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흡연과 근감소증의 상관관계: 국민건강영양조사 2008–2011년도 자료를 이용한 단면연구

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Smoking and its Relationship with Sarcopenia: Result from the 2008–2011 Korean National Health and Nutrition Examination Survey

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Background: This study investigated whether smoking defined as smoking status and smoking level is associated with sarcopenia after the age of 50 years by sex using data from the Korea National Health and Nutrition Examination Survey.

Methods: The total number of subjects in this analysis was 8,622. Participants were queried on smoking status (current, past, never) and smoking level (light, ≤11.3 pack-years; medium, >11.3–24.5 pack-years; heavy, >24.5 pack-years). Sarcopenia was evaluated by dividing the body weight by the appendicular skeletal muscle mass (ASM/Wt). Logistic regression analysis was performed to examine the association between sarcopenia and smoking, after adjusting for potential confounders.

Results: Smoking status was not associated with sarcopenia in men and women, but smoking level and sarcopenia were significantly related in women. After adjusting for confounding factors, the multivariate-adjusted odds ratio (95% confidence interval) of sarcopenia in smokers was 0.383 (0.153–0.964) in the medium smoking group of women, and 3.456 (1.542–7.742) and 3.052 (1.292–7.207) in the heavy smoking group of women.

Conclusion: Therefore, our study identified smoking as a reversible and independent risk factor for sarcopenia and smoking defined by smoking level such as pack-years might be an appropriate definition from a sarcopenia perspective.

Keywords: *Sarcopenia; Smoking*

INTRODUCTION

Smoking is probably the single most significant source of toxic chemical exposure to humans and considered one of the main causes of preventable disease and premature deaths worldwide. The health consequences and medical costs associated with smoking are staggering.[1] Cigarette smoking increases the incidence of cardiovascular and cardiopulmonary diseases.[2] In addition to the known harmful effects of smoking, smoking causes changes to the body composition regarding low skeletal muscle and increased abdominal adiposity. Thus, smoking may cause sarcopenia that refers to the loss of skeletal muscle mass and strength, leading to the increased risk of fall-related injuries, metabolic impairments, and overall mortality.[3]

Sarcopenia has multiple causes such as intrinsic and extrinsic factors.[4-6] Intrinsic factors include increased insulin resistance, advancing age, diabetes, metabolic syndrome,[4] hormonal change, loss of repairabil-

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ity, and reduced number of motor units;[5] extrinsic factors include malnutrition, alcohol consumption, reduced physical activity, and smoking.[6] Some cohort studies have identified smoking as a reversible risk factor for sarcopenia.[7] A previous study has reported that older smokers had lower relative lean mass when compared with subjects who had never smoked, suggesting that smoking may increase the risk of sarcopenia by promoting muscle wasting and accelerating the decline in physical functioning.[8]

The strategies that delay or prevent the onset of sarcopenia are likely to have major consequences for public health.[9] Thus, an understanding of smoking as a risk factor for sarcopenia could help in the design of preventive interventions, which is of considerable importance for healthy aging.

In a meta-analysis of individual studies about the relation between cigarette smoking and sarcopenia, the resulting overall odds ratio (OR) of the association between smoking and sarcopenia was 1.12 (95% confidence interval [CI], 1.03–1.21), indicating that smoking as an isolated risk factor may contribute to the development of sarcopenia.[10] However, the results of individual studies were largely inconsistent. In a previous study, the estimation of men was significantly below OR=1,11) whereas, the estimate of another study of men was significantly above OR=1.12) This could be influenced by the design of the study; smoking was not the main topic and the different approaches to measuring the main variables including sarcopenia and smoking affected the results.

In the case of smoking status, nearly every study involved in this meta-analysis was based on the subjective evaluation of participants. A uniform assessment method of smoking status was not used, even though a method of smoking level was developed, such as pack-years regarding the period and quantity of smoking, so, the assignment to categories of smokers and non-smokers could not be as objective as in the case of sarcopenia categories.[10] In the aging process, declining sex hormone levels in adults over 50 years of age begin to expedite the changes in body composition by gender.[11] We examined the relationship between smoking status and smoking level (pack-years) and sarcopenia among individuals aged 50 years or older by sex, who participated in the Korea National Health and Nutrition Examination Survey (KNHANES).

