JOURNAL OF WOMEN'S HEALTH
Volume 00, Number 00, 2019

DOI: 10.1089/jwh.2018.7527

Smoking and Diabetes as Predictive Factors of Accelerated Loss of Muscle Mass in Middle-Aged and Older Women: A Six-Year Retrospective Cohort Study

Nara Lee, MD, and Chang-Jin Choi, MD, PhD

Abstract

Background: Preservation of muscle mass during aging reduces the risk of frailty and age-related chronic diseases. We investigated the lifestyle, psychological factors, and common cardiometabolic diseases associated with accelerated muscle loss in middle-aged and older women.

Materials and Methods: A total of 881 women aged 40 years and older who underwent regular health checkup at a tertiary care hospital in Korea in 2010–2011 and underwent a 6-year follow-up were included in this study. Lifestyle and health statuses were evaluated through a standardized questionnaire and laboratory testing. Muscle mass was estimated using bioelectrical impedance analysis.

Results: The accelerated loss group showing appendicular skeletal muscle mass (ASM) loss >3% for 6 years represented 24.4% ($n=215$) of the total participants. Current smoking women presented a higher odds ratio (OR) for accelerated loss of ASM than nonsmoking individuals after adjusting for age, body mass index, exercise, caloric intake, alcohol consumption, menopausal state, and diabetes mellitus (DM) (OR 3.53, confidence interval [95% CI] 1.28–9.74, $p=0.015$). Women with DM showed a higher OR than non-DM individuals after adjusting for the aforementioned variables and smoking status (OR 2.92, 95% CI 1.39–6.14, $p=0.005$).

Conclusion: Current smoking and DM are predictors for accelerated muscle mass loss in middle-aged and older women. Smokers and DM patients need to monitor muscle mass changes and apply preventive intervention steps. Smoking cessation and good glycemic control are required not only for reducing cardiovascular risk but also for improving muscle health.

Keywords: muscle, skeletal, smoking, diabetes mellitus, retrospective study

Introduction

SKELETAL MUSCLES PROVIDE the requisite contractile force for locomotive activities and play a crucial role in the regulation of energy metabolism. Preservation of muscle mass during aging reduces the risk of frailty and age-related chronic diseases.[1] Muscle mass in later life depends on both the peak mass achieved in early life and the rate of muscle loss. Women have a smaller muscle mass than men[2] and experience accelerated loss in muscle mass after menopause.[3] Moreover, the life expectancy of women is longer than that of men. With rapid population aging, sarcopenia has become one of the most important challenges to healthy aging in women.

Prior cross-sectional studies conducted in women reported that skeletal muscle mass could be affected by modifiable lifestyle factors such as physical activity,[4] nutrition,[5] cigarette smoking,[6] alcohol consumption,[7] and psychological factors such as depressive symptoms.[8] However, the temporal association between these factors and skeletal muscle mass did not yield consistent results. High-risk alcohol drinking or binge drinking was associated with a higher risk of sarcopenia in elderly Korean women,[7,9] whereas a systemic review and meta-analysis showed that alcohol consumption did not contribute to the development of sarcopenia.[10] An inverse association between skeletal muscle mass and depressive symptoms was reported,[8] but other studies failed to find a significant association.[11] Longitudinal study on the associated factors with muscle mass changes in women is scarce.[12] Furthermore, previous studies have been focused on the elderly while investigating the risk factors for sarcopenia, the last stage of muscle loss. To investigate the

Department of Family Medicine, Seoul St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Seoul, Republic of Korea.

lifestyle or psychological risk factors for rapid muscle loss, participants should be younger and healthier to rule out aging or pathological conditions causing muscle loss.

The aim of this study was to analyze lifestyle or psychological factors associated with accelerated loss of skeletal muscle mass in middle-aged and older women. We also investigated the relationship between common cardiometabolic diseases and accelerated loss in skeletal muscle.

Materials and Methods

Study population

We enrolled 2132 women 40 years of age or older who underwent regular health examinations including body composition assessment in 2010–2011 and underwent a 6-year follow-up at the Health Promotion Center at a tertiary care hospital in Korea. We excluded women diagnosed with a malignant neoplasm, liver cirrhosis, chronic kidney disease, thyroid disease, rheumatoid arthritis, stroke, or cardiovascular disease from the study to rule out other pathological conditions beyond aging ($n=227$). However, we did not exclude individuals with simple hypertension, diabetes mellitus (DM), or metabolic syndrome without cardiovascular complication, which are common lifestyle-related diseases. We also excluded women who received hormone or steroid therapy ($n=106$) and those with missing baseline data ($n=918$) other than stress and depression. A total of 881 women were included in the analyses of the association between accelerated muscle loss and lifestyle or psychological factors (Fig. 1). Written informed consent was obtained from all individuals before their health checkups, and the study was approved by the Institutional Review Board of Catholic Medical Center (No. KC18RESI0093).

