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Prevalence of Sarcopenia and Frailty in Community Dwelling Korean Older Adults with Diabetes

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Abstract

Prevalence of Sarcopenia and Frailty in Community Dwelling Korean Older Adults with Diabetes

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Objective Diabetes is considered one prevalent risk factor contributing to physical disability in older adults. The aim of this study is to identify the prevalence of sarcopenia and frailty in older Korean adults with diabetes as compared to non-diabetic adults.

Methods We analyzed 1,241 adults aged 70-84 years enrolled in

the Korean Frailty and Aging Cohort Study (KFACS). Skeletal muscle mass was assessed by dual-energy X-ray absorptiometry, and muscle strength was measured by a digital grip strength dynamometer. Physical performance was assessed using the Short Physical Performance Battery (SPPB), and the Timed Up and Go (TUG) test. Sarcopenia was defined according to criteria put forth by the Asian Working Group for Sarcopenia (AWGS), the Foundation for the National Institutes of Health (FNIH), and the Korean Geriatric Society (KGS). Frailty was defined using Cardiovascular Health Study Frailty Phenotype (CHS) criteria, the Korean version of the FRAIL Scale (K-FS), and the Korean version of the Frailty Index (K-FI). Diagnosis of diabetes was followed by clinical recommendation, according to the American Diabetes Association.

Results The mean age of the study subjects was 76.2 ± 9.3 years, and 46.8% of the subjects were men. Prevalence of diabetes was 31.1% in men and 23.8% in women. In both genders, subjects with diabetes had higher levels of fasting glucose, insulin, HbA1c, and HOMA-IR, compared to the non-diabetic group. Subjects with diabetes were more likely to have hypertension and dyslipidemia. In men, the prevalence of sarcopenia and the mean value of the muscle mass index was not different between diabetic and non-diabetic groups, but the diabetic subjects had lower hand grip strength and gait speed. The diabetic male group also took a longer time on TUG

test, compared to the non-diabetic group. In women, the prevalence of sarcopenia defined by AWGS was higher in the diabetic group, compared to the non-diabetic group. Women with diabetes also had a lower gait speed and SPPB score, and took a longer time on the TUG test, compared to the non-diabetic group, although hand grip strength and muscle mass index were not different between the two groups. Men with diabetes showed increased prevalence of the composition of pre-frail and frail, defined by CHS and K-FS, compared to the non-diabetic men. Women with diabetes also showed higher prevalence of frailty defined by K-FI, compared to their non-diabetic counterparts.

Conclusion Prevalence of sarcopenia was higher in older women with diabetes compared to the non-diabetic group, but this prevalence was not different in men. Physical performance and muscle strength in older adults with diabetes were reduced compared to the non-diabetic group, whereas muscle mass was relatively preserved in subjects with diabetes. Thus, diabetes might be associated with developing sarcopenia, especially in a form of decreased muscle quality, in older adults.

Keyword Type 2 diabetes, Sarcopenia, Frailty, Hand grip strength

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Chapter 1. Introduction

1.1. Study Background

The elderly (age ≥65 years) population worldwide is rapidly increasing. In 2017, Korea has become an “aged society” (the elderly ≥ 14% of the total Korean population), and it took only 17 years to become an “aging society” (the elderly ≥7%)[1]. The speed of societal aging in Korea is faster than that of Japan, which took 24 years to become an “aged” from “aging”’ society and had been considered the world’s fastest aging nation [2]. The rise in the aging population leads to increased medical expenditures. With the shortage of healthcare resources, this issue poses a problem.

As people age, their body composition changes, including decreases in muscle mass or strength, and/or increases in fat mass. These changes can lead to increases in functional disability [3, 4]. In 1989, Irwin Rosenberg suggested the word *sarcopenia*, which originated from the Greek *sarx*, meaning flesh, and *penia*, meaning loss. [5]. Since then, sarcopenia has been defined as age−related progressive loss of muscle mass and function [6, 7]. It has been reported that sarcopenia is closely related to poor quality of life, functional impairment, and increased mortality [8−10].

Besides aging itself, multiple contributing risk factors to sarcopenia have been suggested, including − malnutrition, sedentary lifestyle, multiple drug use, and chronic diseases, such as

diabetes, obesity, osteoporosis, cancer, heart failure, chronic obstructive pulmonary disease, chronic kidney disease [11]. Several suggested mechanisms for developing sarcopenia include mitochondrial dysfunction, a pro-inflammatory status, oxidative stress, loss of motor neurons, and hormonal changes [12].

Diabetes is one of the most common age-related diseases. According to the 2016 diabetes fact sheet by the Korean Diabetes Association, the prevalence of diabetes among adults aged ≥30 years is 13.7% (4.8 million), and more than 30% of adults aged ≥65 years have diabetes [13]. Previous studies regarding the relationship between sarcopenia and diabetes have been controversial. Several studies suggested that individuals with diabetes were highly associated with decreases of muscle mass [14, 15] and strength [16, 17]. It was also reported that insulin resistance is inversely associated with quadriceps muscle strength [18] and gait speed [19]. However, other studies reported no significant association between diabetes and handgrip strength [20, 21].

Prevalence of sarcopenia has been reported in a wide range of cases in 8%-40% of the population, depending on the definitions and the racial/ethnic characteristics of the study groups [22]. There are few studies regarding prevalence of sarcopenia in diabetic patients in Korea, but these studies are not representative samplings of nationwide community dwellings of older adults. In the

Korea Sarcopenic Obesity Study (KSOS) [14], the prevalence of sarcopenia in the diabetic group and control group was 15.7% and 6.9% respectively, but they recruited only healthy volunteers living in Seoul for the control group, and tertiary hospital outpatient clinic diabetic patients for the diabetic group . The diagnosis of sarcopenia in the KSOS was made only by using a low skeletal muscle index (SMI (%): total skeletal muscle mass (kg)/weight (kg)*100) below the mean of the young reference group without considering muscle function and strength. Kim et al. [23] also compared muscle mass between older adults with diabetes and those without diabetes, but did not estimate muscle function or strength. On the contrary, Lee et al. [24] only identified association between handgrip strength and diabetes.

Considering clinical importance of sarcopenia in older adults, identifying the prevalence of sarcopenia and potential contributing risk factors in diabetic patients would be helpful to manage and prevent functional deterioration.