METHODS

1. Study Population

This study extracted participant results from the KNHANES from the year 2008 to 2011. The KNHANES is composed of a health interview survey, a health examination survey, and a nutrition survey conducted by trained investigators. The KNHANES employed a rolling sampling design that implemented a complex, stratified, multistage probability-cluster survey of a representative Korean population sample.[13] Of the 37,753 participants from the KNHANES of 2008–2011, we initially selected those over 50 years of age, and then excluded participants who had any malignancy, whose data for variables included in the analysis were missing, or who were pregnant. The total number of participants in this analysis was 8,622 (3,696 men and 4,926 women) among those who participated in the survey between January 2008 and August 2011. The present study used data from the KNHANES-V, which received institutional review board approval Pukyong National University (IRB no. 2008-04 EXP-01-C, 2009-01CON-03-2C, 2010-02CON-21-C, 2011-02CON-06-C).

2. Measurements

1) Smoking

Participants were categorized on smoking status. According to the self-report response, participants indicated whether they were never smokers, past smokers, or current smokers. Past smokers were defined as individuals who had smoked in the past, but no longer smoked and current smokers were individuals who reported smoking at the survey. Never smokers were individuals who reported never having a cigarette or <100 cigarettes in their lifetime. Participants who were current or past smokers were asked about the number of cigarettes smoked per day, the age of smoking onset, and if quit, the total number of years of smoking. Pack-years, a measure of smoking exposure that takes into account both the amount and duration of smoking, was calculated by multiplying the number of packs smoked per day by the number of years a person has smoked. We grouped the pack-year data for smokers into quartile: light smoking (≤11.3 pack-years), medium smoking (>11.3–24.5 pack-years), or heavy smoking (>24.5 pack-years).[14]

2) Sarcopenia

Appendicular skeletal muscle mass (ASM) was measured by dual-energy X-ray absorptiometry (Discovery-W; Hologic, Inc., Bedford, MA, USA). ASM (kg) was defined as the sum of the lean soft tissue masses of the arms and legs.[15] Sarcopenia was defined as an ASM/Wt (%) that was less than 1 standard deviation below the mean of a sample of healthy adults aged 20 to 39 years.[3] The reference group of this study included

4,987 healthy adults without any history of chronic diseases such as diabetes, stroke, coronary artery disease, thyroid disease, arthritis, tuberculosis, asthma, chronic obstructive lung disease, liver cirrhosis, and cancer.[16] The cutoff value for sarcopenia was 23.8% (ASM/Wt) for women and 30.3% (ASM/Wt) for men, defined as less than 1 standard deviation below the sex-specific normal mean for the reference group in this study.

3) Covariates

Covariates consisted of age, family structure, education, income, job, drinking, physical activity, total energy, protein, fat, blood pressure, fasting glucose level, triglyceride level, high-density lipoprotein (HDL)-cholesterol level, and waist circumference. Family structure was categorized as living alone or living with another family member. Education level was divided into 2 categories as ≤middle school or ≥high school. Monthly income was divided into quartiles according to the equivalent household income, as low, medium, or high. Drinking was classified according to the reported amount of drinks consumed on average per week or month: ≥a times/week, 1–4 times/month, or <1 time/month.[17] Physical activity was assessed using the International Physical Activity Questionnaire.[18] The subjects were categorized into low, medium and high levels of physical activity based on their total physical activity (metabolic equivalent task min/week) and the frequency of the activities. Dietary intake such as total energy, protein and fat were measured by the single 24-hour dietary recall method. Among metabolic risk factors, based on the National Cholesterol Education Program Adult Treatment Panel III guidelines, high blood pressure levels referred to values of more than 130 mmHg of systolic blood pressure or 85 mmHg diastolic blood pressure, or taking anti-hypertensive medication. High fasting glucose levels were more than 100 mg/dL or taking a hypoglycemic agent or insulin therapy. High triglyceride levels were more than 150 mg/dL or taking medication for dyslipidemia treatment. An HDL-cholesterol level of less than 40 mg/dL for men and 50 mg/dL for women, or taking medication for dyslipidemia treatment was considered high. High waist circumference was more than 90 cm for men and 80 cm for women.[19]