Lifestyle and psychological variables

Age, menopausal status, education status, lifestyle habits, psychological states, history of diseases, and medication use were collected through a standardized self-administered questionnaire. Lifestyle and psychological factors included alcohol consumption, smoking habits, physical activity, daily caloric intake, degree of stress, and depression.

Alcohol consumption was classified by Alcohol Use Disorders Identification Test scores developed by the World Health Organization: low-risk drinking (0–7 points), intermediate risk drinking (8–15 points), and high-risk drinking (≥16 points).[13] Regarding smoking habits, smoking status was subdivided into current smoking, past smoking, and never smoking. The number of cigarettes per day was further investigated for current smokers, for example, 1–24 cigarettes or ≥25 cigarettes. Physical activity was classified into two groups according to the amount of regular exercise time spent per week, <3 h/week, or ≥3 h/week. Stress was classified by Stress Response Inventory as normal (<78 points) or abnormal (≥78 points).[14] Depression was classified by Beck Depression Inventory as normal (<16 points) or abnormal (≥16 points).[15]

Cardiometabolic diseases

Health statuses were evaluated through self-reported questionnaire and laboratory testing. Blood samples were collected by venipuncture after the participants fasted for at least 8 hours. Hypertension was defined as mean systolic blood pressure (BP) ≥140 mmHg or mean diastolic BP ≥90 mmHg on examination and/or current intake of antihypertensive medication. DM was defined by fasting glucose ≥126 mg/dL, hemoglobin A1c (HbA1c) ≥6.5%, or current use of oral hypoglycemic agents or insulin.[16] Definitions of metabolic syndrome and its components were based on the revised National Cholesterol Education Program Adult Treatment Panel III Criteria.[17]

Anthropometrics and the changes of appendicular skeletal muscle mass

Body weight and height were measured in light clothing with no shoes, and body mass index (BMI) was calculated as weight (kg) divided by height squared (m^2). Waist

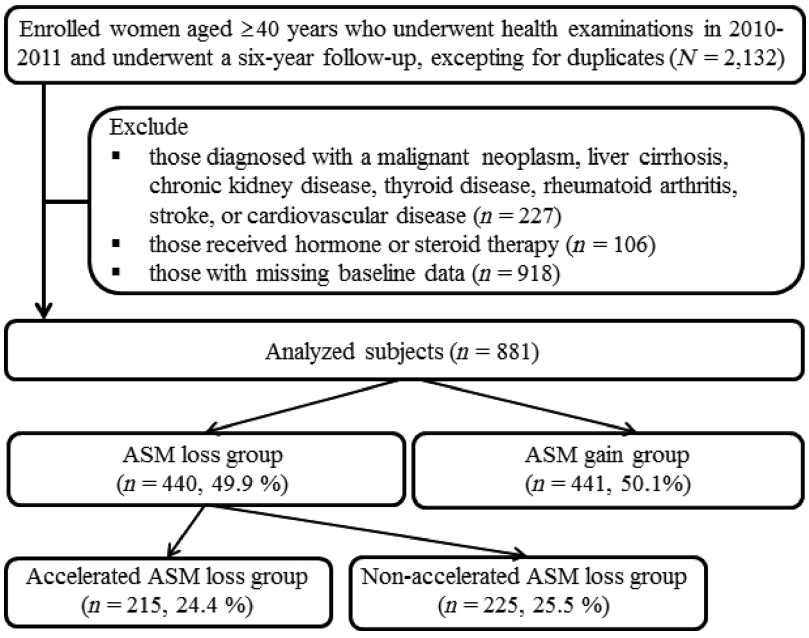

FIG. 1. Flowchart of study participants. The participants were categorized according to the changes (%) of ASM for 6 years. The accelerated loss group with ASM that decreased >3% for 6 years comprised 24.4% ($n=215$) of the total. The gain or non-accelerated loss group comprised 75.6% ($n=666$). ASM, appendicular skeletal muscle mass.

circumference was examined at the point between the upper iliac crest and the lowest rib after normal expiration. Skeletal muscle mass for each limb (kg), body fat mass (kg), and body fat percentage (%) were estimated through bioelectrical impedance analysis (BIA) using a multifrequency BIA device according to the manufacturer's instruction (InBody 720 or InBody 770; Biospace, Inc., Seoul, Korea) after an overnight fast.[18] A tetrapolar eight-point tactile electrode system was used and impedance of an individual's trunk, arms, and legs was separately measured at six different frequencies (1, 5, 50, 250, 500, and 1000 kHz). Total body impedance values were calculated by summing the segmental impedance values, whereas total muscle mass and appendicular skeletal muscle mass (ASM) were estimated according to manufacturer's equation.[19] The ASM was calculated as the sum of lean soft tissue in both arms and legs. Relative change in ASM was calculated as the difference in ASM between baseline and follow-up examination, divided by baseline value and multiplied by 100. We defined accelerated loss of muscle mass as ASM decreases >3% for 6 years.[20,21] This cutoff point was approximated to the lowest quartile of muscle mass change of the participants.

