumference [24]. Another study in Japan among community-dwelling individuals suggested that those with ALSMM had larger WC than non-ALSMM individuals [23]. The possible underlying reason for the higher waist circumference in adults with ALSMM is the mutually interdependent relationship between enhanced fat mass and lower muscle mass [25]. ALSMM individuals often face issues with muscle power and function due to muscle loss, leading to reduced physical activity levels, such as difficulties in sitting-to-stand and walking long distances indoors and outdoors [26]. The decreased physical activity is strongly linked to decreased total daily energy expenditure and increased fat stores, particularly in the visceral and abdominal areas, which increases the waist volume [26]. On the other hand, a higher fat volume, particularly visceral fat, produces pro-inflammatory cytokines, such as interleukin 6 and C-reactive protein, which can hinder the anabolic response of muscle tissue [27]. Therefore, the relationship between decreased muscle mass and increased fat mass in ALSMM is bidirectional and mutually reinforcing [28].

These findings show that SBP and DBP are other risk factors for men, which is consistent with previous studies on this population [29-32]. Atkins et al. [30] conducted a British cohort study on ALSMM with 4,252 participants and reported that the SBP and DBP in the ALSMM group were significantly higher than the normal group. Androga et al. [31] conducted a US cohort study and reported that hypertension in the ALSMM group was greater than in the normal group. Yin et al. [32] conducted a study on 14,926 Chinese individuals. They reported that males with ALSMM had significantly higher SBP and DBP than normal adults. Possible mechanisms underlying the higher SBP and DBP in men with ALSMM include metabolic alterations and muscle mass loss because of skeletal muscle loss, resulting in reduced energy expenditure and physical activity, insulin resistance, and arterial stiffness in adults [33-35]. Furthermore, the accumulation of visceral fat mass may trigger an inflammatory response, leading to thickening of the blood vessel walls, constriction of vascular passages, and obstruction of blood flow [36].

Alcohol consumption is a risk factor for age-related muscle loss. The study finding is in line with previous studies [37,38]. Pang et al. [38] assessed 542 Singaporean community-dwelling adults and concluded that alcohol consumption is highly related to ALSMM. Daskalopoulou et al. [37] conducted a multicenter population-based study with 8694 individuals and mentioned that alcohol consumption is one of the risk factors for ALSMM. The following provides a plausible underlying mechanism for the association between alcohol consumption and ALSMM. Alcohol adversely affects protein synthesis, which is the process by which the body builds muscle. This can lead to a decrease in muscle mass and strength over time [39]. Furthermore, alcohol can interfere with the body's ability to absorb important nutrients, such as protein and amino acids, which are necessary for muscle growth and repair. Alcohol consumption can also lead to dehydration, which can further impair muscle function and recovery [40].

The fasting glucose levels have been identified as a risk factor for ALSMM in males, showing average values

of 107.61 mg/dL and 99.50 mg/dL in the ALSMM and normal groups, respectively. This outcome is parallel to previous research [29,41-44]. Lu et al. [29] examined six hundred people living in the community and reported that individuals in the ALSMM group had elevated levels of fasting blood glucose of 110 mg/dL (6.1 mmol/L) compared to 99 mg/dL (5.4 mmol/L) in the normal group. Bersemi et al. [44] conducted a cohort study on 150 community-dwelling people with ALSMM. They reported that the ALSMM group exhibited higher fasting glucose levels than the non-ALSMM group. Similarly, a Turkish study involving 147 participants showed that ALSMM patients experienced difficulties in controlling their blood glucose [41]. A plausible theoretical mechanism for the elevated fasting glucose levels in ALSMM individuals is the role of muscle mass in regulating postprandial glucose levels. Skeletal muscle is crucial for storing approximately 80% of ingested glucose after meals to prevent hyperglycemia in the blood [19]. ALSMM patients, particularly males, tend to show reduced sensitivity to insulin, resulting in decreased glucose uptake by skeletal muscles. This can be attributed to lower proportions of type I muscle fibers and capillary density, which are less responsive to insulin [45]. As a result, the decreased skeletal muscle mass and compromised insulin sensitivity in males with ALSMM may contribute to diminished glucose uptake by muscles from the bloodstream. This can lead to accelerated elevation of blood glucose levels in ALSMM males.

Triglyceride is also a risk factor for men, showing an average level of 231.74 mg/dL in the ALSMM group and 178.14 mg/dL in the normal group. This factor was consistent with previous ALSMM studies [29,46,47]. Lu et al. [29] assessed 600 northern Taiwan community-dwelling elderly people. They reported that 1.9 mmol/L in the ALSMM group had a significantly higher triglyceride level than 1.3 mmol/L in the normal group. Similarly, Buchmann et al. [46] investigated 1420 elderly people living in Berlin. They concluded that triglyceride in ALSMM (108.7 mg/dL) was greater than in the non-ALSMM group (92.1 mg/dL). Du et al. [47] conducted a cross-section study on community-dwelling elderly in East China. They suggested that the male ALSMM group had increased serum triglycerides level. A possible underlying mechanism for the higher triglyceride and total cholesterol levels is related to insulin resistance [48] and high volume of inflammatory cytokines [49].

The important aspect of this study is the investigation of male risk factors in a representative population of those in their 40s, when the loss of skeletal muscles starts, unlike most combined sex, into a single group [4,14,50]. Nevertheless, this study had a limitation that should be considered for future research. Owing to the cross-sectional design used in this study, despite including a large sample size of 1,564 participants representative of the entire population through statistical weighting, there may be limitations in establishing causal relationships for the identified risk factors. Therefore, future studies should consider employing a longitudinal or randomized case-control study design to strengthen the findings.

Ⅴ. Conclusion

The present study is the first to provide clinical evidence of the risk factors for ALSMM in middle-aged men. The findings of this study showed that height, BMI, WC, SMI, fasting glucose, triglyceride, systolic blood pressure, diastolic blood pressure, and alcohol consumption status clinical factors might increase the risk of developing ALSMM in this specific age group. These results contribute to the existing literature on ALSMM and shed light on the potential risk factors that may be associated with the development of this condition in middle-aged males. Further research will be needed to understand the underlying mechanisms and to develop targeted interventions for individuals at risk for ALSMM.

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