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Keywords

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ABSTRACT

Aims/Introduction: We aimed to examine the prevalence of sarcopenia and frailty in Korean older adults with diabetes compared with individuals without diabetes.

Materials and Methods: We analyzed the data of 2,403 participants aged 70–84 years enrolled in the Korean Frailty and Aging Cohort Study. Sarcopenia was defined using the Asian Working Group for Sarcopenia and the Foundation for the National Institutes of Health. Frailty was assessed by the Cardiovascular Health Study frailty phenotype criteria.

Results: The mean age of the participants was 76.0 ± 3.9 years, and 47.2% were men. The prevalence of diabetes was 30.2% in men and 25.8% in women. Adults with diabetes showed a lower muscle mass index (appendicular skeletal muscle mass/body mass index) and handgrip strength in both sexes, but only the women showed decreased physical performance. Women with diabetes presented a higher prevalence of sarcopenia diagnosed by the Foundation for the National Institutes of Health criteria, and frailty compared with participants without diabetes (sarcopenia 14.7% vs 8.5%, $P = 0.001$; frailty 9.5% vs 4.9%, $P = 0.003$). Men in the high and middle tertiles for homeostatic model assessment of insulin resistance presented a significantly higher prevalence of sarcopenia, compared with men in the low tertile homeostatic model assessment of insulin resistance (high tertile 16.6%, middle tertile 13.3%, low tertile 8.6%).

Conclusions: In older adults with diabetes, muscle mass index and muscle strength were lower than in those without diabetes. However, the prevalence of sarcopenia and frailty was higher and physical performance was lower only in women with diabetes.

INTRODUCTION

The worldwide population of older people (aged ≥ 65 years) is increasing rapidly. Korea became an “aged society” (older people $\geq 14\%$ of the total Korean population) in 2017; it had taken just 17 years to make the transition from an “aging society” (older people $\geq 7\%$)¹. The speed of aging in Korea is more rapid than that of Japan, which had taken 24 years to become an

“aged” from an “aging” society and had been known as the world’s most rapidly aging nation². Increasing numbers of aged persons in a population leads to huge social and health burdens, including increased medical expenditures. Combined with limited healthcare resources, this issue poses several problems for societies.

Sarcopenia is generally defined as the progressive decrease of muscle mass and function associated with the aging process^{3,4}. Sarcopenia has been reported to relate to poor quality of life,

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and increased morbidity and mortality^{5–7}. In addition to aging itself, other risk factors have been proposed for sarcopenia, including malnutrition, polypharmacy, physical inactivity, chronic metabolic diseases and cancer⁸.

Diabetes is one of the most common metabolic diseases in older people. According to the Diabetes Fact Sheet published in Korea (2016), the prevalence of diabetes in adults aged ≥ 30 years was 13.7%, and that in older people (aged ≥ 65 years) was $>30\%$ ⁹. The association between sarcopenia and diabetes has not yet been fully elucidated. Several studies have advocated that individuals with diabetes show marked decreases in muscle mass^{10,11} and strength^{12,13}. It was also shown that insulin resistance has a negative effect on muscle strength¹⁴ and gait speed¹⁵. In contrast, several studies pointed out that there is no significant relationship between muscle strength and diabetes^{16,17}.

The prevalence of sarcopenia has been estimated to vary from 8% to 40% of the population, according to the definitions of sarcopenia and the racial characteristics of the study group¹⁸. There have been several studies in regard to the prevalence of sarcopenia in individuals with diabetes in Korea^{10,19,20}, but these were not representative of the nationwide community-dwelling population. Considering the clinical significance of sarcopenia in the older adult population, assessing the prevalence and determining potential risk factors in patients with diabetes would be beneficial in the management and prevention of functional declines.

Here, we assessed the prevalence of sarcopenia and frailty in Korean adults with diabetes compared with individuals without diabetes. We also evaluated the associations between insulin resistance or hyperglycemia, and sarcopenia.

METHODS

Participants

This study was carried out as a part of the Korean Frailty and Aging Cohort Study (KFACS), recruiting participants from among community-dwelling older people in diverse areas nationwide in 10 study centers across different regions covering different residential locations (urban, suburban and rural). The detailed study design and recruitment plan have been published²¹. Briefly, each center recruited participants by a 1:1 face-to-face approach using quota sampling stratified by age (70–74, 75–79 and 80–84 years with a ratio of 6:5:4, respectively) and sex (male and female), with the aim of recruiting approximately 1,500 men and 1,500 women from May 2016 to November 2017. To minimize selection bias, participants were recruited from diverse settings: local senior welfare centers, community health centers, apartments, housing complexes and outpatient clinics. A detailed flow diagram of the present study is shown in Figure 1.

Eligibility criteria were as follows: individuals aged 70–84 years who can present their thoughts with no cognitive impairment and who were planning to live in the area for at least 2 years from recruitment. The protocol for KFACS was

permitted by the institutional review boards of each center (IRB Number: B-1607/354-402). We received written informed consent from all participants.