Table 1. Baseline Characteristics of Study Participants According to Age Group

	40s (n = *577*)	*50s* (n = *243*)	*≥60s* (n = *61*)	p
Age (years)	44.59 ± 2.85[a,b]	53.14 ± 2.70[b,c]	64.64 ± 4.60[a,c]	<0.001
Menopausal status	87 (15.1)	136 (56.0)	61 (100.0)	<0.001
Height (cm)	159.62 ± 4.68[a,b]	158.24 ± 5.04[b,c]	155.66 ± 5.20[a,c]	<0.001
Weight (kg)	56.35 ± 7.53	56.16 ± 7.41	57.79 ± 8.37	0.314
BMI (kg/m^2)	22.11 ± 2.75[b]	22.42 ± 2.70[b]	23.83 ± 3.10[a,c]	<0.001
WC (cm)	78.99 ± 7.95[b]	80.31 ± 7.60[b]	83.77 ± 9.24[a,c]	<0.001
ASM (kg)	15.59 ± 1.97	15.38 ± 2.01	15.08 ± 2.27	0.09
Body fat mass (kg)	16.74 ± 4.71[b]	17.25 ± 4.79[b]	19.51 ± 5.19[a,c]	<0.001
Body fat percentage	29.30 ± 4.98[a,b]	30.33 ± 5.45[b,c]	33.29 ± 5.37[a,c]	<0.001
Education				
High school	133 (23.1)	108 (44.4)	35 (57.4)	<0.001
Undergraduate	326 (56.5)	97 (39.9)	22 (36.1)	
Graduate	118 (20.5)	38 (15.6)	4 (6.6)	
Alcohol (AUDIT)				
Low (0–7)	529 (91.7)	225 (92.6)	60 (98.4)	0.47
Intermediate (8–15)	43 (7.5)	17 (7.0)	1 (1.6)	
High (≥16)	5 (0.9)	1 (0.4)	0 (0.0)	
Smoking				
Never	562 (97.4)	234 (96.3)	59 (96.7)	0.53
Past	4 (0.7)	4 (1.7)	0 (0.0)	
Current	11 (1.9)	5 (2.1)	2 (3.3)	
Cigarettes/day				
1–24	9 (81.8)	5 (100.0)	1 (50.0)	0.461
≥25	2 (18.2)	0 (0.0)	1 (50.0)	
Exercise				
<3 h/week	489 (84.8)	181 (74.5)	40 (65.6)	<0.001
≥3 h/week	88 (15.3)	62 (25.5)	21 (34.4)	
Caloric intake (cal/day)				
<1000	103 (17.9)	53 (21.8)	17 (27.9)	0.295
1000 to <2000	459 (79.6)	185 (76.1)	42 (68.9)	
≥2000	15 (2.6)	5 (2.1)	2 (3.3)	
Stress (SRI)[d]				
Normal (<78)	533 (97.8)	225 (97.4)	57 (100.0)	0.728
Abnormal (≥78)	12 (2.2)	6 (2.6)	0 (0.0)	
Depression (BDI)[e]				
Normal (<16)	505 (93.2)	212 (91.8)	46 (82.1)	0.015
Abnormal (≥16)	37 (6.8)	19 (8.2)	10 (17.9)	
Hypertension	53 (9.2)	50 (20.6)	25 (41.0)	<0.001
Diabetes mellitus	14 (2.4)	8 (3.3)	13 (21.3)	<0.001
Metabolic syndrome	59 (10.2)	34 (14.0)	29 (47.5)	<0.001

p Values were based on analysis of variance or independent *t*-test.
[a]Significant with 50s.
[b]Significant with 60s.
[c]Significant with 40s.
[d]A total of 833 subjects were analyzed due to missing data for stress.
[e]A total of 829 subjects were analyzed due to missing data for depression.
ASM, appendicular skeletal muscle mass; AUDIT, Alcohol Use Disorders Identification Test; BDI, Beck Depression Inventory; BMI, body mass index; SRI, Stress Response Inventory; WC, waist circumference.

