ORIGINAL

Low skeletal muscle mass is associated with insulin resistance, diabetes, and metabolic syndrome in the Korean population: The Korea National Health and Nutrition Examination Survey (KNHANES) 2009-2010

Seong-Su Moon^{1), 2)}

¹⁾Department of Internal Medicine, Dongguk University College of Medicine, Gyeongju, South Korea

²⁾Medical Institute of Dongguk University, Gyeongju, South Korea

Abstract. Sarcopenia is an emerging risk factor for metabolic disorders. No study of the association of sarcopenia with insulin resistance, diabetes, and metabolic syndrome (MS) according to age group and obesity status in the general population has been reported. We investigated these associations in the Korean population. Participants included 4558 males and 5874 females, who were ≥ 20 years of age or older from the fourth and fifth Korea National Health and Nutritional Examination Surveys of the Korean population (2009 and 2010). Age was categorized according to three groups (20-39, 40-59, and ≥ 60 years). Obesity was defined according to body mass index. Sarcopenia was defined as the appendicular skeletal muscle mass (ASM) divided by weight (Wt) (%) of > 2 SD below the sex-specific mean for young adults. Homeostasis model assessment of insulin resistance (HOMA-IR) was calculated. After adjustment for confounding variables, sarcopenia showed a significant association with HOMA-IR in the non-obese group ($P < 0.001$). Sarcopenia was found to be a risk factor for diabetes in the non-obese group ($OR, 2.140$; 95% $CI, 1.549-2.956$; $P < 0.001$). Sarcopenia also showed an association with MS in the non-obese group ($OR, 2.209$; 95% $CI, 1.679-2.906$; $P < 0.001$), but not in the obese-group. However, these results were not relevant to young age group. In conclusion, sarcopenia showed an association with insulin resistance, diabetes, and MS, in the non-obese population. Sarcopenia may be an early predictor for diabetes and MS susceptibility in the non-obese population, particularly in elderly people.

Keywords: Sarcopenia, Insulin resistance, Diabetes, Metabolic syndrome

SARCOPENIA specifically refers to the loss of muscle mass associated with aging [1-3]. Sarcopenia is known to be related to metabolic disorders, including obesity, insulin resistance, and diabetes [4-7]. Obesity is believed to be the most important underlying cause of insulin resistance. By turns, insulin resistance has been suggested as a pathogenetic mechanism of sarcopenia [5, 8].

Inversely, sarcopenia may cause an increase in insulin resistance without obesity. Because skeletal muscle is a primary site for glucose uptake and deposition [9], sarcopenia promotes insulin resistance, leading to

development of metabolic syndrome (MS) and diabetes [4]. In addition, myokines secreted by skeletal muscle have been suggested to prevent insulin resistance by counteracting the metabolic effect of adipokines produced in adipose tissue [10]. Paucity of myokines from sarcopenia could play a role in development of insulin resistance [11]. Improvement of whole-body lean mass in elderly subjects with sarcopenia has been reported to result in increased insulin sensitivity [12].

Insulin resistance is also an underlying mechanism for type 2 diabetes and MS, which is characterized by a constellation of cardiovascular risk factors, including obesity, hypertension, dyslipidemia, and dysglycemia [13]. Therefore, it could be inferred that sarcopenia induces type 2 diabetes or MS through increasing insulin resistance without obesity.

Sarcopenia has so far been regarded as a geriatric and aging disease; therefore, it has been studied mainly

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Correspondence to: Seong-Su Moon, M.D., Ph.D., Assistant Professor, Department of Internal Medicine, Dongguk University College of Medicine, Dongdae-ro 87, Gyeongju, Gyeongbuk Province 780-350, South Korea. E-mail: drmoonss@hanmail.net

among members of the elderly population. Total lean body mass shows a decline after the age of 45, however, onset of the decline in total lean body mass percentage of total body mass can be detected as early as the third decade; therefore, among younger members of the population, there must be some individuals with sarcopenia [14]. However, etiology of sarcopenia could differ among age groups. Muscle type II fibers, which are less sensitive to insulin than type I fibers, have shown greater vulnerability to atrophy with aging than type I fibers [15, 16]. In addition, the relationship of sarcopenia to insulin resistance or pre-diabetes has been suggested to differ according to age and coexistence of obesity [17].

To the best of our knowledge, no study of the association of sarcopenia with insulin resistance, diabetes, and metabolic syndrome according to age group and obesity status in the general population has been reported. In order to elucidate these relationships, we investigated the relationship of sarcopenia with insulin resistance, diabetes, and metabolic syndrome in the Korean population based on the Korea National Health and Nutrition Examination Survey conducted in 2009 and 2010.