Of 3,014 participants enrolled in the KFACS from 2016 to 2017, 2,403 who completed handgrip strength (HGS) tests and dual-energy X-ray absorptiometry (DXA), were finally included for analysis.

Anthropometric measurements

Height and bodyweight were examined with a digital scale to the nearest 0.1 cm or 0.1 kg, respectively. Body mass index (BMI) was calculated as bodyweight (kg) / height² (m²). Waist circumference was checked at the midpoint between the lowest rib margin and the highest point of the iliac crest. Blood pressure (BP) was taken three times at 2-min intervals, using an automatic BP monitor (Omron Electronics Co., Ltd., Seoul, Korea) and the mean BP were used for analysis. Hypertension was determined if systolic BP was ≥ 140 mmHg or diastolic BP was ≥ 90 mmHg, or if participants were taking antihypertensive medications.

Definition of diabetes

Diabetes was assessed from a self-report of diabetes diagnosed by a physician and any current use of antidiabetic medication. Newly diagnosed diabetes was determined if the baseline laboratory results of fasting plasma glucose were ≥ 126 mg/dL or glycated hemoglobin (HbA1c) was $\geq 6.5\%$ according to the American Diabetes Association recommendations²².

Definition of sarcopenia

Skeletal muscle mass was assessed by DXA (GE Healthcare Lunar, Madison, WI, USA; and Hologic DXA Systems, Hologic Inc., Bedford, MA, USA), and muscle strength was examined with HGS using a digital grip strength dynamometer (TTK-5401; Takei Ltd, Tokyo, Japan). The HGS was evaluated with the participant's arms hanging down, but without touching the trunk. Each hand was tested twice, with left and right hands alternating between trials and 3-min rests between measurements of the same hand. The mean HGS of the dominant hand was used for analysis. Physical performance was evaluated with a gait speed, the Short Physical Performance Battery (SPPB) test, and the Timed Up and Go (TUG) test. The SPPB test²³ comprises of three tests: balance, gait speed and chair stand. The TUG test²⁴ measures the total time of the following: standing up from a chair, walking toward a 3-m designated point, turning around the point, walking back to the chair and sitting down.

Diagnosis of sarcopenia was determined if a decrease of muscle mass accompanied either a decrement in physical performance or muscle strength, following the criteria of the Asian Working Group for Sarcopenia (AWGS)⁴ or the Foundation for the National Institutes of Health (FNIH)²⁵. The cut-off values of AWGS criteria are as follows: muscle mass index (MMI), defined as appendicular skeletal muscle mass (ASM)/

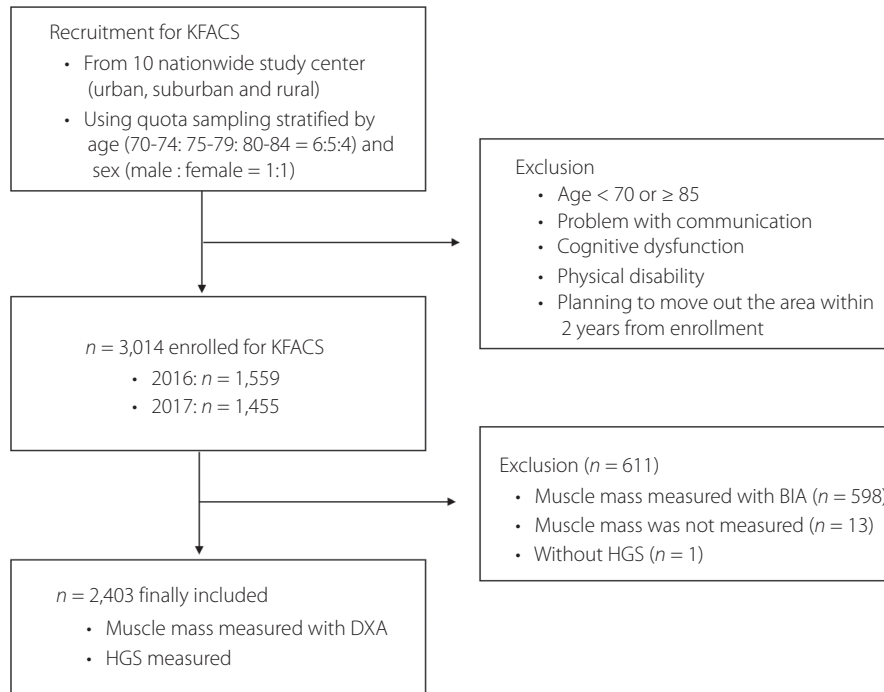


Figure 1 | Flow diagram showing the number of participants who were enrolled in the Korean Frailty and Aging Cohort Study (KFACS) study. Of a total 3,014 enrolled participants, 2,403 participants were finally included for analysis. BIA, bioimpedance analysis; DXA, dual-energy X-ray absorptiometry; HGS, handgrip strength.

height², <7.0 kg/m² for men and <5.4 kg/m² for women; HGS <26 kg for men and < 18 kg for women; and gait speed ≤0.8 m/s. Those of FNIH criteria are as follows: MMI, defined by ASM/BMI, <0.789 for men and <0.512 for women; HGS, <26 kg for men and <16 kg for women; gait speed, ≤0.8 m/s.