1.2. Purpose of Research

In this study, we evaluated the prevalence of sarcopenia and frailty in older Korean adults with diabetes compared to their non-diabetic counterparts. We also compared the prevalence of sarcopenia according to HOMA-IR and HbA1c levels to evaluate the relationship between insulin resistance/hyperglycemia and

sarcopenia.

Chapter 2. Methods

2.1. Participants

This study was a part of the Korean Frailty and Aging Cohort Study (KFACS) [25]. KFACS is a multicenter, longitudinal study, aiming to identify risk factors and adverse outcomes of frailty and to develop means of prevention. Recruitment was conducted in 10 nationwide local centers located in different urban and rural areas. Recruitment targeted 3 neighboring eup/myeon (towns/townships) in each center. Each center recruited participants using quota sampling methods stratified by sex and gender from one of the following 5 places: local senior welfare center, community health center, apartment complex, housing complex, medical institution.

Eligibility criteria included the following: adults aged 70–84 years who were able to express their opinions without cognitive impairment and who planned to reside in the local community at least 2 years from the time of the survey start. All participants voluntarily agreed to informed consent. The following was excluded from the study: (1) subjects who had difficulty in expressing their opinion clearly, (2) subjects who did not perform dual-energy X-ray absorptiometry (DXA) and hand grip strength (HGS), and (3) subjects deemed inadequate to enroll in the study or have poor compliance.

A recruitment total of 3,000 older adults was planned in 2016–2017. Of 1,559 participants enrolled in the KFACS study in 2016, all subjects performed HGS and 1,241 participants conducted DXA. Thus, 1,241 participants were finally included in this study. The study protocol for KFASC was approved by the Institutional Review Boards of each center. This study is a cross sectional and observational study.

2.2. Assessment of Diabetes Status

Previously diagnosed diabetes was made by using a self–report of physician–diagnosed diabetes, the current use of oral hypoglycemic medications, or insulin. Undiagnosed diabetes was identified using the baseline laboratory results of fasting plasma glucose and HbA1c. Diagnosis of diabetes was followed by using the American Diabetes Association (ADA) recommendation [26]. Subjects with HbA1c ≥6.5% or fasting plasma glucose ≥126 mg/dL were considered diabetic.

2.3. Assessment of Sarcopenia

Muscle mass was assessed by DXA and muscle strength was evaluated by HGS using a digital grip strength dynamometer (GRIP–D, Takei Scientific Instruments Co., Japan). HGS of each

hand was measured twice alternately in sitting positions with the elbow bent at 90° . There was a time gap of at least 1 minute for each measurement. Maximal HGS of the dominant hand was used for analysis. Physical performance was assessed by the Short Physical Performance Battery (SPPB) test and the Timed Up and Go (TUG) test. The SPPB test [27] consists of the balance test, gait speed and chair stand. The scores of SPPB test range from 0 (worst performance) to 12 (best performance), and ≤9 points, which showed increased all-cause mortality in the previous meta-analysis study [28], were considered abnormal. The TUG test [29] measures the total time from starting while standing from a chair and walking to the marked point (3 meter distance) to turning around and walking back to the chair and sitting down. The total time of <10 seconds was considered normal, <20 seconds was considered able to go outside alone, >30 seconds is considered requiring a gait aid. The total time of ≥14 seconds on the TUG test has been shown to indicate high risk of falling.

Diagnosis of sarcopenia was made if loss of muscle mass was accompanied with either decrease of muscle strength or physical performance [6], using the criteria of the Asian Working Group for Sarcopenia (AWGS) [30], the Foundation for the National Institutes of Health (FNIH) [31], and the Korean Geriatric Society (KGS) [32]. Prevalence of sarcopenia varies depending on the definition and ethnic characteristics, so we tried to compare prevalence of

sarcopenia using different diagnostic criteria.

In the AWGS criteria, cut-off values for sarcopenia were <7.0 kg/m^2 in men and <5.4 kg/m^2 in women for muscle mass index (MMI), defined as appendicular skeletal muscle mass (ASM) in kilograms divided by the square of height in meters; <26 kg in men and <18 kg in women for the HGS; and ≤0.8 m/s for the gait speed.

The cut-off values from the KGS were <6.43 kg/m^2 in men and <5.34 kg/m^2 in women for the MMI; <26 kg in men and <16 kg in women for the HGS; and ≤0.8 m/s for the gait speed.

The FNIH used ASM divided by body mass index (BMI), instead of $height^2$, for the MMI (cut-off value of <0.789 in men and <0.512 in women), and the cut-off values for the HGS and gait speed were the same as those for the KGS.

2.4. Assessment of Frailty

Frailty was defined using Cardiovascular Health Study Frailty Phenotype (CHS) criteria [33], the Korean version of the FRAIL Scale (K-FS) [34], and the Korean version of the Frailty Index (K-FI) [35]. We also assessed frailty by using the Korean Activities of Daily Living (K-ADL) index and the Korean-Instrumental Activities of Daily Living (K-IADL) index to evaluate functional performance [36].

CHS frailty phenotype criteria include the following 5 items: unintentional weight loss; ≥5% of weight loss in the prior year; self-reported exhaustion; weakness defined as the lowest20% grip strength; slowness defined as the slowest 20% in walk time; and low physical activity. To assess slowness, gait speeds of 4 meters were estimated twice, and the mean values were used for analysis. The cut-off point of slowness was <1.0 m/s for both men and women. To assess physical activity, we surveyed the total amount of physical activity time according to activity intensity (vigorous/ moderate/ low) during the prior week. The lowest 20% were considered to have low physical activity and the cut-off values were 494.65kcal for men and 283.50kcal for women. The total score of 0 was considered as robust, 1-2 as pre-frail, and 3-5 as frail.

K-FS was based on the original FRAIL scale suggested by Morley et al. [37], which was translated into the Korean version. FRAIL scale is established in order to assess frailty in a simpler way, and it includes a 5-question questionnaire: for fatigue, the question is ‘How much of the time did you feel tired during the last month?’ and if the patient answers more than ‘most of the time’, then the patient receives a score of 1; for resistance, ‘Do you have difficulty walking up 10 steps without resting?’; for ambulation, ‘Do you have difficulty walking 300 meters without aid?’; for illness, ‘Do you have any diagnosed disease among the

listed illnesses (hypertension, diabetes, cancer, chronic lung disease, heart attack, congestive heart failure, angina, asthma, arthritis, stroke, and kidney disease)? ‘and having ≥5 illness was scored as 1; for loss of weight, >5% of weight loss gets a score 1. The scoring for diagnosing frailty is the same as that of the CHS frailty criteria.