Subjects and Methods

Study population

This study was based on data acquired during the third year (2009) of the Korea National Health and Nutrition Examination Survey (KNHANES) IV (2007-2009) and the first year (2010) of KNHANES V (2010-2012). These surveys have been conducted periodically since 1998, using a rolling sampling design involving a complex, stratified, multistage, probability-cluster survey of a representative sample of the non-institutionalized civilian population in order to assess the health and nutritional status of the Korean population [18-20]. The survey, which was conducted by the Korean Ministry of Health and Welfare, consists of the health interview survey, the health examination survey, and the nutrition survey. These surveys were completed by 10,078 (79.2% of the total target population of 12,722) participants and 8473 (77.5% of the total target population of 10,938) participants in 2009 and 2010, respectively. The current cross-sectional study was restricted to participants who were ≥ 20 years of age who completed the health examination survey, including whole body DXA ($n=10432$). During conduct of the survey, blood samples were collected from each participant in the morning following an

overnight fast and were processed, immediately refrigerated, and transported in cold storage to the Central Testing Institute in Seoul, Korea. Analysis of all blood samples was performed within 24 h after transportation. Measurements of the concentration of glucose, high density lipoprotein (HDL) cholesterol, low density lipoprotein (LDL) cholesterol, total cholesterol, and triglycerides were performed using a Hitachi automatic analyzer 7600 (Tokyo, Japan). Immunoradiometric assay using a 1470 WIZARD gamma-counter (PerkinElmer, Finland) was used for measurement of insulin. Homeostasis model assessment of insulin resistance (HOMA-IR) was calculated using the following formula: $\text{HOMA-IR} = \text{fasting plasma glucose (mg/dL)} \times \text{fasting insulin (}\mu\text{IU/mL)} / 405$ [21]. Obesity was defined as a body mass index $\geq 27.5 \text{ kg/m}^2$, the cutoff associated with increased mortality rates in Asians, including Koreans [22, 23]. Waist circumference was measured at the mid-point between the lower margin of the last palpable rib and the top of the iliac crest at the end of a normal expiration with the arms relaxed at the sides. According to the National Cholesterol Education Program Adult Treatment Panel III criteria [24] and the Korean abdominal obesity criteria for waist circumference [25], subjects were classified as having MS if they had any three of the following five characteristics: central obesity (waist circumference $\geq 90 \text{ cm}$ in men and $\geq 85 \text{ cm}$ in women), hypertriglyceridemia (triglycerides $\geq 150 \text{ mg/dL}$ or triglyceride-lowering medication), HDL cholesterol ($<40 \text{ mg/dL}$ in males or $<50 \text{ mg/dL}$ in females), hypertension ($\geq 130 \text{ mmHg}$ systolic or $\geq 85 \text{ mmHg}$ diastolic pressure, or use of anti-hypertensive medication), dysglycemia (fasting plasma glucose $\geq 100 \text{ mg/dL}$ or use of anti-hyperglycemic medication, or previously diagnosed type 2 diabetes). The study was approved by the Institutional Review Board of the Korea Center for Disease Control and prevention (2012-01EXP-01-2C).

Definition of sarcopenia

Dualenergy X-ray absorptiometry (DXA) (Discovery-W; Hologic, Waltham, MA, USA) was used for measurement of appendicular skeletal muscle mass (ASM) [26]. Sarcopenia was defined as ASM divided by body weight (ASM/Wt) (%) more than two standard deviations (SD) below mean value of sex-specific normal young people [27, 28]. The definition was modified from the studies of Janssen *et al.* [29]. The sex-specific young reference group included 3343 healthy adults aged 20-40 yr (1449 men, 1894 women). As cutoff points,

the two SDs of sex-specific normal young people were 26.98% in men and 21.14% in women, respectively. All participants in this survey signed an informed consent form.