Definition of frailty

Frailty was determined by Cardiovascular Health Study Frailty Phenotype criteria²⁶ based on five components: (i) unintended weight loss of ≥4.5 kg in the last 1 year; (ii) weakness defined as maximal HGS <26 kg for men and <18 kg for women; (iii) exhaustion evaluated using the questions from the Center for Epidemiological Studies Depression scale; (iv) slowness defined as a gait speed <1 m/s; and (v) reduced physical activity based on calories used for physical activities calculated using the International Physical Activity Questionnaire, where 1 point was given if <494.65 kcal/week in men and <283.50 kcal/week in women. Participants with a total score ≥3 were categorized as frail; those with scores of 1 or 2 were categorized as prefrail and the rest of the participants were categorized as robust.

Metabolic measurements

Blood samples were collected at 07:30 to 08:30 AM after an overnight fast of at least 8 h in each center, and all tests were carried out in a core laboratory (Seegene Co., Seoul, Korea). HbA1c and plasma insulin levels were analyzed using Cobas

8000 e602 equipment (Roche, Mannheim, Germany) and a Tosoh HLC-723 G8 analyzer (Tosoh Corp., Tokyo, Japan), respectively. For other blood chemistry tests – including concentrations of glucose, liver function, lipid profile, renal function and C-reactive protein – we used the Cobas 8000 C702 (Roche). To evaluate insulin resistance, the homeostatic model assessment of insulin resistance (HOMA-IR) was calculated as (fasting glucose [mg/dL] × fasting insulin [μU/mL]) / 405. For assessing pancreatic β-cell function, the HOMA pancreatic β-cell function index (HOMA-β) was calculated as 360 × insulin (μU/mL) / (glucose [mg/dL] – 63)%.

Statistical analysis

Data are described as the mean ± standard deviation for continuous variables, and numbers and percentages for categorical variables. To compare mean values between the two groups, Student's *t*-test and the Mann–Whitney non-parametric *U*-test were used for normally distributed data and non-normally distributed data, respectively. To compare the mean values of three groups divided according to HbA1c percentage level and HOMA-IR tertiles, analysis of variance (ANOVA) and the Kruskal–Wallis test were used for normally distributed data and non-normally distributed data, respectively. For post-hoc analysis, Tukey's method was used in normally distributed data, and the Mann–Whitney nonparametric *U*-test was used in non-normally distributed data. For categorical variables, the χ^2 -

test was used. All statistical analyses were conducted using IBM SPSS Statistics version 23.0 (IBM Corp., Armonk, NY, USA). All results with $P < 0.05$ were considered statistically significant.

RESULTS

The prevalence of diabetes was 30.2% in men and 25.8% in women (Table 1). In both sexes, waist circumference and BMI were higher in the groups with diabetes than in the groups without diabetes. Adults with diabetes presented higher levels of HbA1c, fasting glucose, plasma insulin and HOMA-IR, and lower HOMA- β . Adults with diabetes also showed higher levels of triglycerides, and lower LDL and HDL cholesterol levels. The proportion of smokers was similar in all groups.

The prevalence of sarcopenia by the presence of diabetes was compared in both men and women (Table 2). The prevalence of sarcopenia assessed by both AWGS and FNIH in men was not statistically different between the participants with diabetes and participants without diabetes. Men with diabetes showed a higher prevalence of being prefrail than the group without diabetes (54.2% vs 45.1%, $P = 0.005$). Among Cardiovascular

Health Study Frailty Phenotype components, the prevalence of exhaustion was significantly higher in men with diabetes. In men, the ASM/height² of the two groups was similar, but ASM/BMI and HGS were significantly lower in the group with diabetes than in the group without diabetes. Muscle functions, including gait speed, SPPB score and TUG test, were not statistically different between the two groups among men.

The prevalence of sarcopenia in women assessed by the FNIH criteria was significantly higher in the participants with diabetes than in the participants without diabetes, whereas that defined by AWGS criteria was not different between the two groups (Table 2). Women with diabetes presented lower HGS, ASM/BMI, SPPB score and gait speed, and they took a longer time on the TUG test than women without diabetes. Women with diabetes presented a higher prevalence of frailty. They showed a higher prevalence of weakness, slowness and decreased physical activity compared with women without diabetes.