K-FI was established by the Korean Geriatrics Society and consists of 8 items: frequencies of hospital administration; self-assessment of health status; polypharmacy; loss of weight during the last 1year; depressive mood; urinary or fecal incontinence; TUG test; and having visual or auditory problem. The cut-off points in K-FI were >4.5 for frail and >2.5 for pre-frail.

K-ADL consists of a 7-item questionnaire regarding basic daily activities: dressing, washing of the face and hands, bathing, eating, transfer, toileting, and continence. The total score ranges from 7 (normal) to 21 (the worst function).

K-IADL includes a 10-item questionnaire related to more skillful activities using instruments: decorating, housework, preparing meals, laundry, going out for a short distance, using transportation, shopping, handling money, using the telephone, and taking medicine. The total scores range from 10 (normal) to 30 (the worst function).

2.5. Metabolic Measurement

Blood samples were collected in each center and all tests were conducted in core laboratory (Seegene). Fasting plasma glucose, insulin, and HbA1c were measured at 8am to 9am, after overnight fasting of at least 8 hours. Fasting blood samples (10 mL) were collected into EDTA-containing tubes, and immediately centrifuged at 1000g for 10 minutes at 4℃. Plasma glucose levels and insulin concentrations were analyzed using the Cobas 8000 C702 (Roche, Germany) and Cobas 8000 e602 (Roche, Germany) respectively. For the HbA1c levels, blood samples in EDTA were analyzed using the Tosoh HLC-723 G8 analyzer (Tosoh, Japan). For other blood chemistry tests, including alanine aminotransferase (ALT), aspartate aminotransferase (AST), total cholesterol, low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol, triglyceride, blood urea nitrogen (BUN), creatinine, C-reactive protein, we used the Cobas 8000 C702 (Roche, Germany).

Before measuring blood pressure, subjects were instructed to refrain from ingesting caffeine, smoking, and exercising, and were encouraged to take at least 30 minutes of rest. Blood pressure was measured three times with a time gap of 2 minutes, using an automatic blood pressure monitor (Omron, Korea). The mean value of the blood pressure was used for analysis. Blood samples and measurement of blood pressure, weight, height, and waist circumference were taken by trained study nurses in each center.

2.6. Statistical Analysis

Data are presented as the mean ± SD for continuous variables, and numbers in percent for categorical variables. To compare the mean values between the diabetic and the non-diabetic group, the Student's t-test was used for normally distributed data and Mann-Whitney U test was used for the non-normally distributed data. To compare the mean values of three groups divided by HbA1c and HOMA-IR, the ANOVA test was used for normally distributed data and Kruskal-Wallis test was used for non-normally distributed data. Turkey's method was used for post-hoc analysis in normally distributed data, and Mann-Whitney test was used for post-hoc analysis in non-normally distributed data. The Chi-square test was used for the categorical variables. All statistical analyses were performed using IBM SPSS Statistics version 23.0 (IBM Corp., Armonk, NY, USA). All tests with a p-values less than 0.05 were considered statistically significant.

Chapter 3. Results

Table 1 shows clinical characteristics of study participants according to the presence of diabetes. Of the total 1,241 enrolled subjects, 27.2% had diabetes and 46.8% were men. The mean age was 76.2 ± 9.3 years in total, and this mean was similar between the diabetic- and non-diabetic groups. The percentage of men was much higher in the diabetes group (53.6%) compared to their non-diabetic counterparts (44.3%). BMI and waist circumference were higher in adults with diabetes compared to those in adults without diabetes. Subjects with diabetes had higher levels of fasting glucose, HbA1c, insulin and HOMA-IR, and lower HOMA-beta, compared to the non-diabetic group. The percentages of smoker and ex-smoker were higher in the diabetic group. Systolic and diastolic blood pressures were not different between the two groups. The prevalence of sarcopenia defined by AWGS was 12.4% in subjects with diabetes and 9.1% in subjects without diabetes. The prevalence of frailty defined by CHS was 11.5% in subjects with diabetes, and 8.6% in subjects without diabetes.

We compared each clinical parameter between the diabetic and the non-diabetic group in each gender group (Table 2). The prevalence of diabetes was 31.1% in men and 23.8% in women. In

both gender groups, waist circumference was higher in the diabetic groups compared to the non-diabetic groups. Men with diabetes showed increased BMI compared to the non-diabetic adults. Subjects with diabetes had higher levels of fasting glucose, HbA1c, plasma insulin, and HOMA-IR, and lower HOMA-beta. Subjects with diabetes had higher levels of triglyceride, ALT, and lower levels of HDL-cholesterol. Men with diabetes had elevated BUN, creatinine compared to their non-diabetic counterparts. Frequencies of smoker and ex-smoker were comparable between the two groups.

Next, we compared the prevalence of sarcopenia according to the presence of diabetes in each gender group (Table 3). In men, prevalence of sarcopenia, defined by AWGS, FNIH and KGS, was not different between the diabetic and non-diabetic groups. Men with diabetes showed higher prevalence of the composition of pre-frail and frail, defined by CHS and K-FS, compared to the non-diabetic adults (CHS, 56.4% vs 44%, p = 0.006; K-FRAIL, 52.5% vs 42.3%, p = 0.022), but the prevalence of frailty defined by K-FI was not different. In men, MMI was not different between the two groups, but HGS was significantly lower in adults with diabetes compared to the non-diabetic adults (30.91± 5.2 vs 32.48 ± 6.0 kg, p <0.001). Compared to the non-diabetic group, men with diabetes took longer on the TUG test (10.38 ± 2.2 vs 10.05 ± 2.5 sec, p <0.026) and had decreased gait speed (1.18 ± 0.3 vs 1.23 ± 0.3 m/s,

p <0.001). The percentage of diabetic men with abnormal gait speed, defined as gait speed ≤0.8m/s, was also significantly higher compared to that of non-diabetic men (8.3% vs 4.0%, p = 0.033). However, the total scores of SPPB, K-ADL and K-IADL were not different between the two groups.