Statistical analyses

Levels of HOMA-IR were log-transformed because their distributions were positively skewed. Geometric means with standard errors of HOMA-IR were calculated using analysis of covariance (ANCOVA) after adjustment for age, sex, region, smoking, alcohol consumption, regular exercise, and family income. Age was categorized according to three groups (20-39 years, 40-59 years, and ≥ 60 years). Logistic regression models were used for calculation of multivariate-adjusted odds ratios (ORs). Adjusted variables included age, sex, region, smoking, alcohol consumption, regular exercise, and family income. Subgroup analyses stratified according to age, sex, region, smoking, alcohol drinking, regular exercise, and family income were performed. Region was categorized as rural and urban. Among the 16 administrative districts where this survey was conducted, Seoul, Gyeonggi, and six other metropolitan cities (Busan, Daegu, Incheon, Gwangju, Daejeon, and Ulsan) were grouped as urban areas. The remaining regions were grouped as rural areas. Smoking status was divided into three categories: never, former, and current smoker. Alcohol consumption was indicated as 'yes' for participants who consumed at least two units of alcohol every week over the last year. Regular exercise was indicated as 'yes' when the participant performed moderate or strenuous exercise on a regular basis, regardless of indoor or outdoor exercise (for more than 30 min at a time and more than five times per week in the case of moderate exercise, such as swimming slowly, tennis doubles, volleyball, badminton, table tennis, and carrying light objects; for more than 20 min at a time in the case of strenuous exercise, such as running, climbing, cycling fast, swimming fast, football, basketball, jump rope, squash, tennis singles, and carrying heavy objects or when subject walked for more than 30 min at a time and more than five times per week. Family income was categorized into four groups according to quartile. All tests were two-sided, and $P < 0.05$ was considered statistically significant. Statistical Package for Social Science 15.0 software (SPSS, Chicago, IL, USA) was used in performance of all analyses.

Results

Insulin resistance according to the category of sarcopenia and obesity

The baseline characteristics according to sarcopenic status are shown in Table 1. Among sarcopenic participants, compared with nonsarcopenic participants, higher HOMA-IR was observed only in the non-obese group ($P < 0.001$). While sarcopenic subjects had a higher HOMA-IR than those without sarcopenia in 40-59 years and ≥ 60 years age group of the non-obese group ($P = 0.002$ and < 0.001 , respectively), after adjustment for age, sex, region, smoking, alcohol consumption, exercise, and family income, the 20-39 years age group showed the tendency without significance (2.20 ± 1.07 vs. 1.98 ± 1.01 , among sarcopenic and nonsarcopenic subjects, respectively, $P = 0.144$). Subjects in the obese group did not show that tendency ($P = 0.238$) (Table 2).

Prevalence of diabetes according to the category of sarcopenia and obesity

Prevalence of diabetes was higher among sarcopenic participants than among nonsarcopenic participants only in the non-obese group (23.1% vs. 7.8%, $P < 0.001$). Sarcopenic subjects had a higher prevalence of diabetes than those without sarcopenia only in ≥ 60 years age group of the non-obese group ($OR = 2.448$; 95%CI, 1.695-3.538; $P < 0.001$). No significant association was observed between diabetes and sarcopenia in other age groups (Table 3).

Prevalence of MS according to the category of sarcopenia and obesity after stratification

Prevalence of MS was higher among sarcopenic subjects, compared to nonsarcopenic subjects in the non-obese group ($OR = 2.209$; 95%CI, 1.679-2.906; $P < 0.001$), however, that relationship was not observed in the obese group. After stratification according to age, sex, region, smoking, alcohol drinking, regular exercise, and family income, MS was found to be more prevalent among nonobese and sarcopenic participants in every subgroup except the 20-39 years age group and the 75th-100th family income group, compared with nonobese and nonsarcopenic subjects after adjustment for confounding variables (Table 4).

Association of sarcopenia with individual components of MS in non-obese participants

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Table 1 Baseline characteristics of participants according to sarcopenic status^a