Table 3 shows the prevalence of sarcopenia by the HbA1c levels. Individuals were classified into three groups in each sex: individuals with normal glucose tolerance, diabetes patients

Table 1 | Clinical characteristics according to the presence of diabetes by sex

	Men (<i>n</i> = 1,135)			Women (<i>n</i> = 1,268)		
	Non-DM	DM	<i>P</i>	Non-DM	DM	<i>P</i>
<i>n</i> (%)	792 (69.8%)	343 (30.2%)		941 (74.2%)	327 (25.8%)	
Age (years)	76.4 ± 4.0	76.4 ± 3.8	0.974	75.5 ± 3.9	76.0 ± 3.8	0.032
Height (cm)	164.8 ± 5.8	164.9 ± 5.3	0.749	151.9 ± 5.3	151.7 ± 5.0	0.492
BMI (kg/m ²)	23.7 ± 2.8	24.6 ± 2.9	<0.001	24.6 ± 3.0	25.2 ± 3.0	0.004
Waist circumference (cm)	87.8 ± 8.4	90.8 ± 8.2	<0.001	86.3 ± 8.5	88.5 ± 8.2	<0.001
SBP (mmHg)	130.5 ± 15.3	131.9 ± 14.6	0.147	130.9 ± 15.9	132.2 ± 14.8	0.193
DBP (mmHg)	78.3 ± 9.4	76.9 ± 8.6	0.014	77.2 ± 9.3	76.3 ± 8.9	0.151
Fasting glucose (mg/dL)	95.8 ± 11.5	126.4 ± 30.2	<0.001	94.5 ± 9.3	127.0 ± 30.9	<0.001
HbA1c (%)	5.6 ± 0.3	6.8 ± 0.9	<0.001	5.7 ± 0.3	7.0 ± 1.0	<0.001
Insulin (mU/L)	6.4 ± 4.7	8.1 ± 6.1	<0.001	7.6 ± 4.5	9.7 ± 5.9	<0.001
HOMA-IR	1.6 ± 1.4	2.6 ± 3.0	<0.001	1.8 ± 1.2	3.1 ± 2.3	<0.001
HOMA- β (%)	75.7 ± 103.0	52.5 ± 51.2	<0.001	86.5 ± 99.6	67.9 ± 62.8	0.002
Cholesterol (mg/dL)	177.4 ± 34.4	164.9 ± 39.5	<0.001	191.6 ± 35.7	172.2 ± 37.9	<0.001
Triglycerides (mg/dL)	109.2 ± 58.5	133.6 ± 74.0	<0.001	120.1 ± 54.8	135.7 ± 67.0	0.001
HDL-C (mg/dL)	52.4 ± 14.6	46.3 ± 12.7	<0.001	55.6 ± 13.8	51.6 ± 13.8	<0.001
LDL-C (mg/dL)	107.1 ± 30.6	96.1 ± 32.9	<0.001	116.3 ± 33.2	98.4 ± 31.8	<0.001
BUN (mg/dL)	16.8 ± 4.8	18.3 ± 7.1	<0.001	15.8 ± 4.5	16.6 ± 5.0	0.005
Creatinine (mg/dL)	1.01 ± 0.2	1.10 ± 0.6	<0.001	0.96 ± 0.2	0.97 ± 0.2	0.261
AST (IU/L)	22.8 ± 7.5	23.8 ± 13.4	0.183	22.3 ± 8.0	22.3 ± 8.2	0.958
ALT (IU/L)	18.9 ± 9.9	21.9 ± 13.6	<0.001	17.5 ± 8.8	20.6 ± 10.7	<0.001
CRP (mg/dL)	1.4 ± 2.3	1.3 ± 1.7	0.516	1.3 ± 1.7	1.2 ± 1.9	0.678
HTN, <i>n</i> (%)	380 (48.0%)	230 (67.1%)	<0.001	517 (54.9%)	237 (72.5%)	<0.001
Hyperlipidemia, <i>n</i> (%)	162 (20.5%)	117 (34.1%)	<0.001	326 (34.6%)	185 (56.6%)	<0.001
Current smoker, <i>n</i> (%)	90 (11.4%)	33 (9.6%)	0.241	9 (1.0%)	4 (1.2%)	0.833
Ex-smoker, <i>n</i> (%)	511 (64.5%)	239 (69.7%)		18 (1.9%)	5 (1.5%)	

Data are reported as the mean ± standard deviation or number (%). ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMI, body mass index; BUN, blood urea nitrogen; CRP, C-reactive protein; DM, diabetes mellitus; HbA1c, glycated hemoglobin; HDL-C, high-density lipoprotein cholesterol; HOMA- β , homeostatic model assessment of β -cell function index; HOMA-IR, homeostatic model assessment of insulin resistance; HTN, hypertension LDL-C, low-density lipoprotein cholesterol; SBP/DBP, systolic/diastolic blood pressure.