In women, the prevalence of sarcopenia defined by AWGS was significantly higher in the diabetic group (12.7% vs 7.6%, p = 0.045) compared to the non-diabetic group, and the prevalence of frailty defined by K-FI was significantly higher in the diabetic group (18.5% vs 10.5%, p = 0.009) than in the non-diabetic group. Women with diabetes had lower gait speed (1.04 ± 0.2 vs 1.10 ± 0.3 m/s, p <0.018) and SPPB score (10.11 ± 1.9 vs 10.45 ± 0.3, p = 0.057) compared to the adults without diabetes. The percentage of diabetic women with abnormal SPPB test, defined as the total score of SPPB test ≤9, was also significantly higher than that of their non-diabetic counterparts (31.2% vs 22.9%, p = 0.035). Subjects with diabetes got a higher K-ADL score (7.24 ± 0.6 vs 7.14 ± 0.5, p <0.045) and took longer on the TUG test (11.42 ± 3.5 vs 10.68 ± 2.8 sec, p <0.057), but MMI and HGS were not different between the two groups.

Table 4 shows the prevalence of sarcopenia according to the HbA1c (%) in each gender group. In each gender group, subjects were divided into three groups: subjects without diabetes, diabetic

subjects with HbA1c <7%, and diabetic subjects with HbA1c ≥7.0%. In men, the prevalence of sarcopenia and physical performance were not different among the three groups. Diabetic men with HbA1c <7% showed lower HGS compared to the non-diabetic group (31.49 ± 5.4 vs 30.6 ± 5.04 kg, p <0.05). The total score of SPPB, TUG, K-ADL and K-IADL were not different among the three groups. In women, diabetic subjects with HbA1c ≥7.0% showed higher prevalence of sarcopenia defined by AWGS compared to the non-diabetic group (20.0 vs 7.6%, p <0.001) and diabetic group with HbA1c <7% (20.0 vs 8.2%, p = 0.031) respectively, and the diabetic group took longer on TUG test compared to the non-diabetic group. However, MMI, HGS, and the total score of SPPB, K-ADL and K-IADL were not different among the three groups in women.

Table 5 presents prevalence of sarcopenia according to HOMA-IR in each gender group. We divided each gender group into 3 groups according to HOMA-IR: high 1/3, middle 1/3, and low 1/3. In men, subjects with high HOMA-IR showed higher prevalence of sarcopenia defined by FNIH compared to those in the groups with low HOMA-IR (17.3 vs 6.3%, p <0.001) and middle HOMA-IR (17.3 vs 10.5%, p = 0.05), respectively. Men with high HOMA-IR showed decreased gait speed compared to the subjects with low HOMA-IR and middle HOMA-IR. Men with high HOMA-IR also took longer on TUG tests compared to the subjects with the low

HOMA-IR and middle HOMA-IR. The percentage of men with abnormal gait speed in the high HOMA-IR group was significantly higher than that in the low HOMA-IR and middle HOMA-IR groups, respectively. The percentage of men with an abnormal TUG test, defined as the total time of TUG test ≥14 seconds, was also higher in high HOMA-IR group compared to the percentage in the middle HOMA-IR group.

In women, subjects with high HOMA-IR had a decreased gait speed and SPPB score compared to the subjects with low HOMA-IR, but the prevalence of sarcopenia among the three groups was not different.

Chapter 4. Discussion

We identified the prevalence of sarcopenia and frailty in a community-dwelling of older Korean adults aged 70-84 years, according to the presence of type 2 diabetes. Among 1,241 participants enrolled in KFACS, 27.2% had diabetes. Prevalence of sarcopenia defined by AWGS was 12.4% in the diabetic group, and 9.1% in the non-diabetic group. Prevalence of frailty defined by CHS was 11.5% in the diabetic group, and 8.6% in the non-diabetic group. Subjects with diabetes were more likely to have hypertension, dyslipidemia, renal dysfunction, and insulin resistance.

The prevalence of sarcopenia in this study is lower than previously reported data in KSOS (diabetic group, 15.7%; non-diabetic group, 6.9%) [14]. However, in KSOS, the prevalence of sarcopenia in the diabetic group may be overestimated because the diabetic patients were recruited only from a tertiary hospital, so more severe stages of diabetic patients may be included. In the same manner, the prevalence of sarcopenia in the control group might be underestimated, since they only recruited from healthy volunteers from one urban city, Seoul. As we know, our study is the first study that identified the prevalence of sarcopenia in Korea using both muscle mass and muscle strength/function and represented a local community-dwelling of older adults. Our data

were consistent with the previous study using the Korea National Health and Nutrition Examination Survey (KNHANES), which showed an inverse relationship between handgrip strength and type 2 DM / insulin resistance [24].

We compared clinical parameters of sarcopenia according to gender, because muscle mass and strength are well-known to be largely affected by gender. The prevalence of diabetes was significantly different in each gender group in our study (Men, 31.1%; Women, 23.8%; p <0.05), and 11.5% of men and 8.8% of women were identified to have sarcopenia defined by AWGS. Men with diabetes showed decreased muscle strength (HGS) and physical performance, assessed according to gait speed and the TUG test. Muscle mass and prevalence of sarcopenia were not different between the diabetic- and non-diabetic groups. Women with diabetes showed higher prevalence of sarcopenia using AWGS criteria (12.7%) and frailty using K-FI (18.5%), compared to the non-diabetic group (AGWS, 7.6%; K-FI, 10.5%). Women with diabetes had decreased physical performance, including gait speed, SPPB test, TUG test and K-ADL, but muscle mass and strength were not different compared with the non-diabetic women. Overall, subjects with diabetes had decreased muscle function and strength, though muscle mass was preserved in both gender groups.