Statistical analysis

All statistical analyses were performed with SAS software, version 9.4 (SAS Institute, Inc., Cary, NC). Continuous variables are expressed as means with standard deviations, whereas categorical variables are presented as cases per category and frequency of responses. Baseline characteristics of participants based on age group or changes of ASM were compared using analysis of variance followed by Bonferroni *post hoc* test or independent *t*-test for continuous variables and chi-square test or Fisher's exact test for categorical variables. Multiple logistic regression analysis was used to investigate the associations between baseline lifestyle factors, psychological factors, and cardiometabolic diseases (independent variables) and accelerated loss of ASM (dependent variable). Odds ratio (OR) and confidence interval (CI) were assessed considering baseline variables. The percentage changes of ASM for 6 years, expressed as mean with standard error, were compared in statistically significant variables. All tests were two sided and a p-value of <0.05 was taken as statistically significant

Results

Characteristics of study participants

The study was performed in 881 women aged 48.33 ± 6.54 years at baseline. The number of participants by age group was as follows: 577 (65%) in the 40s age group, 243 (28%) in the 50s age group, and 61 (7%) in the 60s and older age group.

Table 2. Clinical Characteristics According to Changes of Appendicular Skeletal Muscle Mass

	Gain/nonaccelerated loss (n = *666*)	*Accelerated loss* (n = *215*)	p
Age (years)	47.61 ± 0.24	50.60 ± 0.48	<0.001
Age group			
40s	461 (79.9)	116 (20.1)	<0.001
50s	171 (70.4)	72 (29.6)	
≥60s	34 (55.7)	27 (44.3)	
Menopausal status	200 (30.0)	84 (39.1)	0.014
Height (cm)	159.01 ± 0.19	158.84 ± 0.35	0.655
Weight (kg)	56.06 ± 0.28	57.46 ± 0.56	0.027
BMI (kg/m^2)	22.17 ± 0.10	22.76 ± 0.21	0.01
ASM (kg)	15.36 ± 0.08	15.92 ± 0.14	<0.001
WC (cm)	79.42 ± 0.30	80.49 ± 0.58	0.09
Body fat mass (kg)	16.92 ± 0.18	17.54 ± 0.37	0.137
Body fat percentage	29.82 ± 0.19	30.00 ± 0.41	0.685
Education			
High school	202 (30.3)	74 (34.4)	0.279
Undergraduate	336 (50.5)	109 (50.7)	
Graduate	128 (19.2)	32 (14.9)	
Alcohol (AUDIT)			
Low (0–7)	616 (92.5)	198 (92.1)	0.833
Intermediate (8–15)	46 (6.9)	15 (7.0)	
High (≥16)	4 (0.6)	2 (0.9)	
Smoking			
Never	653 (98.1)	202 (94.0)	0.007
Past	5 (0.8)	3 (1.4)	
Current	8 (1.2)	10 (4.7)	
Exercise			
<3 h/week	549 (82.4)	161 (74.9)	0.015
≥3 h/week	117 (17.6)	54 (25.1)	
Caloric intake (cal/day)			
<1000	134 (20.1)	39 (18.1)	0.795
1000 to <2000	515 (77.3)	171 (79.5)	
≥2000	17 (2.6)	5 (2.3)	
Stress (SRI)[a]			
Normal (<78)	617 (98.3)	198 (96.6)	0.169
Abnormal (≥78)	11 (1.8)	7 (3.4)	
Depression (BDI)[b]			
Normal (<16)	579 (92.5)	184 (90.6)	0.397
Abnormal (≥16)	47 (7.5)	19 (9.4)	
Hypertension	92 (13.8)	36 (16.7)	0.289
Diabetes mellitus	15 (2.3)	20 (9.3)	<0.001
Metabolic syndrome	76 (11.4)	46 (21.4)	<0.001

[a]A total of 833 subjects were analyzed due to missing data for stress.
[b]A total of 829 subjects were analyzed due to missing data for depression.

The baseline BMI, waist circumference, body fat mass, and body fat percentage had greater mean values in the older age group. The proportion of regular exercise group for ≥3 h/week and patients with hypertension, DM, or metabolic syndrome were higher in the older age group (Table 1).

The ASM decreased for 6 years in 440 (49.9%) women. The ASM decreased >3% for 6 years in 215 (24.4%) women (Fig. 1). The proportions of accelerated muscle loss group were higher in the older age group (20.1%, 29.6%, and 44.3% among the 40s, 50s, and 60s and older age groups, respectively). The accelerated muscle loss group displayed greater mean values of baseline weight, BMI, and ASM than the gain or nonaccelerated muscle loss group. The proportions of postmenopausal women, current smokers, regular exercise group for ≥3 h/week, and patients with DM or metabolic syndrome were higher in the accelerated muscle loss group (Table 2).

Lifestyle, psychological, or cardiometabolic factors related to accelerated loss of ASM

Current smoking women presented higher OR for accelerated loss of ASM than never and past smoking women after adjustment for age and BMI (OR 3.98, 95% CI 1.51–10.48, $p = 0.005$). Women with DM showed significantly higher OR than non-DM women after adjustment for age and BMI (OR 2.97, 95% CI 1.43–6.17, $p = 0.003$). Lifestyle consideration such as caloric intake, alcohol consumption, exercise as well as psychological stress and depression was not significantly associated with accelerated muscle loss after adjustment for age and BMI (Table 3).