Table 2 | Prevalence of sarcopenia according to the presence of diabetes by sex

	Men (n = 1,135)			Women (n = 1,268)		
	Non-DM	DM	P	Non-DM	DM	P
n (%)	792 (69.8%)	343 (30.2%)		941 (74.2%)	327 (25.8%)	
Sarcopenia						
AWGS (%)	102 (12.9%)	47 (13.7%)	0.706	94 (10.0%)	41 (12.5%)	0.198
FNIH (%)	98 (12.4%)	49 (14.3%)	0.378	80 (8.5%)	48 (14.7%)	0.001
CHS frailty						
Frail, n (%)	42 (5.3%)	19 (5.5%)	0.871	46 (4.9%)	31 (9.5%)	0.003
Prefrail, n (%)	357 (45.1%)	186 (54.2%)	0.005	568 (60.4%)	199 (60.9%)	0.875
Frail + prefrail, n (%)	399 (50.4%)	205 (59.8%)	0.004	614 (65.2%)	230 (70.3%)	0.093
Weakness	103 (13.0%)	51 (14.9%)	0.404	177 (18.8%)	78 (23.9%)	0.050
Slowness	170 (21.5%)	85 (24.8%)	0.219	286 (30.4%)	135 (41.3%)	<0.001
Reduced physical activity	75 (9.6%)	41 (12.1%)	0.201	82 (8.8%)	45 (13.9%)	0.008
Exhaustion	135 (17.0%)	81 (23.6%)	0.010	345 (36.7%)	135 (41.3%)	0.138
Weight loss	44 (5.6%)	19 (5.5%)	0.991	32 (3.4%)	16 (4.9%)	0.223
Muscle mass and function						
ASM/height ² (kg/m ²)	7.0 ± 0.9	7.1 ± 0.9	0.384	5.8 ± 0.7	5.8 ± 0.7	0.686
ASM/BMI	0.81 ± 0.1	0.78 ± 0.1	<0.001	0.55 ± 0.1	0.53 ± 0.1	0.016
HGS (kg)	31.8 ± 6.0	30.6 ± 5.4	<0.001	20.6 ± 4.0	20.1 ± 3.7	0.038
Gait speed (m/s)	1.20 ± 0.3	1.16 ± 0.3	0.089	1.10 ± 0.3	1.04 ± 0.2	<0.001
SPPB (score)	11.1 ± 1.5	11.0 ± 1.4	0.247	10.6 ± 1.6	10.2 ± 1.8	<0.001
TUG test (s)	10.0 ± 2.8	10.4 ± 2.3	0.062	10.5 ± 2.6	11.2 ± 3.1	<0.001

Data are reported as the mean ± standard deviation or number and (%). ASM, appendicular skeletal muscle mass; AWGS, Asian Working Group for Sarcopenia; BMI, body mass index; CHS criteria, Cardiovascular Health Study frailty phenotype criteria; DM, diabetes mellitus; FNIH, Foundation for the National Institutes of Health; HGS, handgrip strength; SPPB, short physical performance battery; TUG test, Timed Up and Go test.

with HbA1c <7% and diabetes patients with HbA1c ≥7.0%. In both men and women, the prevalence of sarcopenia in participants with diabetes was not different according to the HbA1c levels.

Table 4 presents the prevalence of sarcopenia by HOMA-IR. In each sex, individuals were classified into three groups using three tertiles of HOMA-IR: high, middle and low. In men, individuals in the high and middle tertiles HOMA-IR groups presented a higher prevalence of sarcopenia, assessed by FNIH, compared with those in the low tertile HOMA-IR group. Men in the high tertile HOMA-IR group showed lower ASM/BMI and gait speed compared with men in the low tertile group. In women, as HOMA-IR increased, the BMI and ASM/height² values increased, and the prevalence of sarcopenia assessed by AWGS decreased accordingly. Women in the high tertile HOMA-IR group also showed lower ASM/BMI, SPPB scores and gait speed compared with the women in the low tertile HOMA-IR group, although the HGS were not different among the three groups.

DISCUSSION

Here, we investigated the prevalence of sarcopenia and frailty in older Korean adults aged 70–84 years, in accordance with the presence of diabetes. Among 2,403 participants included in the KFACS, 27.8% had diabetes. In women, the prevalence of sarcopenia assessed by FNIH criteria and that of frailty defined

by Cardiovascular Health Study Frailty Phenotype criteria were significantly higher in those with diabetes compared with the group without diabetes, whereas these were not different in men.

The results of the present study showed the similarity to those of a study using the Korea National Health and Nutrition Examination Survey, which reported an inverse linear association between HGS and diabetes/insulin resistance²⁰. The prevalence of sarcopenia in the present study is lower than previous results shown in the Korean Sarcopenic Obesity Study¹⁰. However, in the Korean Sarcopenic Obesity Study, the prevalence of sarcopenia in the participants with diabetes might have been overestimated, as the patients with diabetes were recruited from a tertiary hospital, and Korean Sarcopenic Obesity Study defined sarcopenia only using a skeletal muscle index (ASM/height²) and a different cut-off point from that used here.

The prevalence of frailty in patients with diabetes has been documented to be three- to fivefold higher than in the general population^{27,28}. Here, we found that the prevalence of frailty was twofold times higher only among the women with diabetes compared with those without diabetes. As we know, this is the first study to show the prevalence of frailty in older adults with diabetes in Korea.