Muscle mass is generally positively correlated with body size, so when evaluating loss of muscle mass, the absolute level of skeletal

muscle mass index (SMI), adjusted by height squared or BMI, is used instead of skeletal muscle mass. ASM/height^2 was first suggested by Baumgartner et al. [38] and many research groups, including AWGS, started to use this index to sarcopenia, but this index has a limitation— the underestimation of the prevalence of sarcopenia in cases of subjects with large fat mass [39]. Recently, the FNIH introduced new diagnostic criteria using ASM/BMI as SMI. In our study, the prevalence of sarcopenia defined by the FNIH in men with diabetes was higher compared to the prevalence defined by the AWGS or the KGS. This might indicate that the prevalence of sarcopenia in diabetic men is largely affected by body weight. However, in women with diabetes, the prevalence of sarcopenia defined by the AWGS was higher than the prevalence defined by the FNIH or the KGS. The reason for the difference in prevalence of sarcopenia according to criteria and gender may be explained by the previous study conducted in Korea which used the data from the Korean National Health and Nutrition Examination Survey (KNHANES) from 2008 to 2010 [40]. In the KNHANES study, men showed a peak level of total muscle mass and ASM in their 30s and then this decreased continuously. This trend was similar to ASM divided by BMI. In women, total muscle mass and ASM increased gradually until their 40s, plateaued during their 50–60s, and then started to decrease after that. This trend was similar to ASM/height^2 . These results indicate that ASM/BMI in men and

ASM/height^2 may better reflect absolute level of SMI compared to other parameters, and suggest the necessity of applying different diagnostic criteria according to gender, when defining sarcopenia.

To identify potential contributing risk factors of sarcopenia, we compared the prevalence of sarcopenia according to HOMA-IR. Men with high HOMA-IR showed increased prevalence of sarcopenia and decreased physical performance in gait speed and on the TUG test. In women, prevalence of sarcopenia was not different among the three groups divided by HOMA-IR, though subjects with high HOMA-IR showed decreased physical performance in gait speed and on the SPPB test. Several pathophysiology accelerating sarcopenia in diabetes have been suggested, including insulin resistance, glucose toxicity, presence of diabetic peripheral neuropathy or peripheral vascular disease, and genetic factors [11, 41]. Among them, insulin resistance has been known to be one of the major contributing factors [18, 42]. Insulin is an important anabolic signal and stimulates protein synthesis. Thus, insulin resistance can lead to a catabolic status, including protein degradation, in muscles of diabetic patients.

Lee et al. compared percentages of muscle loss among 5 groups— normoglycemia, impaired fasting glucose (IFG), untreated DM, DM treated with insulin sensitizers (IS), and DM treated without IS. Adults with IFG, untreated DM, and DM treated without IS showed significantly greater decline of muscle mass than their

normoglycemic counterparts. Interestingly, loss of muscle mass in diabetic patients treated with IS was significantly less than the loss of mass in normoglycemic group, untreated DM, and DM treated without IS, respectively [43]. These data suggest that IS may attenuate the loss of muscle mass in the diabetic group. Other studies showed that amounts of loss of muscle mass and strength in diabetic patients were greater with longer diabetes duration and higher HbA1c.

There were several studies showing that the rates of loss of muscle strength or functions were more rapid than those of muscle mass, and muscle strength was more important than muscle mass in predicting mortality and mobility limitation [10, 44-46]. Given that previous study showing that the gain of muscle mass did not help to improve muscle strength in older adults with sarcopenia [10], earlier assessments for muscle function using the SPPB or TUG test, and appropriate intervention would be helpful in high risk populations.

There are several possible reasons for preserved muscle mass in older adults with diabetes in our study. First, most of the enrolled participants were community-dwelling, well-functioning adults. Although DM durations were not evaluated, subjects with diabetes seem to have well-controlled, early stage diabetes, taking into consideration a low HbA1c (6.86%). Thus, only loss of muscle

function might have come and muscle loss had not yet manifested. Secondly, some oral hypoglycemic agents (OHA) and insulin may have positive effects on muscle mass. Although medications for diabetes had not been evaluated in an initial survey, most diagnosed diabetic patients are supposed to take insulin sensitizers such as metformin which is the first treatment option for diabetes in Korea and known to attenuate muscle loss.

Our study has several limitations. Due to the characteristics of the cross-sectional study, we could not assess causality between diabetes and sarcopenia. To assess a causal relationship and possible risk factors of sarcopenia in diabetes, a longitudinal observation should be conducted. Secondly, DM durations and complications were not evaluated. Longer DM duration has been known to be related with high incidence of sarcopenia due to increased insulin resistance and complications. Diabetic neuropathy is also known to be closely related to muscle wasting and weakness. Thirdly, DM medications are not assessed in initial surveys. Some medications have been known to be related to sarcopenia [47-49]. For example, using insulin sensitizers, sulfonylureas or insulin may attenuate the loss of muscle mass. Additional surveys on diabetic medications and disease duration should be conducted.

In older women with diabetes, prevalence of sarcopenia was higher compared to the non-diabetic group, but this was not

different in men. Physical performance and muscle strength in the diabetic group were reduced compared to the non-diabetic group, whereas muscle mass was relatively preserved in subjects with diabetes. Thus, in older adults, diabetes might be associated with developing sarcopenia, especially with respect to decreased muscle quality. In subjects with diabetes, loss of muscle function itself, regardless of muscle loss, is related to increase in mobility limitation and mortality. Thus, appropriate assessment of sarcopenia may help to decrease functional deterioration in older adults with diabetes.

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국문 초록

지역 사회에 거주하는 노인 당뇨병 환자에서 근감소증 및 노쇠의 유병률

목적: 당뇨는 노인의 근감소증의 중요한 위험인자 중 하나이다. 하지만 지금까지 한국의 노인 당뇨 환자에서 근감소증 및 노쇠의 유병률에 대하여 시행한 연구는 거의 없었다. 이번 연구의 목적은 당뇨환자에서 근감소증 및 노쇠의 유병률에 대하여 알아보고자 한다.

방법: 한국인의 노쇠 및 노화 코호트 연구 (Korean Frailty and Aging Cohort Stuty, KFACS)에 2016년에 등록된 70-84세 노인 1241명을 대상으로 하였다. 골격근량은 골밀도 검사 (DXA)를 통하여, 근력은 손 악력 검사 (hang grip strength)를 통하여 측정하였고, 신체 수행 능력은 Short physical performance Battery (SPPB) 및 Timed Up and Go (TUG) test로 평가하였다. 근감소증의 정의는 Asian Working Group for Sarcopenia (AWGS), the Foundation for the National Institutes of Health (FNIH) 및 Korean Geriatric Society (KGS)를 사용하였고, 당뇨의 진단은 미국 당뇨병학회 진단 기준을 따랐다. 노쇠는 Cardiovascular Health Study Frailty Phenotype (CHS) criteria, Korean version of the FRAIL Scale (K-FS), and Korean version of the Frailty Index (K-FI)를 따라 정의하였다.

