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Nationwide Cross-sectional Analysis of Determinant Agents for Sarcopenia in Men in Their Forties: Based on the EWGSOP Criteria

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| **Abstract** |

PURPOSE: This study examined sarcopenia in middle-aged men aged 40 to 49 years.

METHODS: The study design was a nationwide cross-sectional study involving 1,564 participants. The participants were divided into two groups based on their skeletal muscle mass index scores, with 36 and 1,528 individuals classified into the sarcopenia and normal groups, respectively. The variables examined included age, height, weight, body mass index (BMI), waist circumference, skeletal muscle mass index, and systolic and diastolic blood pressure. The results from blood tests included fasting glucose, triglycerides, and total cholesterol levels. The smoking and drinking status were also recorded.

RESULTS: The anthropometric variables, such as weight, BMI, and waist circumference, revealed significant differences between the two groups (p < .05), except for height (p > .05). In addition, total cholesterol in the laboratory test and drink

status were significant between the two groups (p < .05).

CONCLUSION: This study identified significant determinants for sarcopenia among community-dwelling middle-aged men.

Key Words: Determinant agents, Middle aged men, Sarcopenia, Odds ratio

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Ⅰ. Introduction

Sarcopenia is characterized by the age-related reduction of skeletal muscle mass that leads to diminished muscle strength, function, and quality of life [1]. Critchley initially introduced the concept of skeletal muscle loss and weakness in 1931. Subsequently, sarcopenia has emerged as a significant health issue for the elderly population [2]. Although the precise mechanism of sarcopenia is not completely understood, various studies have suggested that hormonal changes, immobility, age-related muscle changes, nutrition, and neurodegenerative factors may contribute to its development. Elderly individuals aged 65 years and above are more susceptible to sarcopenia [3].

The aging demographic in Asia is experiencing rapid expansion, with Korea emerging as one of the world's most rapidly aging nations. In 2021, approximately 16.5% of

the Korean population were aged 65 years and above, which is expected to increase to 39.8% by 2050 [4]. As a result, age-related ailments, such as sarcopenia, are poised to exert a more pronounced impact on Korea and the broader Asian region compared to other countries.

Moreover, the age-related loss of skeletal muscle mass is higher in men than women. Brown et al. [5], Liu et al. [6], Hai et al. [7], and Chan et al. [8] examined a community-dwelling elderly population in US and China. They reported that men have a higher prevalence of skeletal muscle mass loss than women. These studies collectively suggest a higher prevalence of sarcopenia in males than females. Despite the substantial number of older adults at risk of sarcopenia and the significant proportion of affected males, there are challenges in identifying the determinant agents and addressing sarcopenia within this population, which is in contrast to the well-studied sarcopenia in females [9-12]. Although Silva et al. [13] examined the decline in age-related skeletal muscle mass in a cohort of 108 participants with an average age of 43 years, their approach of grouping males and females together might have hindered the identification of gender-specific determinant agents.

The majority of sarcopenia studies have predominantly targeted individuals aged 50 and above [14-20]. Nevertheless, research indicates that age-related muscle loss could commence as early as the fourth decade of life [21-25]. Recognizing the determinant agents specific to middle-aged men between 40 and 49 years of age is paramount for formulating early intervention strategies against age-related muscle decline. Consequently, this study examined distinctive clinical determinant agents among middle-aged men. The underlying hypothesis posits that middle-aged men exhibit unique determinant agents associated with muscle loss.

Ⅱ. Methods

1. Subject Selection

The present nationwide cross-sectional study was conducted using data from the Korea National Health and Nutrition Examination Survey conducted by the Centers for Disease Control and Prevention to monitor the health-risk behaviors of the population The Korea National Health and Nutrition Examination Survey only offers muscle data from dual-energy X-ray absorptiometry (DEXA) scans for diagnosing sarcopenia from 2008 to 2011, with no data available for the subsequent years. Consequently, the analysis was conducted using the data from this period. The survey used a stratified, clustered, multistage probability sampling design. Among the 35,737 individuals who participated in the survey between 2008 and 2011, 32,325 were excluded from the study because they did not meet the age criteria, resulting in 5,428 participants. Subsequently, 3,864 subjects were excluded because of a lack of available health survey and DEXA measurement data. Thus, the data from only 1,564 male participants aged 40 to 49 years were included in the final analysis. The inclusion criteria specified individuals aged between 40 and 49 years, while the exclusion criteria encompassed individuals lacking DEXA measurements and health survey data and those hospitalized for any reason. Overall, 36 and 1,564 middle-aged individuals were categorized into a sarcopenia and normal group, respectively.