Both current smoking and DM were independent predictors for accelerated loss of ASM. Current smokers had higher OR for accelerated loss of ASM than never and past smokers after adjusting for age, BMI, and DM (OR 3.64, 95% CI 1.36–9.74, $p = 0.010$). Women with DM showed higher OR than non-DM women after adjusting for age, BMI, and smoking status (OR 2.78, 95% CI 1.33–5.81, $p = 0.007$). These relationships remained significant after adjustment for age, BMI, exercise, caloric intake, alcohol consumption, and menopausal state (Table 4).

The average percentage changes from baseline of ASM after 6 years were $-2.17\% \pm 1.23\%$ in current smoking women versus $0.20\% \pm 0.18\%$ in never and past smoking women ($p = 0.055$). Women with DM had higher loss percentage changes of ASM than women without DM ($-3.71\% \pm 0.87\%$ vs. $0.30\% \pm 0.18\%$, $p < 0.001$) (Fig. 2).

Discussion

This study found that current smoking is a predictor of accelerated muscle mass loss for 6 years in healthy middle-aged and older women. Women who currently smoke had a 3.53 times higher risk of accelerated ASM loss than nonsmoking women regardless of age, BMI, exercise, caloric intake, alcohol consumption, menopause, and DM.

Previous cross-sectional studies in older adults suggested that cigarette smoking is a risk factor for sarcopenia. Current smokers were more likely to have sarcopenia in community-dwelling men and women aged 55–98 years.[6] Current smokers had lower relative ASM than those who never smoked and showed a dose–effect relationship among the smokers.[22] The effects of smoking cessation on body composition have been reported as being associated with increased muscle mass in women.[23,24] These findings suggest that smoking cessation might help increase muscle mass reversibly.

Although the underlying mechanism is not clear, cigarette smoking could accelerate muscle loss by both depressing muscle protein synthesis and promoting muscle catabolism. The fractional synthesis rate of muscle was lower and presented greater expression of genes, including the muscle growth inhibitor myostatin and E3 ubiquitin ligase muscle atrophy F-box (MAFBx), in skeletal muscle of smokers compared with those in nonsmokers.[25] Structural and metabolic damages including type I fiber atrophy, increased

Table 3. Age and Body Mass Index Adjusted Odds Ratios for Accelerated Loss of Appendicular Skeletal Muscle Mass According to Lifestyle, Psychological Factors, or Cardiometabolic Diseases

	Reference	*OR (95% CI)*	*OR (95% CI)*	p
Caloric intake	1000 to <2000	<1000 cal/day	≥2000 cal/day	
	1	0.80 (0.53–1.20)	0.81 (0.28–2.34)	0.533
Alcohol (AUDIT)	Low (0–7)	Intermediate (8–15)	High (≥16)	
	1	1.15 (0.63–2.13)	2.03 (0.36–11.36)	0.66
Exercise	<3 h/week	≥3 h/week		
	1	1.33 (0.91–1.95)		0.142
Smoking	Never and past	Current		
	1	3.98 (1.51–10.48)		0.005
Stress (SRI)	Normal (<78)	Abnormal (≥78)		
	1	2.47 (0.93–6.56)		0.071
Depression (BDI)	Normal (<16)	Abnormal (≥16)		
	1	1.05 (0.59–1.89)		0.869
Hypertension	No	Yes		
	1	0.87 (0.55–1.37)		0.321
Metabolic syndrome	No	Yes		
	1	1.43 (0.91–2.26)		0.126
Diabetes mellitus	No	Yes		
	1	2.97 (1.43–6.17)		0.003

CI, confidence interval, OR, odds ratio.

Table 4. Smoking and Diabetes Mellitus as Predictive Factors of Accelerated Loss of Appendicular Skeletal Muscle Mass

	OR (95% CI)	p
Model 1		
Current smoking	3.64 (1.36–9.74)	0.010
Diabetes mellitus	2.78 (1.33–5.81)	0.007
Model 2		
Current smoking	3.60 (1.31–9.91)	0.013
Diabetes mellitus	2.92 (1.39–6.14)	0.005
Model 3		
Current smoking	3.53 (1.28–9.74)	0.015
Diabetes mellitus	2.92 (1.39–6.14)	0.005

Model 1: Adjusted for age, BMI, and diabetes mellitus or smoking. Model 2: As model 1, with additional adjustment for exercise, caloric intake, and AUDIT score. Model 3: As model 2, with additional adjustment for menopausal state.