결과: 대상자의 평균 나이는 76.2 ± 9.3세 였고, 46.8%가 남성이었다. 당뇨 유병률을 남성에서는 31.1%, 여성에서는 23.8%였다. 남, 녀 모두에서 당뇨환자들은 당뇨가 없는 환자들에 비하여 공복 혈당 수치, 인슐린, HbA1c 및 HOMA-IR이 유의하게 높았다. 당뇨환자들은 고혈압 및 고지혈증을 동반하는 경우가 더 많았다.

남성에서 당뇨 유무에 따라 근감소증의 유병률 및 사지 근육량은 차이가 없었다. 하지만 당뇨를 동반한 남성 환자들은 당뇨가 없는 군에 비해 손의 근력 및 보행 속도가 감소해 있었고, TUG test에서 더 많은 시간이 걸렸다. 여성에서는 당뇨를 동반한 군이 AWGS에 의해 정의된 근감소증 유병률이 유의하게 더 높았다. 당뇨를 동반한 여성 환자들은 보행속도 및 SPPB 점수가 낮았고, TUG test도 오래 걸렸지만, 속의 근력 및 사지 근육 량은 당뇨 유무에 따른 차이가 없었다. 당뇨를 동반한 남성 환자들은 CHS와 K-FS에 의해 정의된 노쇠와 노쇠 전단계가 당뇨가 없는 남성의 비해서 유의하게 높았고, 당뇨를 동반한 여성은 K-FI에 의하여 정의된 노쇠 유병률이 당뇨가 없는 여성에 비해 유의하게 높았다.

결론: 당뇨를 동반한 여성 노인에서 근감소증이 유의하게 높았지만, 남성에서는 차이가 없었다. 당뇨를 동반한 노인에서 당뇨가 없는 노인에 비하여 신체 수행 능력 및 근력이 유의하게 감소되어 있었다. 그러나 근육 량은 상대적으로 보존되어 있었다. 따라서 당뇨는 근육의 질을 떨어뜨리는 형태로 근감소증의 발생과 관련되는 것으로 보인다.

Keyword 2형 당뇨, 근감소증, 노쇠, 악력

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Table 1. Clinical characteristics according to the presence of diabetes.

	Total	Non-DM	DM	*p*
Number (%)	1241	903 (72.8%)	338 (27.2%)	
Men, n (%)	581 (46.8%)	400 (44.3%)	181 (53.6%)	0.004
Age (year)	76.2 ± 4.0	76.2 ± 4.0	76.3 ± 3.87	0.543
Height (cm)	157.7 ± 8.6	157.4 ± 8.8	158.6 ± 8.1	0.037
BMI (kg/m2)	24.4 ± 3.0	24.2 ± 3.1	25.0 ± 2.8	<0.001
Waist Circumference(cm)	87.9 ± 8.5	87.1 ± 8.5	90.0 ± 8.1	<0.001
SBP (mmHg)	131.5 ± 15.9	131.0 ± 16.1	132.8 ± 15.5	0.077
DBP (mmHg)	77.9 ± 9.3	78.2 ± 9.6	77.2 ± 8.6	0.078
Fasting glucose (mg/dL)	104.5 ± 22.4	96.3 ± 10.4	126.2 ± 30.1	<0.001*
HbA1c (%)	6.0 ± 0.8	5.7 ± 0.3	6.9 ± 1.0	<0.001*
Insulin (mIU/L)	7.7 ± 4.6	7.3 ± 4.6	9.0 ± 4.6	<0.001*
HOMA-IR	2.0 ± 1.4	1.8 ± 1.2	2.8 ± 1.7	<0.001*
HOMA-beta (%)	73.4 ± 91.7	78.5 ± 101.8	59.4 ± 52.6	<0.001*
Current smoker, n (%)	65 (5.2%)	43 (4.8%)	22 (6.5%)	
Ex-smoker, n (%)	403 (32.5%)	278 (30.8%)	125 (37%)	0.033

BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; HDL-Cholesterol, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol; BUN, blood urea nitrogen; CK, creatinine kinase, AST, aspartate aminotransferase; alanine aminotransferase; CRP, C-reactive protein; Data are reported as the means ± SD or number (%).

P values for t-test or chi-square test. ∗*P* for Mann-Whitney test in non-normally distributed data.

Table 2. Clinical characteristics according to the presence of diabetes divided by gender

	Men (n=581)			Women (n=660)		
	Non-DM	DM	P	Non-DM)	DM	P
Number (%)	400 (68.8%)	181 (31.1%)		503 (76.2%)	157 (23.8%)	
Age (yr)	76.6 ± 4.01	76.5 ± 3.8	0.778	75.8 ± 4.0	76.1 ± 4.0	0.424
Height (cm)	165.0 ± 5.9	164.5 ± 5.3	0.286	151.4 ± 5.4	151.7 ± 4.4	0.381
BMI (kg/m2)	23.5 ± 2.9	24.9 ± 2.8	<0.001	24.7 ± 3.1	25.2 ± 2.9	0.107
Waist Circumference (cm)	87.5 ± 8.7	91.4 ± 7.8	<0.001	86.7 ± 8.4	88.3 ± 8.1	0.041
SBP (mmHg)	130.9 ± 15.7	133.3 ± 15.8	0.092	131.1 ± 16.4	132.3 ± 15.2	0.428
DBP (mmHg)	79.1 ± 9.9	78.5 ± 8.3	0.452	77.5 ± 9.3	75.7 ± 8.8	0.034
Fasting glucose (mg/dL)	97.0 ± 11.1	126.3 ± 26.9	<0.001*	95.8 ± 9.7	126.0 ± 33.4	<0.001*
HbA1c (%)	5.7 ± 0.3	6.8 ± 0.8	<0.001*	5.8 ± 0.3	7.0 ± 1.11	<0.001*
Insulin (mU/L)	6.4 ± 4.1	8.5 ± 4.5	<0.001*	8.0 ± 4.8	9.4 ± 4.7	<0.001*
HOMA-IR	1.6 ± 1.1	2.7 ± 1.7	<0.001*	1.9 ± 1.3	2.9 ± 1.6	<0.001*
HOMA-beta (%)	70.8 ± 48.0	51.8 ± 49.2	<0.001*	84.6 ± 129.3	68.2 ± 55.2	<0.001*
Cholesterol (mg/dL)	181.8 ± 35.2	175.3 ± 41.6	0.051	196.0 ± 36.6	182.4 ± 38.6	<0.001
Triglyceride (mg/dL)	108.1 ± 56.4	140.9 ± 77.7	<0.001	118.6 ± 52.3	139.8 ± 70.9	0.001