3. Statistical Analysis

All sampling and weight variables were stratified, and the statistical analyses were performed using SPSS version 20.0 (IBM Corp., Armonk, NY, USA) to account for the complex sampling design. In order to calculate the total population that the sample would represent, we employed the stratification variables and sampling weights designated by the Korea Centers for Disease Control and Prevention. All data were described as unweighted frequencies, weighted percentages, means, and standard deviations. Subjects' characteristics were compared according to the presence or absence of sarcopenia, using the t-test or chi-square test for categorical variables and the generalized linear model for continuous variables. Multiple logistic regression analyses were used to determine the association between sarcopenia and smoking.

RESULTS

1. Characteristics of the Study Subjects by Sex

The general characteristics of the subjects are shown in Table 1. Among the men, the percentage of past smokers was higher in sarcopenia than non-sarcopenia. Among the women, the number of heavy level smokers was higher in sarcopenia than non-sarcopenia. Also, subjects with sarcopenia had lower protein intake amounts. In both sexes, age, job, physical activity, total energy, blood pressure, fasting glucose, triglyceride, HDL-cholesterol and waist circumference demonstrated statistically significant differences according to the presence or absence of sarcopenia. Subjects with sarcopenia were older and were unemployed. The levels of blood pressure, fasting glucose, triglycerides, and waist circumference were significantly higher in sarcopenia than non-sarcopenia. Also, HDL-cholesterol levels were lower in subjects with sarcopenia. The prevalence of sarcopenia was 36.0% among men and 37.8% among women.

2. Association between Smoking Status and Sarcopenia

To identify the association between smoking status and sarcopenia, multiple logistic regression analysis was performed (Table 2). Among the men, after adjustment for age, family structure, education, income, job, drinking, physical activity, total energy, protein and fat (model 1), the ORs for sarcopenia were 1.222 (95% CI, 0.924–1.615) in the past smoking group and 0.924 (95% CI, 0.695–1.227) in the current smoking group compared with the never smoking group. Controlling further for blood pressure, fasting glucose, triglyceride, HDL-cholesterol, and waist circumference (model 2), the ORs for sarcopenia were 1.218 (95% CI, 0.901–1.648) in the past smoking group and 0.976 (95% CI, 0.711–1.340) in the current smoking group compared with the never smoking group. Among women, after adjustment for age, family structure, education, in-

Table 1. Characteristics of subjects according to sarcopenia by sex (n=8,622)