Both groups used the same equipment and tools to diagnose sarcopenia and measure the variables. The study received approval from the institutional review board of the Center for Disease Control and Prevention, and all participants provided written informed consent.

2. Variables

1) Anthropometric Variables:

The participants were instructed to remove footwear, socks, headwear, and hairpins and wear lightweight clothing for anthropometric measurements. The heights and weights were assessed using calibrated automatic body measurement equipment, with measurements recorded to

the nearest 0.1 cm and kg, respectively. The body mass index (BMI) was derived from the weight (kg) divided by the square of height (m^2). The waist circumference (WC) was measured to the nearest 0.1 cm on a horizontal plane at the midpoint between the last rib and the iliac crest during normal expiration.

2) Blood Pressure and Blood Laboratory Test Variables:

Trained practitioners measured the systolic blood pressure (SBP) and diastolic blood pressure (DBP) using a mercury sphygmomanometer. The measurements were taken with the blood pressure cuff positioned at heart level while participants were seated, following at least five minutes of rest. Blood laboratory tests included the fasting glucose (FG), triglyceride, and total cholesterol (TC) levels, which were analyzed using the LABOSPECT 008AS platform (Hitachi High-Tech Co., Tokyo, Japan). Blood samples were drawn from the non-dominant arm after an overnight fast of at least eight hours. The collected blood was promptly mixed with a coagulation promoter and centrifuged in a mobile examination vehicle. All analyses were conducted within 24 hours of sample collection.

3) Drinking and Smoking Variables:

Data on smoking and drinking habits were collected through survey questions, categorizing participants as non-users, ex-users, or current users of both cigarettes and alcohol. These variables are essential for assessing the various aspects of health and disease risk within the study population.

3. Diagnosis of Sarcopenia

The diagnostic criteria for sarcopenia include an assessment of the skeletal muscle mass in the limbs. This condition is classified under the ICD-10-CM code M62.84. DEXA (QDR4500A, Hologic, Inc., Bedford, MA) was used to quantify the skeletal muscle mass in the limbs [26]. Establishing cut-off points was contingent upon the chosen measurement technique and the availability of relevant

reference studies. The European Working Group on Sarcopenia in Older People (EWGSOP) advises using normative data from healthy young adults rather than other predictive reference populations to define these cut-off points based on a Rosetta study in sarcopenia [27-29]. In particular, the recommended cut-off points were set to two standard deviations below the mean reference value, ensuring a more accurate and standardized assessment. A muscle mass assessment was performed by calculating the appendicular skeletal muscle mass (ASM) divided by the square of the height, commonly known as the skeletal muscle mass index (SMI)

4. Statistical analysis

This study used descriptive statistics, including mean and standard deviation, to present the measurements. Complex sampling analysis, incorporating the individual weights provided by KNHANES, was used to represent a nationwide analysis of Korea. Data analysis was conducted using SPSS 27.0 software (IBM Corporation, Armonk, NY, USA). This study used a stratified, clustered, multistage probability sampling design.

Independent t-tests and chi-square analyses were used to compare the chemical parameters between the participants with and without sarcopenia. Multiple logistic regression was used to calculate the odds ratio of sarcopenia. The statistical significance level was set at $p = .05$.

Ⅲ. Results

1. Clinical Risk Factors

1) Anthropometric Variables

The variables of interest included the weight, body mass index, and waist circumference, which exhibited statistically significant disparities between the two groups ($p < .05$), unlike height, which lacks significance ($p > .05$). Table 1 lists these determinant agents in anthropometric measures.

2) Blood lab tests variables and blood pressure

The two groups displayed a statistically significant discrepancy in the total cholesterol (TC) levels (p < .05). In contrast, the FG and triglyceride levels were similar in the two groups (p > .05). Similarly, SBP and DBP were similar in the two groups (p > .05)(Table 2).

3) Drinking and Smoking Variables

The drinking status showed statistical significance (p < .05), whereas the smoking status did not (p > .05)(Table 3).