''Never and past smoking'' or ''nondiabetes mellitus'' is a reference group.

glycolytic capacity, and reduced expression of the constitutive nitric oxide synthases were found in the skeletal muscle of smokers.[26]

In contrast to our study results, in a longitudinal study of older men aged 60–85 years, smoking was not associated with acceleration of muscle loss.[27] The causes of this discordance are unclear. The magnitude of the effects of smoking on muscle mass could be different for each gender or age group. Further studies are needed to clarify gender- or age-specific relationships.

We found that accelerated loss of muscle mass in middle-aged and older women is associated with DM. Women with DM had a 2.92 times higher risk of accelerated ASM loss than non-DM women for 6 years regardless of age, BMI, exercise, calorie intake, alcohol consumption, menopausal state, and smoking status.

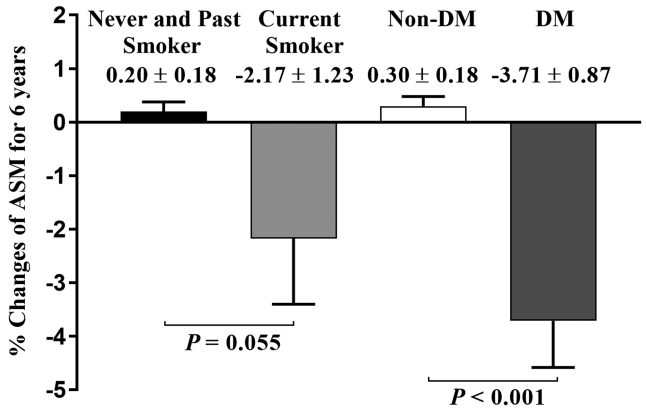

FIG. 2. Comparison of changes (%) of ASM for 6 years according to smoking and DM. The percentage changes (mean ± standard error) from baseline of ASM after 6 years were −2.17% ± 1.23% in current smoking women versus 0.20% ± 0.18% in never and past smoking women ($p = 0.055$). Women with DM had higher loss percentage changes of ASM than women without DM (−3.71% ± 0.87% versus 0.30% ± 0.18%, $p < 0.001$). DM, diabetes mellitus.

In a longitudinal study of 1587 community-living women aged ≥65 years, ASM loss in women with DM was 1.8 times higher than that of those without DM over 4 years.[21] Loss of muscle mass was greater with higher HbA1c and was attenuated by use of medications such as oral hypoglycemic agents or insulin in other longitudinal studies.[28–31] These results suggest that good glycemic control through improving insulin resistance might help prevent muscle mass loss.

Insulin is an anabolic signal and stimulates muscle protein synthesis. Insulin resistance could contribute to acceleration of muscle loss in type 2 DM patients by decreasing stimulation of protein synthesis pathways and increasing activation of protein degradation pathways.[32,33] Overproduction of proinflammatory cytokines such as tumor necrosis factor-α and interleukin-6 could not only influence insulin resistance[34,35] but also promote muscle atrophy through activation of the proinflammatory transcription factor nuclear factor-κ B in type 2 DM individuals.[36] Altered muscle fiber distribution, such as reduction in oxidative type I fibers and an increase in glycolytic type II fibers, as well as mitochondrial dysfunction in skeletal muscle of patients with type 2 DM could also lead to muscle loss.[37–39] Conversely, as skeletal muscle is the main site of glucose consumption, diminished skeletal muscle mass could increase type 2 DM risk.[40]

In this study, physical activity, daily calorie intake, high-risk alcohol drinking, depression, or stress were not significantly associated with accelerated muscle loss. Our study did not account for specific types and intensity of physical activity or nutritional composition, which could contribute to changes in skeletal muscle mass. We recognize other limitations that should be considered when interpreting the results. This study examined 18 smokers that accounted for 2% of the total participants. According to a 2010 report by Korean Statistical Information Service, smoking rate among women 20 years or older was 3.1%.[41] This rate was the lowest among countries belonging to Organisation for Economic Co-operation and Development. Therefore, the relationship between smoking and muscle mass loss derived from this study is limited and do not necessarily generalize to a larger potentially more diverse population. The evaluation of lifestyle or psychological factors was based on a self-reported questionnaire, the answers to which could have been influenced by recall bias. Participants might have under-reported their smoking habit because cigarette smoking is relatively less acceptable for women in Korean culture. Therefore, it could be more accurate to evaluate smoking status with an objective test such as urine cotinine or expiratory carbon monoxide. Independent variables were utilized only from the baseline data, but the lifestyle habit, psychological state, and health state could have changed for 6 years. Lastly, the cohort consisted of women who underwent regular health examinations in a single center, which may limit the ability to generalize our results.

Despite the abovementioned limitations, to our knowledge, this is the first study that analyzes the lifestyle or psychological factors associated with accelerated loss of muscle mass in middle-aged and older women from longitudinal data. Future studies are needed to evaluate the association considering the age of onset of smoking or cumulative smoking amounts among a larger number of smokers. Also, prospective studies are needed to establish casual roles for the multiple factors

associated with loss of not only muscle mass but also muscle strength.