HDL−C (mg/dL)	52.2 ± 14.4	45.6 ± 12.7	<0.001	55.2 ± 13.6	50.7 ± 13.5	<0.001
LDL−C (mg/dL)	108.0 ± 30.1	101.5 ± 34.4	0.031	117.1 ± 34.1	103.7 ± 32.4	<0.001
BUN (mg/dL)	16.7 ± 4.8	18.1 ± 7.1	0.018	15.9 ± 4.8	16.5 ± 4.8	0.175
Creatinine (mg/dL)	0.9 ± 0.2	1.1 ± 0.5	0.003	0.7 ± 0.2	0.7 ± 0.2	0.292
AST(SGOT) (IU/L)	23.1 ± 8.1	23.1 ± 12.6	0.995	22.0 ± 8.1	21.5 ± 8.0	0.523
ALT(SGPT) (IU/L)	18.9 ± 9.4	22.4 ± 15.0	0.005	17.5 ± 9.8	19.5 ± 10.3	0.033
CRP (mg/dL)	1.4 ± 2.1	1.5 ± 1.9	0.392	1.2 ± 1.6	1.2 ± 1.9	0.838
HTN hx, n (%)	190 (47.5%)	123 (68.0%)	<0.001	279 (55.5%)	113 (72.0%)	<0.001
Hyperlipidemia hx (%)	76 (19.0%)	51 (28.2%)	0.013	166 (33.0%)	83 (52.9%)	<0.001
Current smoker, n (%)	39 (9.8%)	20 (11.0%)		4 (0.8%)	2 (1.3%)	
Ex−smoker, n (%)	268 (67%)	124 (68.5%)	0.709	10 (2.0%)	1 (0.6%)	0.445

BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; HDL−Cholesterol, high density lipoprotein cholesterol; LDL−C, low density lipoprotein cholesterol; BUN, blood urea nitrogen; CK, creatinine kinase, AST, aspartate aminotransferase; alanine aminotransferase; CRP, C−reactive protein; HTN hx, history of hypertension; Data are reported as the means ± SD or number (%).

P values for t−test or chi−square test. *P* for Mann−Whitney test in non−normally distributed data.

Table 3. Prevalence of sarcopenia according to the presence of diabetes in each gender group

	Men (n=581)			Women (n=660)		
	Non-DM	DM	P	Non-DM	DM	P
Number (%)	400 (68.8%)	181 (31.1%)		503 (76.2%)	157 (23.8%)	
Sarcopenia						
AWGS (%)	45 (11.3%)	22 (12.2%)	0.752	38 (7.6%)	20 (12.7%)	0.045
KGS (%)	30 (7.5%)	9 (5.0%)	0.260	24 (4.8%)	12 (7.6%)	0.167
FNIH (%)	43 (10.8%)	24 (13.3%)	0.380	43 (8.5%)	18 (11.5%)	0.271
Frailty						
CHS criteria						
Frail, n (%)	21 (5.3%)	13 (7.2%)	0.358	57 (11.3%)	26 (16.6%)	0.085
Pre-frail, n (%)	155 (38.8%)	89 (49.2%)	0.018	274 (54.5%)	77 (49.0%)	0.234
Frail + pre-frail, n (%)	176 (44%)	102 (56.4%)	0.006	331 (65.8%)	103 (65.6%)	0.963
K-FRAIL scale						
Frail, n (%)	28 (7.0%)	13 (7.2%)	0.937	96 (19.1%)	38 (24.2%)	0.164
Pre-frail, n (%)	141 (35.3%)	82 (45.3%)	0.021	253 (50.3%)	73 (46.5%)	0.406
Frail + pre-frail, n (%)	169 (42.3%)	95 (52.5%)	0.022	349 (69.4%)	111 (70.7%)	0.754
K-Frailty index						

Frail, n (%)	26 (6.5%)	19 (10.5%)	0.095	53 (10.5%)	29 (18.5%)	0.009
Pre−frail, n (%)	97 (24.3%)	39 (21.5%)	0.476	160 (31.8%)	59 (37.6%)	0.180
Frail + pre−frail, n (%)	123 (30.8%)	58 (32.0%)	0.755	213 (42.3%)	88 (56.1%)	0.003
Muscle Mass and function						
MMI (kg/m²)	6.99 ± 0.9	7.14 ± 0.8	0.061	5.91 ± 0.7	5.84 ± 0.7	*0.360
HGS (kg)	32.48 ± 6.0	30.91 ± 5.2	0.001	20.69 ± 4.1	20.56 ± 3.7	*0.647
Gait speed (m/s)	1.23 ± 0.3	1.18 ± 0.3	0.036	1.10 ± 0.3	1.04 ± 0.2	*0.018
SPPB (score)	10.97 ± 1.4	10.94 ± 1.4	*0.884	10.45 ± 1.7	10.11 ± 1.9	*0.057
TUG test (s)	10.05 ± 2.5	10.38 ± 2.2	*0.026	10.68 ± 2.8	11.42 ± 3.5	*0.019
K−ADL (score)	7.13 ± 0.5	7.13 ± 0.5	0.846	7.14 ± 0.4	7.24 ± 0.6	0.045
K−IADL (score)	10.32 ± 1.2	10.35 ± 1.2	0.803	10.29 ± 1.0	10.37 ± 1.2	0.460
Abnormal Gait Speed, n (%)	16 (4.0%)	15 (8.3%)	0.033.	53 (10.5%)	23 (14.6%)	0.159
Abnormal SPPB test, n (%)	54 (13.5%)	23 (12.7%)	0.794	115 (22.9%)	49 (31.2%)	0.035
Abnormal TUG test, n (%)	22 (5.5%)	10 (5.5%)	0.990	48 (9.5%)	20 (12.7%)	0.250

Abnormal gait speed, ≤0.8m/s; Abnormal SPPB test, ≤9; abnormal TUG test, ≥14 seconds. MMI, muscle mass index defined as appendicular skeletal muscle mass (ASM) in kilograms divided by the square of height; HGS, hand grip strength; SPPB, short physical performance battery; TUG test, timed up and go test; K−ADL, Korean activities of daily living; K−IADL, Korean−instrumental activities of daily living; AWGS, Asian working group for sarcopenia;

KGS, Korean Geriatric Society; FNIH, Foundation for the National Institutes of Health; CHS criteria, cardiovascular health study frailty phenotype criteria; K-FRAIL scale, Korean version of the FRAIL Scale; K-Frailty index, Korean version of Frailty index. Data are reported as the means ± SD or number (%). *P* values for t-test or chi-square test. *P* for Mann-Whitney test in non-normally distributed data.