	Non-Sarcopenic	sarcopenic	<i>P</i>
No. of total participants	9988	444	
Age, years	48.3 ± 15.5	59.8 ± 14.3	<0.001
Men, %	4392 (44.0)	166 (37.4)	0.006
Body height, cm	162.6 ± 9.1	157.4 ± 8.8	<0.001
Body weight, kg	62.4 ± 11.2	67.6 ± 12.2	<0.001
BMI, kg/cm ²	23.5 ± 3.2	27.2 ± 3.7	<0.001
WC, cm	80.4 ± 9.6	91.1 ± 10.0	<0.001
FPG, mg/dL	97.3 ± 22.1	106.5 ± 26.5	<0.001
Insulin μ IU/mL	10.0 ± 5.2	12.8 ± 8.1	<0.001
HOMA-IR ^b	2.46 ± 1.87	3.42 ± 2.46	<0.001
T-chol, mg/dL	187.5 ± 35.8	199.5 ± 40.7	<0.001
Triglyceride, mg/dL	134.6 ± 114.9	154.4 ± 98.2	<0.001
HDL-C, mg/dL	52.5 ± 12.7	50.0 ± 12.4	<0.001
LDL-C, mg/dL	111.9 ± 30.9	118.5 ± 35.4	0.018
Metabolic syndrome	2333 (23.4)	254 (57.2)	<0.001
ASM, kg	17.8 ± 4.7	15.1 ± 4.1	<0.001
ASM/Wt, %	28.4 ± 4.1	22.2 ± 3.0	<0.001
Regions ^c			0.691
Rural area	2450 (24.5)	105 (23.6)	
Urban area	7538 (75.5)	339 (76.4)	
Smoking status ^d			0.001
Never	5792 (58.0)	272 (61.3)	
Former	1060 (10.6)	65 (14.6)	
Current	3136 (31.4)	107 (24.1)	
Alcohol consumption ^e			0.178
Yes	2186 (21.9)	85 (19.1)	
No	7802 (78.1)	359 (80.9)	
Regular exercise ^f			0.052
Yes	5316 (53.2)	215 (48.4)	
No	4672 (46.8)	229 (51.6)	
Family income ^g			<0.001
< 25th	1808 (18.3)	139 (31.8)	
25th to 50th	2411 (24.5)	118 (27.0)	
50th to 75th	2824 (28.6)	93 (21.3)	
75th to 100th	2815 (28.6)	87 (19.9)	

BMI, body mass index; WC, waist circumference; FPG, fasting plasma glucose; HOMA-IR, homeostasis model assessment of insulin resistance; T-chol, total cholesterol; HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol; ASM, appendicular skeletal muscle mass; ASM/Wt, appendicular skeletal muscle mass/body weight.

^aValues are presented as number(%) or mean (SD). ^bGeometric mean ± SE. ^cRegion was categorized as urban (Seoul, Gyeonggi, Busan, Daegu, Incheon, Gwangju, Daejeon, and Ulsan) and rural (eight other administrative districts) area. ^dSmoking status was divided into three categories: never, former, and current smoker. ^eAlcohol consumption was indicated as 'yes' for participants who consumed at least two units of alcohol every week over the last year.

^fRegular exercise was indicated as 'yes' when the participant performed moderate or strenuous exercise on a regular basis (for more than 30 min at a time and more than five times per week in the case of moderate exercise; for more than 20 min at a time in the case of strenuous exercise) or when the subject walked for more than 30 min at a time and more than five times per week.

^gFamily income was categorized into four groups according to quartile.

Table 2 Adjusted geometric means and SEs of HOMA-IR according to category of sarcopenia and obesity

	Non-obese		<i>P</i>	Obese		<i>P</i>
	Non-sarcopenic	Sarcopenic		Non-sarcopenic	Sarcopenic	
Total participants						
No of participants	8164	192		850	134	
HOMA-IR ^a	2.00±1.00	2.32±1.03	<0.001 [†]	3.02±1.02	3.15±1.04	0.309
Age group						
20-39 year						
No of participants	2942	28		298	19	
HOMA-IR ^a	1.98±1.01	2.20±1.07	0.144	3.10±1.02	3.14±1.09	0.892
40-59 year						
No of participants	3256	70		365	53	
HOMA-IR ^a	1.97±1.01	2.28±1.05	0.002 [†]	2.95±1.07	3.21±1.07	0.219
≥60 years						
No of participants	1966	94		187	62	
HOMA-IR ^a	2.10±1.01	2.42±1.04	<0.001 [†]	3.03±1.03	3.03±1.06	0.981

Data are presented as adjusted geometric mean ± SE.

^a Adjusted for age, sex, region, smoking, alcohol consumption, exercise, and family income. [†] *P*<0.01.**Table 3** Adjusted ORs and 95% CIs of prevalence of diabetes according to category of sarcopenia and obesity