Skeletal muscle mass is known to be proportional to the body size, so when assessing the muscle quantity, the MMI, adjusted by height squared, has been used rather than total

Table 3 | Prevalence of sarcopenia according to glycated hemoglobin percentage by sex

		Non-DM	DM		P^{\dagger}	P^{\ddagger}	P^{\S}	P^{\parallel}
			(HbA1c <7%)	(HbA1c \geq 7.0%)				
Men	<i>n</i> (%)	792 (69.8%)	224 (19.7%)	119 (10.5%)				
	HbA1c (%)	5.6 \pm 0.47	6.3 \pm 0.5	7.7 \pm 0.8	<0.001			
	Age (years)	76.4 \pm 3.9	76.3 \pm 3.8	76.6 \pm 3.8	0.843			
	Sarcopenia							
	AWGS (%)	102 (12.9%)	31 (13.8%)	16 (13.4%)	0.926			
	FNIH (%)	98 (12.4%)	34 (15.2%)	15 (12.6%)	0.540			
	Muscle mass and function							
	ASM/height ² (kg/m ²)	7.02 \pm 0.85	7.04 \pm 0.84	7.11 \pm 0.91	0.512			
	ASM/BMI	0.81 \pm 0.1	0.78 \pm 0.1	0.79 \pm 0.1	0.002	0.006	0.120	0.999
	HGS (kg)	31.83 \pm 5.85	30.66 \pm 5.62	30.54 \pm 4.93	0.005	0.021	0.032	0.996
	Gait speed (m/s)	1.20 \pm 0.3	1.18 \pm 0.3	1.15 \pm 0.3	0.077			
	SPPB (score)	11.07 \pm 1.49	11.00 \pm 1.28	10.91 \pm 1.62	0.115			
TUG test(s)	10.09 \pm 2.79	10.42 \pm 2.18	10.37 \pm 2.49	0.003	0.003	0.180	0.999	
Women	<i>n</i> (%)	941 (74.2%)	190 (15.0%)	137 (10.8%)				
	HbA1c (%)	5.8 \pm 0.3	6.4 \pm 0.5	7.9 \pm 1.2	<0.001			
	Age (years)	75.51 \pm 3.86	75.88 \pm 3.85	76.27 \pm 3.75	0.051			
	Sarcopenia							
	AWGS (%)	94 (10.0%)	20 (10.5%)	21 (15.3%)	0.166			
	FNIH (%)	80 (8.5%)	28 (14.7%)	20 (14.6%)	0.006	0.008	0.021	0.972
	Muscle mass and function							
	ASM/height ² (kg/m ²)	5.83 \pm 0.75	5.85 \pm 0.73	5.85 \pm 0.69	0.895			
	ASM/BMI	0.55 \pm 0.1	0.53 \pm 0.1	0.54 \pm 0.1	0.050	0.049	0.51	0.999
	HGS (kg)	20.65 \pm 3.96	20.09 \pm 3.64	20.17 \pm 3.89	0.077			
	Gait speed (m/s)	1.12 \pm 0.3	1.04 \pm 0.20	1.04 \pm 0.21	<0.001	0.001	0.006	0.999
	SPPB (score)	10.63 \pm 1.59	10.23 \pm 1.84	10.24 \pm 1.78	0.002	0.010	0.039	0.999
TUG test (s)	10.46 \pm 2.59	11.10 \pm 3.14	11.28 \pm 3.10	<0.001	0.042	0.002	0.956	

Data are reported as the mean \pm standard deviation or number and (%). P^{\dagger} , P for ANOVA in normally distributed data; P for Kruskal–Wallis in non-normally distributed data; P^{\ddagger} , normal versus diabetes mellitus (DM; glycated hemoglobin [HbA1c] <7%); P^{\S} , normal versus DM (HbA1c \geq 7.0%); P^{\parallel} , DM (HbA1c <7%) versus DM (HbA1c \geq 7.0%). ASM, appendicular skeletal muscle mass; AWGS, Asian Working Group for Sarcopenia; BMI, body mass index; FNIH, Foundation for the National Institutes of Health; HGS, handgrip strength; SPPB, short physical performance battery; TUG test, Timed Up and Go test.

skeletal muscle mass. Using ASM/height² as MMI was first suggested by Baumgartner *et al.*²⁹, and many organizations including the European Working Group on Sarcopenia in Older People and AWGS have recommended this index for sarcopenia; however, ASM/height² has a limitation, namely, the underestimation of the prevalence of sarcopenia among individuals with a large fat mass³⁰. More recently, the FNIH proposed a new MMI using the ASM/BMI ratio. In a previous study using data from the Korea National Health and Nutrition Examination Survey³¹, men presented a peak level of total muscle mass and ASM during their 30s, and these declined steadily as they aged. However, in women, total muscle mass and ASM showed an increment until their 40s, plateaued during their 50s, and then started to diminish after that. These age trends were similar to ASM/BMI, whereas the age trends of ASM/height² showed a peak in the 60s among women, which was clinically unexpected. The present results for both sexes showed that participants with diabetes had decreased ASM/BMI, compared with participants without diabetes, whereas the ASM/height²

was not different between the two groups. Thus, in the Korean population, ASM/BMI might better predict metabolic disease than ASM/height², and this is consistent with studies showing that BMI, rather than height, is more strongly associated with metabolic syndrome.