Characteristics	Categories	Men (n=3,696)			Women (n=4,926)		
		Sarcopenia (-)	Sarcopenia (+)	P-value	Sarcopenia (-)	Sarcopenia (+)	P-value
Age (y)		59.91±0.38	63.04±0.32	<0.001	62.75±0.37	63.57±0.28	0.025
Family structure	Single	118 (4.2)	80 (5.3)	0.163	469 (12.2)	299 (13.2)	0.384
	With family	2,227 (95.8)	1,265 (94.7)		2,583 (87.8)	1,567 (86.8)	
Education	≤Middle	1,332 (54.0)	751 (54.7)	0.758	2,396 (77.8)	1,502 (80.5)	0.083
	≥High	993 (46.0)	581 (45.3)		621 (22.2)	342 (19.5)	
Income	Low	662 (23.7)	409 (26.4)	0.119	1,111 (33.4)	676 (34.5)	0.712
	Medium	1,108 (48.7)	637 (49.4)		1,337 (46.7)	830 (46.6)	
	High	547 (27.6)	283 (24.2)		557 (19.9)	333 (18.8)	
Job	No	638 (24.6)	574 (37.0)	<0.001	1,653 (55.1)	1,167 (61.2)	0.001
	Yes	1,686 (75.4)	759 (63.0)		1,365 (44.9)	677 (38.8)	
Smoking status	Never	435 (18.4)	243 (17.6)	<0.001	2,771 (90.9)	1,716 (92.4)	0.232
	Past	1,028 (41.7)	715 (50.2)		94 (3.6)	61 (3.5)	
	Current	862 (39.9)	380 (32.2)		151 (5.5)	67 (4.1)	
Smoking level*	Light	389 (20.5)	236 (20.3)	0.778	149 (62.0)	66 (55.2)	0.004
	Medium	473 (25.5)	268 (24.3)		69 (27.7)	26 (18.3)	
	Heavy	1,023 (54.0)	585 (55.5)		27 (10.4)	36 (26.5)	
Drinking (times)	≥2/wk	1,021 (44.4)	504 (40.8)	0.018	197 (7.0)	96 (5.8)	0.088
	1–4/mo	619 (27.8)	345 (26.4)		582 (21.1)	336 (18.7)	
	<1/mo	684 (27.8)	483 (32.8)		2,237 (71.9)	1,403 (75.5)	
Physical activity	Low	740 (32.4)	528 (41.0)	<0.001	1,207 (40.0)	866 (46.9)	<0.001
	Medium	709 (30.5)	477 (33.3)		1,015 (33.5)	620 (34.3)	
	High	875 (37.1)	330 (25.7)		795 (26.5)	358 (18.8)	
Total energy (kcal/day)		2,214.87±35.51	2,054.79±29.75	<0.001	1,579.29±23.92	1,502.72±18.34	0.001
Protein (g/day)		77.16±1.68	72.16±1.32	0.003	52.30±1.03	51.23±0.83	0.302
Fat (g/day)		36.10±1.38	35.41±1.17	0.617	22.58±0.72	22.71±0.59	0.858
Blood pressure (mmHg)	High	1,345 (55.9)	984 (72.4)	<0.001	1,745 (55.4)	1,311 (69.0)	<0.001
	Low	1,000 (44.1)	365 (27.6)		1,313 (44.6)	557 (31.0)	
Fasting glucose (mg/dL)	High	957 (41.4)	736 (57.4)	<0.001	946 (33.7)	772 (44.8)	<0.001
	Low	1,325 (58.6)	545 (42.6)		1,947 (66.3)	972 (55.2)	
Triglyceride (mg/dL)	High	823 (37.9)	647 (53.7)	<0.001	1,006 (35.1)	832 (46.3)	<0.001
	Low	1,457 (62.1)	628 (46.3)		1,886 (64.9)	914 (53.7)	
HDL-cholesterol (mg/dL)	Low	523 (24.0)	493 (37.7)	<0.001	1,418 (47.8)	972 (53.3)	0.003
	High	1,757 (76.0)	782 (62.3)		1,474 (52.2)	774 (46.7)	
Waist circumstance (cm)	High	443 (19.3)	663 (51.4)	<0.001	1,489 (48.9)	1,473 (79.2)	<0.001
	Low	1,896 (80.7)	684 (48.6)		1,559 (51.1)	388 (20.8)	
Prevalence of sarcopenia (%)		36.0			37.8		

Values are presented as mean±standard deviation or number (weighted %).
HDL, high-density lipoprotein.
*Smoking level was divided into pack-year of smoking ([packs smoked per day]×[years as a smoker]; light ≤11.3; medium >11.3–24.5; heavy >24.5).
P-values were calculated by t-test or chi-square test.