	Non-obese		<i>P</i>	Obese		<i>P</i>
	Non-sarcopenic	Sarcopenic		Non-sarcopenic	Sarcopenic	
Total participants						
Case/n	704/8972	59/255		154/1016	53/189	
Prevalence(%)	7.8	23.1		15.2	28.0	
Adjusted OR (95% CI)	1	2.140 (1.549-2.956)	<0.001 [†]	1	1.346 (0.908-1.995)	0.139
Age group						
20-39 years						
Case/n	24/3001	1/29		14/303	4/23	
Prevalence(%)	0.8	3.4		4.4	17.4	
Adjusted OR (95% CI)	1	3.700 (0.468-29.246)	0.215	1	3.832 (0.996-14.739)	0.051
40-59 years						
Case/n	263/3560	10/80		66/435	12/66	
Prevalence(%)	7.4	12.5		15.2	18.2	
Adjusted OR (95% CI)	1	1.621 (0.809-3.248)	0.173	1	1.223 (0.604-2.479)	0.576
≥60 years						
Case/n	417/2411	48/146		74/264	37/100	
Prevalence(%)	17.3	32.9		28.0	37.0	
Adjusted OR (95% CI)	1	2.448 (1.695-3.538)	<0.001 [†]		1.267 (0.762-2.107)	0.362

Adjusted for age, sex, region, smoking, alcohol consumption, exercise, and family income. [†] *P*<0.01.

component of MS is involved in the significant relationship between sarcopenia and MS in the non-obese group, hypertension, elevated TG, and central obesity were found to have a significant relationship with sarcopenia. In ≥60 years age subgroup of the non-obese group, prevalence of hypertension, elevated TG, dysglycemia (FPG ≥ 100 mg/dl or on diabetes treatment), and central obesity was higher among sarcopenic subjects than among those without sarcopenia. In contrast, subjects in the obese group did not show that tendency (Table 5).

Insulin resistance and prevalence of diabetes and MS according to the category of sarcopenia and obesity in the elderly

To show the data of the elderly, age was categorized according to three groups (60-69, 70-79, and ≥ 80 years). While sarcopenic subjects had higher HOMA-IR and prevalence of diabetes and MS than those without sarcopenia in the non-obese group, after adjustment for age, sex, region, smoking, alcohol consumption, exercise, and family income, subjects in the obese group did not show that tendency. Among sarcopenic partici-

Table 4 Adjusted ORs and 95% CIs of prevalence of MS according to category of sarcopenia and obesity after stratification by age, sex, region, smoking, alcohol consumption, exercise, or family income.

	Non-obese		<i>P</i>	Obese		<i>P</i>
	Non-sarcopenic	Sarcopenic		Non-sarcopenic	Sarcopenic	
Total participants	1	2.209 (1.679-2.906)	<0.001 [†]	1	0.965 (0.664-1.403)	0.853
Age						
20-39 years	1	2.226 (0.633-7.825)	0.212	1	1.055 (0.435-2.562)	0.905
40-59 years	1	1.931 (1.183-3.152)	0.008 [†]	1	0.983 (0.555-1.743)	0.954
≥60 years	1	2.641 (1.859-3.753)	<0.001 [†]	1	0.918 (0.495-1.701)	0.786
Sex						
Men	1	2.763 (1.809-4.220)	<0.001 [†]	1	1.564 (0.793-3.038)	0.197
Women	1	1.965 (1.358-2.845)	<0.001 [†]	1	0.771 (0.486-1.223)	0.269
Region						
Rural area	1	2.770 (1.620-4.737)	<0.001 [†]	1	0.665 (0.305-1.450)	0.305
Urban area	1	2.010 (1.458-2.772)	<0.001 [†]	1	1.064 (0.693-1.634)	0.777
Smoking						
Never	1	2.066 (1.447-2.950)	<0.001 [†]	1	0.796 (0.500-1.267)	0.335
Former	1	3.106 (1.599-6.035)	0.001 [†]	1	0.593 (0.173-2.032)	0.405
Current	1	2.030 (1.125-3.664)	0.019 [‡]	1	2.092 (0.912-4.798)	0.082
Alcohol consumption						
No	1	2.303 (1.686-3.146)	<0.001 [†]	1	0.923 (0.607-1.404)	0.709
Yes	1	1.933 (1.075-3.477)	0.028 [‡]	1	1.089 (0.458-2.591)	0.848
Regular exercise						
Yes	1	2.508 (1.695-3.711)	<0.001 [†]	1	0.960 (0.572-1.610)	0.877
No	1	1.964 (1.336-2.888)	0.001 [†]	1	0.986 (0.572-1.720)	0.960
Family income						
<25 th	1	3.088 (1.919-4.971)	<0.001 [†]	1	1.192 (0.536-2.650)	0.666
25th to <50th	1	1.785 (1.038-3.068)	0.036 [‡]	1	0.833 (0.420-1.651)	0.601
50th to <75th	1	2.340 (1.299-4.215)	0.005 [†]	1	1.484 (0.626-3.518)	0.370
75th to 100th	1	1.504 (0.753-3.001)	0.248	1	0.780 (0.363-1.674)	0.523

Adjusted for age, sex, region, smoking, alcohol consumption, exercise, and family income level. [†]*P*<0.01. [‡]*P*<0.05.

pants, compared with nonsarcopenic participants, higher HOMA-IR was observed in the 70-79 years age group (*P*=0.005), higher prevalence of diabetes was shown in the 60-69 and 70-79 years age groups (*P*=0.001 and *P*<0.001, respectively), and MS was more prevalent in the three age groups (*P*=0.002, *P*<0.001, and *P*=0.041, respectively) (Supplemental Table 1).