In conclusion, current smoking and DM are predictors for accelerated muscle mass loss in middle-aged and older women. Smokers and DM patients need to monitor muscle mass changes and be open to preventive intervention. Smoking cessation and good glycemic control are required for improving muscle health as well as reducing cardiovascular risk.

Acknowledgment

Statistical consultation was supported by the Department of Biostatistics of the Catholic Research Coordinating Center.

Author Disclosure Statement

No competing financial interests exist.

References

1. Janssen I, Heymsfield SB, Ross R. Low relative skeletal muscle mass (sarcopenia) in older persons is associated with functional impairment and physical disability. J Am Geriatr Soc 2002;50:889–896.
2. Melton LJ 3rd, Khosla S, Crowson CS, O'Connor MK, O'Fallon WM, Riggs BL. Epidemiology of sarcopenia. J Am Geriatr Soc 2000;48:625–630.
3. Aloia JF, McGowan DM, Vaswani AN, Ross P, Cohn SH. Relationship of menopause to skeletal and muscle mass. Am J Clin Nutr 1991;53:1378–1383.
4. Steffl M, Bohannon RW, Sontakova L, Tufano JJ, Shiells K, Holmerova I. Relationship between sarcopenia and physical activity in older people: A systematic review and meta-analysis. Clin Interv Aging 2017;12:835–845.
5. Genaro Pde S, Pinheiro Mde M, Szejnfeld VL, Martini LA. Dietary protein intake in elderly women: Association with muscle and bone mass. Nutr Clin Pract 2015;30:283–289.
6. Castillo EM, Goodman-Gruen D, Kritz-Silverstein D, Morton DJ, Wingard DL, Barrett-Connor E. Sarcopenia in elderly men and women: The Rancho Bernardo study. Am J Prev Med 2003;25:226–231.
7. Kwon YJ, Lim HJ, Lee YJ, et al. Associations between high-risk alcohol consumption and sarcopenia among postmenopausal women. Menopause 2017;24:1022–1027.
8. Wu H, Yu B, Meng G, et al. Both muscle mass and muscle strength are inversely associated with depressive symptoms in an elderly Chinese population. Int J Geriatr Psychiatry 2017;32:769–778.
9. Yoo JI, Ha YC, Lee YK, Hana C, Yoo MJ, Koo KH. High prevalence of sarcopenia among binge drinking elderly women: A nationwide population-based study. BMC Geriatr 2017;17:114.
10. Steffl M, Bohannon RW, Petr M, Kohlikova E, Holmerova I. Alcohol consumption as a risk factor for sarcopenia—A meta-analysis. BMC Geriatr 2016;16:99.
11. Ishii S, Chang C, Tanaka T, et al. The association between sarcopenic obesity and depressive symptoms in older Japanese adults. PLoS One 2016;11:e0162898.
12. Visser M, Deeg DJ, Lips P. Low vitamin D and high parathyroid hormone levels as determinants of loss of muscle strength and muscle mass (sarcopenia): The Longitudinal Aging Study Amsterdam. J Clin Endocrinol Metab 2003;88:5766–5772.
13. Skipsey K, Burleson JA, Kranzler HR. Utility of the AUDIT for identification of hazardous or harmful drinking in drug-dependent patients. Drug Alcohol Depend 1997;45:157–163.
14. Koh KB, Park JK, Kim CH, Cho S. Development of the stress response inventory and its application in clinical practice. Psychosom Med 2001;63:668–678.
15. Beck AT, Ward CH, Mendelson M, Mock J, Erbaugh J. An inventory for measuring depression. Arch Gen Psychiatry 1961;4:561–571.
16. Kerner W, Brückel J. Definition, classification and diagnosis of diabetes mellitus. Exp Clin Endocrinol Diabetes 2014;122:384–386.
17. Grundy SM, Cleeman JI, Daniels SR, et al. Diagnosis and management of the metabolic syndrome: An American Heart Association/National Heart, Lung, and Blood Institute Scientific Statement. Circulation 2005;112:2735–2752.
18. Kim JH, Choi SH, Lim S, et al. Assessment of appendicular skeletal muscle mass by bioimpedance in older community-dwelling Korean adults. Arch Gerontol Geriatr 2014;58:303–307.
19. Ling CH, de Craen AJ, Slagboom PE, et al. Accuracy of direct segmental multi-frequency bioimpedance analysis in the assessment of total body and segmental body composition in middle-aged adult population. Clin Nutr 2011;30:610–615.
20. Kitamura I, Koda M, Otsuka R, Ando F, Shimokata H. Six-year longitudinal changes in body composition of middle-aged and elderly Japanese: Age and sex differences in appendicular skeletal muscle mass. Geriatr Gerontol Int 2014;14:354–361.
21. Lee JS, Auyeung TW, Leung J, Kwok T, Leung PC, Woo J. The effect of diabetes mellitus on age-associated lean mass loss in 3153 older adults. Diabet Med 2010;27:1366–1371.
22. Szulc P, Duboeuf F, Marchand F, Delmas PD. Hormonal and lifestyle determinants of appendicular skeletal muscle mass in men: The MINOS study. Am J Clin Nutr 2004;80:496–503.
23. Rom O, Reznick AZ, Keidar Z, Karkabi K, Aizenbud D. Smoking cessation-related weight gain—Beneficial effects on muscle mass, strength and bone health. Addiction 2015;110:326–335.
24. Kleppinger A, Litt MD, Kenny AM, Oncken CA. Effects of smoking cessation on body composition in postmenopausal women. J Womens Health (Larchmt) 2010;19:1651–1657.
25. Petersen AM, Magkos F, Atherton P, et al. Smoking impairs muscle protein synthesis and increases the expression of myostatin and MAFbx in muscle. Am J Physiol Endocrinol Metab 2007;293:E843–E848.
26. Montes de Oca M, Loeb E, Torres SH, De Sanctis J, Hernández N, Tálamo C. Peripheral muscle alterations in non-COPD smokers. Chest 2008;133:13–18.
27. Renoud A, Ecochard R, Marchand F, Chapurlat R, Szulc P. Predictive parameters of accelerated muscle loss in men-MINOS study. Am J Med 2014;127:554–561.
28. Gougeon R, Styhler K, Morais JA, Jones PJ, Marliss EB. Effects of oral hypoglycemic agents and diet on protein metabolism in type 2 diabetes. Diabetes Care 2000;23:1–8.
29. Gougeon R, Marliss EB, Jones PJ, Pencharz PB, Morais JA. Effect of exogenous insulin on protein metabolism with differing nonprotein energy intakes in Type 2 diabetes mellitus. Int J Obes Relat Metab Disord 1998;22:250–261.