Table 2. Association between smoking status and sarcopenia

Smoking status	Never	Past		Current	
	Reference	OR (95% CI)	P-value	OR (95% CI)	P-value
Men					
Model 1	1	1.222 (0.924–1.615)	0.159	0.924 (0.695–1.227)	0.582
Model 2	1	1.218 (0.901–1.648)	0.200	0.976 (0.711–1.340)	0.881
Women					
Model 1	1	0.808 (0.518–1.260)	0.345	0.677 (0.450–1.020)	0.062
Model 2	1	0.840 (0.524–1.345)	0.467	0.811 (0.523–1.259)	0.350

Odds ratios (ORs) and 95% confidence intervals (CIs) were obtained by logistic regression analysis.
Model 1 was adjusted for age, family structure, education, income, job, drinking, physical activity, total energy, protein and fat; Model 2 was adjusted for all variables in model 1 plus blood pressure, fasting glucose, triglyceride, high density lipoprotein-cholesterol and waist circumstance.

come, job, drinking, physical activity, total energy, protein and fat (model 1), the ORs for sarcopenia were 0.808 (95% CI, 0.518–1.260) in the past smoking group and 0.677 (95% CI, 0.450–1.020) in the current smoking group compared with the never smoking group. Further adjustment for blood pressure, fasting glucose, triglyceride, HDL-cholesterol and waist circumference (model 2), the ORs for sarcopenia were 0.840 (95% CI, 0.524–1.345) in the past smoking group and 0.811 (95% CI, 0.523–1.259) in the current smoking group compared with the never smoking group. There was no statistical significance according to the smoking status in both sexes.

3. Association between Smoking Level and Sarcopenia

To determine the association between smoking level and sarcopenia, multiple logistic regression analysis was performed (Table 3). Among the men, after adjustment for age, family structure, education, income, job, drinking, physical activity, total energy, protein and fat (model 1), the OR for sarcopenia was 0.972 (95% CI, 0.725–1.253) in the heavy level of smoking group compared with the light level of smoking group and was not statistically significant. Controlling further for blood pressure, fasting glucose, triglyceride, HDL-cholesterol and waist circumference (model 2), the OR for sarcopenia was 0.951 (95% CI, 0.722–1.253) in the heavy level of smoking group compared with the light level of smoking group and was not statistically significant. However, among women, compared with the light level of smoking group, the ORs for sarcopenia were 0.383 (95% CI, 0.153–0.964) in the medium level of smoking group and 3.456 (95% CI, 1.542–7.742) in the heavy level of smoking group, controlling for age, family structure, education, income, job, drinking, physical activity, total energy, protein, and fat. Both smoking groups were statistically significant (model 1). After further adjustment for blood pressure, fasting glucose, triglyceride, HDL-cholesterol, and waist circumference (model 2), the OR for sarcopenia was 3.052 (95% CI, 1.292–7.207) in the heavy level of smoking group compared with the light level of smoking group and was statistically significant.

DISCUSSION

The results of this study demonstrated that the prevalence of sarcopenia was 36.0% for men and 37.8% for women older than 50 years defined by only muscle mass of ASM/weight among Koreans. One previous study which used other criteria for sarcopenia defined by muscle mass, muscle strength, and physical performance in middle-aged and elderly Europeans reported that the prevalence of sarcopenia was 11.9% among men.[20] The difference in prevalence of sarcopenia is probably due to the lack of consensus regarding the optimal approach for diagnosis. Some initiatives have been undertaken to find consensus on a standardized definition of sarcopenia.[21] It appeared to be insufficient to diagnose sarcopenia by measuring only muscle mass. Therefore, two consensus definitions were suggested, including loss of muscle function or muscle strength and physical performance in its definition.[21] According to the definition used, prevalence rate estimates of sarcopenia among people aged 60 years and older can vary between 3% and 52%.[22,23] Early identification of sarcopenia would be of great clinical relevance because the loss of muscle mass and strength with aging can be largely reversed by proper exercise and nutritional intervention.[24,25] For adequate identification of sarcopenia, it is necessary to apply the proper definition of sarcopenia considering muscle mass, strength, and physical performance.