Discussion

Thus far, obesity has been regarded as the most crucial underlying cause of insulin resistance leading to type 2 diabetes and MS. Of note, results of this study demonstrated that sarcopenia may be an early predictor for insulin resistance, diabetes, and MS, even without coexistence of obesity. Sarcopenia showed a significant association with insulin resistance in the non-obese group, but not in the obese group. Sarcopenia was also found to be a risk factor for MS in the non-obese group, but not in the obese-group. In addition, only in the non-obese group, diabetes was more prev-

alent among sarcopenic subjects than among those without sarcopenia. All of these findings were applicable particularly to ≥60 years age subgroup. Taken together, our findings indicated that, regarding metabolic disorders, including insulin resistance, diabetes, and MS, non-obese elderly people in the Korean population, compared with obese elderly people, are more affected by sarcopenia. Because people in Asia tend to develop type 2 diabetes with less degree of obesity [30], these facts are worthy of notice.

Although several studies have suggested that insulin resistance and MS are increased synergistically by sarcopenia and obesity [17, 27, 31, 32], the interaction of sarcopenia and obesity in dysglycemia and MS has been inconsistent among previously published studies. One study reported an association of sarcopenia with dysglycemia in obese individuals but not in non-obese individuals [17]. On the contrary, in obese postmenopausal women, sarcopenia showed an association with a better lipid profile and lower CVD predisposing factors [33]. In the New Mexico Aging Process Study, the

Table 5 Adjusted ORs and 95% CI of individual MS components by sarcopenia

	Non-obese	<i>P</i>	Obese	<i>P</i>
Total participants				
Hypertension ^a	1.721 (1.279-2.315)	<0.001 [†]	1.332 (0.889-1.995)	0.165
Low HDL ^b	1.253 (0.957-1.640)	0.101	0.746 (0.529-1.051)	0.094
Elevated TG ^c	1.550 (1.189-2.022)	0.001 [†]	0.771 (0.552-1.076)	0.126
Dysglycemia ^d	1.270 (0.963-1.675)	0.090	1.304 (0.929-1.829)	0.124
Central obesity ^e	3.442 (2.644-4.481)	<0.001 [†]	2.283 (1.077-4.841)	0.031 [‡]
20-39 years				
Hypertension ^a	1.409 (0.399-4.971)	0.594	2.087 (0.832-5.240)	0.117
Low HDL ^b	1.016 (0.425-2.427)	0.971	0.926 (0.361-2.372)	0.872
Elevated TG ^c	1.601 (0.613-4.185)	0.337	0.842 (0.327-2.166)	0.721
Dysglycemia ^d	1.976 (0.723-5.403)	0.185	1.990 (0.808-4.903)	0.135
Central obesity ^e	5.788 (2.541-13.187)	<0.001 [†]	1.061 (0.296-3.806)	0.928
40-59 years				
Hypertension ^a	1.657 (1.041-2.637)	0.033 [‡]	1.029 (0.578-1.831)	0.922
Low HDL ^b	1.114 (0.686-1.809)	0.663	0.644 (0.357-1.160)	0.143
Elevated TG ^c	1.557 (0.977-2.479)	0.062	0.746 (0.430-1.295)	0.298
Dysglycemia ^d	1.034 (0.625-1.709)	0.897	1.667 (0.961-2.894)	0.069
Central obesity ^e	2.886 (1.812-4.596)	<0.001 [†]	2.144 (0.810-5.672)	0.125
≥60 years				
Hypertension ^a	2.003 (1.313-3.055)	0.001 [†]	1.415 (0.677-2.958)	0.356
Low HDL ^b	1.428 (0.998-2.043)	0.051	0.787 (0.480-1.291)	0.343
Elevated TG ^c	1.706 (1.210-2.404)	0.002 [†]	0.778 (0.482-1.254)	0.303
Dysglycemia ^d	1.451 (1.028-2.078)	0.034 [‡]	1.036 (0.634-1.694)	0.887
Central obesity ^e	3.862 (2.713-5.496)	<0.001 [†]	6.152 (0.000-12.757)	0.996

MS, metabolic syndrome

Adjusted for age, sex, region, smoking, alcohol consumption, exercise, and family income.