Compared with participants without diabetes, women with diabetes showed a higher prevalence of sarcopenia, as defined by FNIH, and of frailty, but these were not different in men. In both sexes, participants with diabetes showed lower ASM/BMI and HGS, but only women with diabetes showed lower physical performance, including gait speed, TUG test, and SPPB test results, compared with women without diabetes. In women, decreased physical performance might be explained by higher intramuscular fat mass compared with men with the same bodyweight. A previous study showed that a high level of intramuscular fat was associated with decreased gait speed and lower grip strength³². Women have a much larger percentage of body fat than men, and there are sex differences in fat distribution. Women are known to accumulate fat tissue in the

Table 4 | Prevalence of sarcopenia according to the homeostatic model assessment of insulin resistance by sex

	HOMA-IR	Low tertile	Middle tertile	High tertile	<i>P</i> [†]	<i>P</i> [‡]	<i>P</i> [§]	<i>P</i>
Men	<i>n</i> (%)	373 (33.1%)	376 (33.3%)	379 (33.6%)				
	HOMA-IR	0.72 ± 0.24	1.45 ± 0.23	3.44 ± 2.98	<0.001			
	Age (years)	76.28 ± 3.8	76.35 ± 3.9	76.6 ± 3.9	0.522			
	Height (cm)	164.6 ± 5.8	164.7 ± 6.0	165.3 ± 5.5	0.144			
	BMI (kg/m ²)	22.21 ± 2.6	24.10 ± 2.4	25.55 ± 2.65	<0.001	<0.001	<0.001	<0.001
	Sarcopenia							
	AWGS (%)	51 (13.7%)	47 (12.5%)	49 (12.9%)	0.890			
	FNIH (%)	32 (8.6%)	50 (13.3%)	63 (16.6%)	0.004	0.038	0.001	0.200
	Muscle mass and function							
	ASM/height ² (kg/m ²)	6.86 ± 0.8	7.03 ± 0.8	7.20 ± 0.9	<0.001	0.014	<0.001	0.013
	ASM/BMI	0.84 ± 0.1	0.79 ± 0.1	0.77 ± 0.1	<0.001	<0.001	<0.001	0.036
	HGS (kg)	31.49 ± 5.7	31.52 ± 5.5	31.46 ± 5.9	0.990			
	Gait speed (m/s)	1.21 ± 0.3	1.20 ± 0.3	1.15 ± 0.3	<0.001	0.999	0.001	0.001
	SPPB total score	11.02 ± 1.38	11.11 ± 1.51	10.99 ± 1.50	0.097			
TUG test(s)	10.04 ± 2.38	10.06 ± 2.67	10.45 ± 2.87	0.113				
Women	<i>n</i> (%)	421 (33.4%)	418 (33.1%)	422 (33.5%)				
	HOMA-IR	0.90 ± 0.25	1.74 ± 0.28	3.75 ± 1.86	<0.001			
	Age (years)	75.38 ± 3.88	75.64 ± 3.9	75.95 ± 3.79	0.083			
	Height (cm)	151.50 ± 5.35	152.06 ± 5.21	151.9 ± 5.05	0.256			
	BMI (kg/m ²)	22.9 ± 2.54	25.1 ± 2.60	26.3 ± 2.96	<0.001	<0.001	<0.001	<0.001
	Sarcopenia							
	AWGS (%)	60 (14.3%)	40 (9.6%)	33 (7.8%)	0.007	0.036	0.002	0.368
	FNIH (%)	33 (7.8%)	47 (11.2%)	47 (11.1%)	0.175			
	Muscle mass and function							
	ASM/height ² (kg/m ²)	5.61 ± 0.7	5.81 ± 0.7	6.07 ± 0.7	<0.001	<0.001	<0.001	0.001
	ASM/BMI	0.565 ± 0.1	0.538 ± 0.1	0.537 ± 0.1	<0.001	0.001	0.001	0.999
	HGS (kg)	20.41 ± 3.7	20.52 ± 4.1	20.61 ± 3.86	0.875			
	Gait speed (m/s)	1.06 ± 0.3	1.06 ± 0.2	1.01 ± 0.2	0.001	0.999	0.002	0.005
	SPPB total score	10.67 ± 1.6	10.61 ± 1.6	10.33 ± 1.7	0.004	0.999	0.009	0.016
TUG test (s)	10.43 ± 2.6	10.57 ± 2.8	10.90 ± 2.8	0.056				

Data are reported as the mean ± standard deviation or number and (%). *P*[†], *P* for ANOVA in normally distributed data; *P* for Kruskal–Wallis in non-normally distributed data; *P*[‡], HOMA-IR low tertile versus middle tertile; *P*[§], HOMA-IR low tertile versus high tertile; *P*^{||}, HOMA-IR middle tertile versus high tertile. ASM, appendicular skeletal muscle mass; AWGS, Asian Working Group for Sarcopenia; BMI, body mass index; DM, diabetes mellitus; FNIH, Foundation for the National Institutes of Health; HGS, handgrip strength; HOMA-IR, homeostatic model assessment of insulin resistance; SPPB, short physical performance battery; TUG test, Timed Up and Go test.