Table 1. Anthropometric variables and skeletal muscle mass index

	Sarcopenia (N =36)	Normal (N =1,528)	p
Age (years)	45.25 ± 2.53	44.22 ± 2.93	.037*
Height (cm)	169.33 ± 6.20	170.64 ± 5.71	.176
Weight (kg)	55.77 ± 6.08	71.66 ± 9.88	.000**
BMI (kg/m^2)	19.45 ± 2.05	24.58 ± 2.91	.000**
WC (cm)	73.22 ± 7.27	85.19 ± 8.29	.000**
SMI (g/m^2)	5907.62 ± 235.17	7916.00 ± 824.78	.000**

Values are expressed as the mean ± standard deviation. The independent t-test was exploited.
BMI, body mass index; WC, waist circumference; SMI, skeletal muscle mass index
*p < .05, **p < .01

Table 2. Blood pressure and blood lab test variables

	Sarcopenia (N =36)	Normal (N =1,528)	p
FG (mg/dL)	102.54 ± 40.51	99.87 ± 22.69	.502
Triglyceride (mg/dL)	139.48 ± 174.54	181.97 ± 155.89	.112
TC (mg/dL)	199.29 ± 33.05	195.71 ± 35.59	.040*
SBP (mmHg)	119.44 ± 17.35	119.49 ± 14.59	.985
DBP (mmHg)	80.13 ± 11.30	82.24 ± 11.05	.259

Values are expressed as the mean ± standard deviation. The independent t-test was exploited.
SBP, systolic blood pressure; DBP, diastolic blood pressure; FG, fasting glucose; TC, total cholesterol.
*p < .05, **p < .01

Table 3. Drinking and smoking variables

	Sarcopenia (N =36)	Normal (N =1,528)	p
Drinking status (%) current-/ex-/non-smoker	89.62 / 6.95 / 3.42	71.55 / 22.20 / 6.23	.007**
Smoking status (%) (current-/ex-/non-smoker)	70.35 / 14.88 / 14.75	55.25 / 17.51 / 27.23	.177

A Chi-square test was used to compare the two groups.
**p < .01

Table 4. Multiple logistic regression for the odds ratios of sarcopenia

Variables	Odd ratios (95% of CI)	p
Weight	1.678(1.376-2.046)	.000**
Waist circumference	1.194(1.058-1.458)	.031*
Total cholesterol	1.118(1.025-1.272)	.048*

The odd ratio values are present as the 95% confidence interval (CI)
Multiple logistic regression was exploited.
*p < .05, **p < .01

2. Odd ratios for determinant agents

The study found significant differences in the variables of weight, waist circumference, and total cholesterol between the two groups (p < .05). The respective values were 1.678 (with a confidence interval of 1.376 to 2.046), 1.194 (confidence interval of 1.058 to 1.458), and 1.118 (confidence interval of 1.025 to 1.272) (Table 4).

Ⅳ. Discussion

This study evaluated the determinant agents of sarcopenia among middle-aged individuals residing in the community. The aging population in Korea and Asia is accelerating, particularly with males. Despite the potential adverse consequences of sarcopenia, healthcare professionals, including physical and occupational therapists, encounter challenges in diagnosing the condition because of insufficient knowledge and diagnostic tools. This gap can lead to missed diagnoses and subsequent complications[18,19,30-38,20, 39-44]. The study variables, which include anthropometric measurements, blood pressure, blood lab test variables, drinking status, and smoking status, offer an inexpensive, convenient, and accessible method to identify potential sarcopenia patients. Understanding the determinant agents is essential for the early detection and prevention of sarcopenia. The identified determinant agents for sarcopenia in this population included weight, body mass index, waist circumference, skeletal muscle index, total cholesterol, and drink status.

Waist circumference and weight are determinant agents for sarcopenia. Several studies have suggested that increased waist circumference and weight could be determinant agents of sarcopenia [32,42,43]. For example, a nationwide study in Korea [32] found that individuals in the sarcopenia group had lower weight compared to the normal group. Similarly, Kim [45] conducted research on community-dwelling older adults, concluding that the sarcopenia group had lower weight and torso body fat mass. Additionally, Qianyun Zhao [46] studied 165 patients in China and reported that the sarcopenia group had significantly smaller waist circumferences and lower weight.

There are several underlying reasons why individuals with sarcopenia tend to have smaller waist circumferences and lower body weight. Sarcopenia is characterized by the progressive loss of skeletal muscle mass and strength. Since muscle tissue is denser and heavier than fat, a reduction in muscle mass leads to an overall decrease in body weight [47]. Moreover, individuals with sarcopenia often experience a reduction in subcutaneous and visceral fat, contributing to a smaller waist circumference. As muscle mass decreases, the body's ability to store fat efficiently also diminishes, resulting in fewer fat deposits around the waist [47]. Sarcopenia is also associated with metabolic changes that affect energy expenditure and fat storage. The reduction in muscle mass lowers the basal metabolic rate, altering how the body processes and stores fat, which often results in a trimmer waistline [48]. Poor nutrition and insufficient protein intake, common among older adults, can further exacerbate muscle loss. Inadequate nutrition not only leads to reduced muscle mass but also contributes to overall weight loss and decreased waist circumference due to insufficient caloric intake needed to maintain body weight [49]. In summary, smaller waist circumference and reduced body weight in individuals with sarcopenia are attributed to the loss of muscle mass and strength, decreased fat storage, and altered metabolism. Poor nutrition and insufficient protein intake further contribute to reduced

weight and waist circumference.