^aHypertension, systolic ≥ 130 mmHg and/or diastolic ≥ 85 mmHg or on treatment. ^bLow HDL, < 40 mg/dl for men or < 50 mg/dl for women. ^cElevated TG, ≤ 150 mg/dL or on treatment. ^dDysglycemia, FPG ≥ 100 mg/dl or on treatment. ^eCentral obesity, waist circumference ≥ 90 cm in men and ≥ 85 cm in women. [†] $P < 0.01$. [‡] $P < 0.05$.

prevalence of MS was higher in the non-sarcopenic obese group than the sarcopenic obese group [34]. The current study showed an additive effect of sarcopenia and obesity on insulin resistance and diabetes, although the effect of sarcopenia on HOMA-IR, MS, and diabetes was insignificant in the obese group. The sarcopenic and obese group showed higher HOMA-IR than either the sarcopenic group or the obese group alone (3.15 ± 1.04 , 2.32 ± 1.03 , and 3.02 ± 1.02 , respectively), the prevalence of diabetes in the sarcopenic and obese group was higher than either in the sarcopenic or in the obese group alone (28.0, 23.1, and 15.2 %, respectively). The discrepancy between studies may be, at least in part, due to study design and population characteristics.

Results of the current study showed that non-obese individuals were more affected by sarcopenia with regard to insulin resistance, and sarcopenia showed a significant association with MS in the non-obese group, but not in the obese group. Diabetes was found

to be more prevalent among sarcopenic subjects only in the non-obese group. Obesity is known to be the most important underlying cause of insulin resistance, which is an underlying mechanism for type 2 diabetes and MS. Although sarcopenia may also result in insulin resistance, the effect of sarcopenia is weaker compared with obesity. In the previous studies, obesity without sarcopenia has shown the higher HOMA-IR than sarcopenia without obesity [17, 27]. In obese subjects, there is greater lipid content within skeletal muscle [35], which may already diminish insulin sensitivity in muscle [36]. Therefore, in that case, sarcopenia may not be a critical determinant for insulin resistance or MS. Therefore we assumed that the pathogenetic mechanism of sarcopenia may differ between in obese individuals and in those without obesity.

No study investigating the association of sarcopenia with insulin resistance or MS specifically in the young age group has been reported, although some studies included subjects who were 20 years of age or older

in their study population [17, 37]. One study reported a stronger association of sarcopenia with dysglycemia in individuals younger than 60 years of age, compared with those older than 60 years [17], which is somewhat incompatible with the result of the current study, which did not show a significant association between dysglycemia among metabolic syndrome components with sarcopenia. The age difference in the metabolic effect of sarcopenia is probably due to the result of differences in the etiology of sarcopenia in the young age group, compared with the elderly group. Elderly sarcopenic individuals have more decreased type II muscle fibers, which are less sensitive to insulin action [38, 39], while sarcopenia in younger individuals is caused primarily by reduced accumulation of skeletal muscle mass not by muscle atrophy. Thus, sarcopenia of older individuals could mean increased insulin sensitivity and improved glucose disposal by insulin.

However, in the current study, we did not observe improved insulin resistance in older participants. In contrast, insulin resistance and prevalence of diabetes and MS were higher among sarcopenic individuals than among non-sarcopenic individuals in the elderly group (≥ 60 years). In this study, sarcopenia of older participants, even among non-obese subjects, did not mean increased insulin sensitivity. We did not examine the muscle type of individual participants; therefore, we cannot explain the definite reasons for the discrepancy. We assume that, with regard to metabolic derangements, sarcopenia has the same harmful meaning to elderly subjects as young people. In the current study, the 20-39 years age group showed no significant relationships of sarcopenia with insulin resistance, diabetes, and MS after an adjustment for confounding factors. The prevalence of sarcopenia in the non-obese young age group was very low as 0.009% in this study, which is inferred as a reason for the insignificant result. The 40-59 years age group showed significant relationships of sarcopenia with insulin resistance and MS but not with diabetes. It seems that sarcopenia becomes more prevalent and more affects metabolic disorders according to aging. However, it remains to be clarified in the future study.