gluteal–femoral (peripheral) area, whereas men are more likely to accumulate fat in abdominal (central) areas, so women have more intramuscular fat³³. In the Health, Aging and Body Composition Study, women showed more than double the thigh subcutaneous fat area than men, but the subcutaneous fat amount in their thighs was independently associated with declines in gait speed³⁴. In that study, although the rate of decrement in gait speed was similar in both sexes, the baseline gait speed was approximately 0.1 m/s lower in women, leading to constantly slower gait speeds at all the following time points. We found similar results for mean gait speed (men 1.19 ± 0.3 m/s; women 1.10 ± 0.3; *P* < 0.001), and this sex difference persisted regardless of having diabetes (men without diabetes 1.20 ± 0.3 vs women without diabetes 1.10 ± 0.3 m/s, *P* < 0.001; men with diabetes 1.16 ± 0.3 vs women with diabetes 1.04 ± 0.2 m/s, *P* < 0.001). With the same cut-off value

for gait speed, this sex difference might well lead to higher proportions of women with decreased gait speed.

Insulin resistance is one of the major contributing factors to sarcopenia^{14,35}. Insulin is one of the major anabolic signals, thus it enhances protein synthesis and decreases protein breakdown³⁶. Therefore, insulin resistance can result in protein degradation³⁷, especially in the muscles of patients with diabetes^{38,39}. In the present study, regarding the development of sarcopenia, the men surveyed might not have been simply affected by the presence of diabetes or the HbA1c levels, but by their degree of insulin resistance, as shown in Table 4. When we assessed the prevalence of sarcopenia with regard to the HOMA-IR results, men in the high tertile group presented decreased gait speed and increased prevalence of sarcopenia compared with those in the low tertile group. However, in women, the prevalence of sarcopenia was not different

according to HOMA-IR status. In fact, as the HOMA-IR increased, the prevalence of sarcopenia assessed by AWGS decreased, which was opposite to what we expected. Increased HOMA-IR status was associated with significantly higher BMI, whereas height was similar among the three tertile groups. Interestingly, as HOMA-IR increased, ASM/BMI decreased, but ASM/height² increased accordingly. As not only fat mass, but also muscle mass and intramuscular fat mass, increases with the increment of bodyweight, the prevalence of sarcopenia can be underestimated when MMI is assessed by the ASM/height² in groups with high HOMA-IR status.

In the present study, the prevalence of sarcopenia was not different according to HbA1c levels, as shown in Table 3. However, this might be due to the relatively low proportion of participants with diabetes with high HbA1c levels. Among 670 patients with diabetes, just 76 (11.3%) patients had HbA1c $\geq 8.0\%$, and 30 (4.5%) patients had HbA1c $\geq 9.0\%$.

Several studies have shown that the loss rates in muscle strength or functions with aging are faster than in muscle mass; thus, muscle strength is more important than muscle mass in estimating the risk of mortality and mobility limitations^{7,40–42}. As a previous study showed that an increment in muscle mass did not enhance muscle strength in older people with sarcopenia⁷, earlier evaluation of muscle strength or function using the HGS or SPPB tests and early interventions would bring a favorable outcome in high-risk populations, especially among older people with diabetes.

The present study had several limitations. First, because it was a cross-sectional study, we could not assess causality between diabetes and sarcopenia. Longitudinal studies should be carried out to evaluate such a causal relationship and the possible contributing factors for sarcopenia among people with diabetes. Second, the duration of diabetes and diabetic complications were not evaluated. Longer durations of diabetes are associated with an increased incidence of sarcopenia from increased insulin resistance and diabetic complications, such as diabetic neuropathy, which is reported to be closely linked with muscle weakness⁴³. Third, antidiabetic medications were not investigated in the initial surveys. Some antidiabetic medications, such as metformin, are known to be linked with sarcopenia^{44–46}. Thus, additional investigations of antidiabetic medications and disease duration should be carried out. Fourth, there is a limitation of the validity of the HOMA-IR in individuals with higher fasting glucose levels⁴⁷. However, HOMA-IR correlates significantly with IR assessed by the clamp test in individuals with type 2 diabetes, and is a less invasive, inexpensive and easily applicable method to assess insulin resistance compared with the clamp test⁴⁸. Finally, we used two kinds of DXA machines; 55% of participants were measured using Lunar equipment, and the rest were measured using Hologic equipment. This might have led to differences in the assessment of muscle mass⁴⁹.

Diabetes was associated with decreased MMI when adjusted for BMI, but not for height² in these older Korean individuals.

In both sexes, the prevalence of sarcopenia, adjusted by height², was not associated with diabetic status. However, only the women with diabetes showed an increased prevalence of sarcopenia when adjusted for BMI and increased frailty. In individuals with diabetes, sarcopenia and frailty are associated with limitations in mobility and with increased mortality. Thus, in older adults with diabetes, early assessment of sarcopenia and frailty, along with timely interventions, might help in preventing functional deterioration.

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DISCLOSURE

The authors declare no conflict of interest.

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