Research findings consistently show that the total cholesterol levels are a contributing factor to sarcopenia in men, and an increase in total cholesterol levels results in a rise in sarcopenia, aligning with previous studies [45,51]. For example, Du et al. [51] reported that men in the sarcopenic group had higher total cholesterol levels than those in the normal group. Similarly, Sanada et al., involving approximately 1,500 Japanese individuals, showed significantly elevated total cholesterol levels in those with sarcopenia compared to the normal group [45]. The potential underlying mechanisms for higher triglyceride and total cholesterol levels in sarcopenia may include insulin resistance [52] and an increased presence of inflammatory cytokines [53]. These factors can disrupt the lipid metabolism, leading to elevated cholesterol levels in individuals with sarcopenia.

Therefore, research has consistently highlighted the significance of higher total cholesterol levels as a contributing factor to sarcopenia in men, corroborating earlier findings. The total cholesterol levels in sarcopenia may be influenced by insulin resistance and increased inflammatory cytokines. Understanding these associations is crucial for effectively managing and preventing sarcopenia in men.

The drinking status was found to be a potential determinant of sarcopenia, aligning with previous research findings [54,55]. Pang et al. examined over 500 adults from the Singaporean community and reported a significant association between alcohol intake and the decline in skeletal muscle mass associated with aging [55]. Similarly, a multicenter population-based study by Daskalopoulou et al., which included 8,694 participants, highlighted alcohol consumption as a determinant agent for sarcopenia [54]. The mechanism through which alcohol consumption impacts sarcopenia is as follows. Alcohol adversely affects protein synthesis, which is essential for muscle development. This detrimental effect can gradually decrease muscle mass and strength over time [56]. In addition, alcohol can hinder the absorption of vital nutrients, such as proteins and amino acids, which are critical for muscle growth and repair. Furthermore, alcohol consumption can lead to dehydration, exacerbate muscle dysfunction, and hinder recovery [57]. The combination of weakened and reduced muscle mass leads to a condition known as sarcopenia.

The key strength of this study was its focus on male-specific susceptibility markers within a representative group of individuals in their 40s, a crucial age when the decline in skeletal muscle mass usually begins. Unlike many studies that grouped both sexes, this research concentrated solely on women, offering valuable gender- specific insights into the factors influencing sarcopenia [5,15,58].

Nevertheless, some limitations should be noted for future research. Despite the large, statistically weighted sample size representing the entire population, the cross-sectional design of this study has limitations in establishing the causal relationships for the identified susceptibility markers. Cross-sectional studies capture data at a single point, making it difficult to infer causality between variables. Future studies should consider using longitudinal or randomized case-control study designs to strengthen the findings, which can provide a better understanding of the temporal relationships and causative factors contributing to sarcopenia among men. Second, this study used outdated data from 2008−2011 by the Korea National Health and Nutrition Examination Survey. The Korea National Health and Nutrition Examination Survey provides muscle data obtained through DEXA for diagnosing sarcopenia only for 2008−2011 but not for subsequent years. Therefore, the data from this period were used for the present analysis. Finally, discrepancies in the group sizes between the sarcopenia and normal groups could limit statistical analysis and potentially compromise the research outcomes. Moreover, the study did not account for sarcopenic obesity, a condition characterized by reduced muscle mass and increased body fat. The sarcopenic obesity is essential for interpreting the results better because it may help explain weight gain and waist circumference expansion.

Ⅴ. Conclusion

This study is the first to provide clinical evidence of determinant agents for sarcopenia in middle-aged men. The findings suggest that weight, body mass index, waist circumference, and total cholesterol may elevate the risk of developing sarcopenia in this age group. These results add to the existing literature on sarcopenia, highlighting potential determinant agents linked to its development in middle-aged males. Nevertheless, further research is needed to elucidate the underlying mechanisms and devise targeted interventions for individuals at risk for sarcopenia. This study highlights the importance of monitoring these determinant agents to mitigate the progression of sarcopenia.

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