We adopted ASM divided by body weight (%) as a skeletal muscle mass index to define sarcopenia, since that ASM/Wt has been widely adopted in many studies to define sarcopenia and that ASM/Wt was suggested to be the more appropriate index for sarcopenic obesity in the Korean population, because ASM/height(m)², which was positively correlated with BMI, visceral fat

area, and the HOMA-IR, could underestimate sarcopenia in overweight or obese subjects [27].

This study has several limitations. First, we could not differentiate type 1 from type 2 diabetes from the KNHANES dataset. Although we selected participants who were older than 20 years of age and prevalence of type 1 diabetes is relatively low in Korea, we could not exclude the possibility that participants with type 1 diabetes were included in this study. Therefore, there could be selection bias. Second, although we restricted the study population to participants without diagnosed diabetes in order to exclude the effect of diabetes on sarcopenia in certain analyses, the cross-sectional study design prevented us from affirming the causal relationship between sarcopenia and insulin resistance, diabetes, and MS. Their causal relationship should be verified in future longitudinal studies. Finally, it was recently suggested that the definition of sarcopenia be restricted to the presence of low muscle strength or poor physical performance in addition to reduced muscle, therefore, because we did not measure muscle strength for determination of sarcopenia; this might also have been a limitation.

Despite these limitations, because the population of the current study was representative of the general Korean population, this study has powerful strength. In conclusion, results of this study showed a greater association of sarcopenia with increased insulin resistance and prevalence of diabetes and MS among non-obese participants. Of particular interest, in non-obese elderly people, sarcopenia was found to be a significant correlate of those metabolic disorders. Therefore, sarcopenia may be a significant predictor of type 2 diabetes and MS susceptibility in non-obese elderly population.

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Conflicts of Interest

There are no conflicts of interest.

Disclosure Summary

The author has nothing to declare.

Supplemental Table 1 Adjusted geometric means and SEs of HOMA-IR, adjusted ORs and 95% CIs of prevalence of diabetes and MS according to category of sarcopenia and obesity in elderly subjects

	Non-obese		<i>P</i>	Obese		<i>P</i>
	Non-sarcopenic	Sarcopenic		Non-sarcopenic	Sarcopenic	
HOMA-IR ^a						
60-69 year	2.07±1.01	2.26±1.06	0.170	3.00±1.04	3.13±1.08	0.589
70-79 year	2.07±1.02	2.49±1.06	0.005 [†]	3.13±1.07	2.88±1.10	0.486
≥80 years	1.97±1.04	2.45±1.13	0.105	NA	NA	NA
Diabetes						
60-69 years						
Case/n	239/1419	21/64		41/166	12/45	
Prevalence(%)	16.8	32.8		24.7	26.7	
Adjusted <i>OR</i> (95% CI) ^a	1	2.528 (1.454~4.398)	0.001 [†]	1	0.908 (0.403~2.043)	0.815
70-79 years						
Case/n	155/852	24/65		30/91	23/50	
Prevalence(%)	18.2	36.9		33.0	46.0	
Adjusted <i>OR</i> (95% CI) ^a	1	2.852 (1.641~4.957)	<0.001 [†]	1	1.817 (0.854~3.864)	0.121
≥80 years						
Case/n	23/140	3/17		3/7	2/5	
Prevalence(%)	16.4	5.6		42.9	40.0	
Adjusted <i>OR</i> (95% CI) ^a	1	1.188 (0.300~4.709)	0.806	1	NA	NA
MS						
60-69 years						
Case/n	516/1419	38/64		130/166	23/45	
Prevalence(%)	36.4	59.4		78.3	75.6	
Adjusted <i>OR</i> (95% CI) ^a	1	2.296 (1.362~3.872)	0.002 [†]	1	0.867 (0.384~1.957)	0.730
70-79 years						
Case/n	320/852	42/65		77/91	43/50	
Prevalence(%)	37.6	64.6		84.6	86.0	
Adjusted <i>OR</i> (95% CI) ^a	1	3.041 (1.762~5.246)	<0.001 [†]	1	1.035 (0.377~2.841)	0.948
≥80 years						
Case/n	46/140	9/17		7/7	5/5	
Prevalence(%)	32.9	52.9		100	100	
Adjusted <i>OR</i> (95% CI) ^a	1	3.183 (1.046~9.684)	0.041 [†]	1	NA	NA

HOMA-IR is presented as adjusted geometric mean ± SE.

^a Adjusted for age, sex, region, smoking, alcohol consumption, exercise, and family income. [†] *P*<0.05. NA, non applicable.

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