30. Lee CG, Boyko EJ, Barrett-Connor E, et al. Insulin sensitizers may attenuate lean mass loss in older men with diabetes. Diabetes Care 2011;34:2381–2386.
31. Park SW, Goodpaster BH, Lee JS, et al. Excessive loss of skeletal muscle mass in older adults with type 2 diabetes. Diabetes Care 2009;32:1993–1997.
32. Fujita S, Glynn EL, Timmerman KL, Rasmussen BB, Volpi E. Supraphysiological hyperinsulinaemia is necessary to stimulate skeletal muscle protein anabolism in older adults: Evidence of a true age-related insulin resistance of muscle protein metabolism. Diabetologia 2009;52:1889–1898.
33. Wang X, Hu Z, Hu J, Du J, Mitch WE. Insulin resistance accelerates muscle protein degradation: Activation of the ubiquitin-proteasome pathway by defects in muscle cell signaling. Endocrinology 2006;147:4160–4168.
34. Lang CH, Frost RA, Nairn AC, MacLean DA, Vary TC. TNF-alpha impairs heart and skeletal muscle protein synthesis by altering translation initiation. Am J Physiol Endocrinol Metab 2002;282:E336–E347.
35. Kim JH, Bachmann RA, Chen J. Interleukin-6 and insulin resistance. Vitam Horm 2009;80:613–633.
36. Perry BD, Caldow MK, Brennan-Speranza TC, et al. Muscle atrophy in patients with Type 2 Diabetes Mellitus: Roles of inflammatory pathways, physical activity and exercise. Exerc Immunol Rev 2016;22:94–109.
37. Oberbach A, Bossenz Y, Lehmann S, et al. Altered fiber distribution and fiber-specific glycolytic and oxidative enzyme activity in skeletal muscle of patients with type 2 diabetes. Diabetes Care 2006;29:895–900.
38. Stuart CA, McCurry MP, Marino A, et al. Slow-twitch fiber proportion in skeletal muscle correlates with insulin responsiveness. J Clin Endocrinol Metab 2013;98:2027–2036.
39. Yoon Y, Galloway CA, Jhun BS, Yu T. Mitochondrial dynamics in diabetes. Antioxid Redox Signal 2011;14:439–457.
40. Srikanthan P, Karlamangla AS. Relative muscle mass is inversely associated with insulin resistance and prediabetes. Findings from the third National Health and Nutrition Examination Survey. J Clin Endocrinol Metab 2011;96:2898–2903.
41. Korean Statistical Information Service. Available at: http://kosis.kr Accessed January 1, 2019.

Address correspondence to:
Chang-Jin Choi, MD, PhD
Department of Family Medicine
Seoul St. Mary's Hospital
College of Medicine
The Catholic University of Korea
222, Banpo-daero
Seocho-gu
Seoul 06591
Republic of Korea

E-mail: fmchcj@gmail.com