We found that the association of smoking level with sarcopenia was significant; after adjusting for confounding factors in women, the dose-

Table 3. Association between smoking level and sarcopenia

Smoking level*	Light	Medium		Heavy	
	Reference	OR (95% CI)	P-value	OR (95% CI)	P-value
Men					
Model 1	1	1.018 (0.771–1.344)	0.897	0.972 (0.725–1.253)	0.469
Model 2	1	1.097 (0.853–1.411)	0.847	0.951 (0.722–1.253)	0.719
Women					
Model 1	1	0.383 (0.153–0.964)	0.042	3.456 (1.542–7.742)	0.003
Model 2	1	0.464 (0.168–1.285)	0.139	3.052 (1.292–7.207)	0.011

Odds ratios (ORs) and 95% confidence intervals (CIs) were obtained by logistic regression analysis.
Model 1 was adjusted for age, family structure, education, income, job, drinking, physical activity, total energy, protein and fat; Model 2 was adjusted for all variables in model 1 plus blood pressure, fasting glucose, triglyceride, high density lipoprotein-cholesterol and waist circumstance.
*Pack-year of smoking=(packs smoked per day)×(years as a smoker); reference: Light ≤11.3; Medium >11.3–24.5; Heavy >24.5.

response relationship for smoking and sarcopenia was stronger in women than in men in this study. This is in line with previous study reporting an association between smoking and the age-related loss of muscle mass.[7] In this cohort study conducted to investigate risk factors for sarcopenia, it has been shown that smokers had lower appendicular skeletal muscle mass than did subjects who never smoked, and among the smokers, appendicular skeletal muscle mass values were lower in those who smoked more.

Recently, according to the model of accelerated muscle loss by smoking, potential metabolites of smoking such as aldehydes and reactive oxygen species that are assumed to be important in this process, enter the bloodstream and reach the skeletal muscles of smokers and accelerate muscle wasting by increasing oxidative stress, promoting muscle catabolic processes, and inhibiting anabolism.[9] Also, smoking can affect systemic processes leading to increased inflammatory activity, insulin resistance, and metabolism. These may also affect skeletal muscle, providing a possible physiological explanation for the catabolic effects of smoking.[26,27] Another study revealed that smoking increased the risk of sarcopenia by impairing synthesis of muscle protein and increasing the expression of genes associated with impaired muscle maintenance.[28] In general, health risk behaviors such as low levels of physical activity and poor nutrition intake have a significant influence on sarcopenia and smoking is known to be associated with physical inactivity and malnutrition.[29] Our study identified smoking as an independent reversible risk factor for sarcopenia. Identification of the association between smoking and sarcopenia may help in developing strategies to prevent and delay the progress of sarcopenia for health promotion among smokers.

In this study, smoking status was not associated with sarcopenia in both sexes. However, another Korean study reported that smoking significantly decreases the risk of sarcopenia in men.[11] These differences might be partially explained by the design of the study, where smoking was not the main topic, unlike this study and sexual characteristics. Of note, smoking defined by smoking level was more closely associated with sarcopenia than that defined by smoking status in women. Sarcopenia refers to the gradual decline in muscle mass and quality noted with advancing age, which includes the concept of time.[6] In this study, the smoking level considering the amount and duration of smoking was more significant than the smoking status by the cross-sectional questionnaire. However, smoking level was not associated with sarcopenia in men. This seems to require more research on the relation between smoking and sarcopenia with more properly designed studies. This result suggests that smoking defined by smoking level might be an appropriate definition from a sarcopenia perspective.

The present study has several strengths. Our study identified smoking as the main topic for risk factors of sarcopenia using a representative nationwide survey. Furthermore, the pack-years method of assessing smoking designed by the World Health Organization[10] was used for evaluating smoking level. However, this study has several limitations. First, a cross-sectional study design precludes our ability to determine a causal relationship between smoking and sarcopenia. Also, we did not evaluate individual muscle strengths or physical performance in assessing sarcopenia.

Smoking is independently associated with sarcopenia in Korean women older than 50 years. Smoking defined by smoking level such as pack-years might be better for predicting the association with sarcopenia than that defined by smoking status in women. It is necessary to develop the health promotion program for assessing the high-risk group of sarcopenia by smoking level among smokers and apply smoking cessation counseling to them. In addition, longitudinal studies are warranted to investigate the role of smoking based on this definition such as pack-years in predicting sarcopenia.

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