Table 4. Prevalence of sarcopenia according to the HbA1c (%) in each gender group.

		Non-DM	DM					
			(A1c<7%)	(A1c≥7.0%)	P^a	P^b	P^c	P^d
Men	Number (%)	400 (68.8%)	120 (20.7%)	61 (10.5%)				
	HbA1c (%)	5.6 ± 0.3	6.3 ± 0.4	7.6 ± 0.6				
	Sarcopenia							
	AWGS (%)	45 (11.3%)	16 (13.3%)	6 (9.8%)	0.746			
	KGS (%)	30 (7.5%)	8 (6.7%)	1 (1.6%)	0.234			
	FNIH (%)	43 (10.8%)	18 (15.0%)	6 (9.8%)	0.401			
	Muscle mass and function							
	MMI (kg/m²)	6.99 ± 0.87	7.1 ± 0.81	7.3 ± 0.8	0.050	0.698	0.041	0.253
	HGS (kg)	32.48 ± 5.97	30.6 ± 5.04	31.49 ± 5.4	0.006	0.005	0.419	0.602
	Gait speed(m/s)	1.23 ± 0.29	1.19 ± 0.3	1.16 ± 0.3	0.233			
	SPPB (score)	10.97 ± 1.36	10.98 ± 1.3	10.89 ± 1.6	0.963			
	TUG test(s)	10.05 ± 2.47	10.38 ± 2.1	10.38 ± 2.2	0.083			
	K-ADL (score)	7.13 ± 0.5	7.18 ± 0.5	7.03 ± 0.2	0.068			
	K-IADL (score)	10.32 ± 1.2	10.43 ± 1.4	10.2 ± 0.7	0.517			
	Abnormal Gait Speed (%)	16 (4.0%)	11 (9.2%)	4 (6.6%)	0.079			
	Abnormal SPPB test (%)	54 (13.5%)	18 (15.0%)	5 (8.2%)	0.428			
	Abnormal TUG test (%)	22 (5.5%)	7 (5.8%)	3 (4.9%)	0.968			

Women	Number (%)	503(76.2%)	97 (14.7%)	60 (9.1%)				
	HbA1c (%)	5.7 ± 0.3	6.4 ± 0.4	7.9 ± 1.2				
	Sarcopenia							
	AWGS (%)	38 (7.6%)	8 (8.2%)	12 (20.0%)	0.006	0.814	0.001	0.031
	KGS (%)	24 (4.8%)	6 (6.2%)	6 (10.0%)	0.288			
	FNIH (%)	43 (8.5%)	9 (9.3%)	9 (15.0%)	0.264			
	Muscle mass and function							
	MMI (kg/m²)	5.91 ± 0.73	5.87 ± 0.75	5.79 ± 0.64	0.486			
	HGS (kg)	20.69 ± 4.11	20.81 ± 3.38	20.17 ± 4.27	0.480			
	Gait speed(m/s)	1.10 ± 0.25	1.04 ± 0.23	1.04 ± 0.23	0.059			
	SPPB (score)	10.45 ± 1.68	10.19 ± 1.94	10.00 ± 1.91	0.128			
	TUG test (s)	10.68 ± 2.76	11.24 ± 3.27	11.70 ± 3.81	0.016	0.198	0.031	0.615
	K-ADL (score)	7.14 ± 0.4	7.24 ± 0.6	7.23 ± 0.5	0.109			
	Abnormal Gait Speed (%)	53 (10.5%)	13 (13.4%)	10 (16.7%)	0.305			
	Abnormal SPPB test (%)	115 (22.9%)	29 (29.9%)	20 (33.3%)	0.095			
	Abnormal TUG test (%)	48 (9.5%)	12 (12.4%)	8 (13.3%)	0.507			
	K-IADL (score)	10.29 ± 1.0	10.39 ± 1.3	10.33 ± 0.9	0.753			

Abnormal gait speed, ≤0.8m/s; Abnormal SPPB test, ≤9; abnormal TUG test, ≥14 seconds.

MMI, muscle mass index defined as appendicular skeletal muscle mass (ASM) in kilograms divided by the square of height; HGS, hand grip strength; SPPB, short physical performance battery; TUG test, timed up and go test; AWGS,

Asian working group for sarcopenia; KGS, Korean Geriatric Society; FNIH, Foundation for the National Institutes of Health. P^a: P for ANOVA in normally distributed data, P for Kruskal–Wallis in non–normally distributed data. P^b: Normal vs DM (A1c <7), P^c: Normal vs DM (A1c≥7.0), P^d: DM (A1c<7) vs DM (A1c≥7.0). Data are mean ± SD in case of normal distribution, otherwise median (range: 95% CI). In normally distributed data Tukey's method was used for post–hoc analysis. In non–normally distributed data, P for Mann–Whitney multiplied by 3, to adjust for multiple comparisons, was used for post–hoc analysis.

Table 5. Prevalence of sarcopenia according to the HOMA-IR in each gender group.

	HOMA-IR	Low 1/3	Middle 1/3	High 1/3	P^a	P^b	P^c	P^d
Men	Number (%)	192 (33.4%)	191 (33.3%)	191 (33.3%)				
	Age	76.3 ± 4.0	76.5 ± 3.9	76.9 ± 3.8	0.403			
	Sarcopenia							
	AWGS (%)	21 (10.9%)	19 (9.9%)	25 (13.1%)	0.612			
	KGS (%)	15 (7.8%)	8 (4.2%)	16 (8.4%)	0.210			
	FNIH (%)	12 (6.3%)	20 (10.5%)	33 (17.3%)	0.003	0.135	<0.001	0.054
	Muscle mass and function							
	MMI (kg/m^2)	6.8 ± 0.8	7.1 ± 0.8	7.2 ± 0.9	<0.001	0.006	<0.001	0.462
	HGS (kg)	32.0 ± 5.8	32.4 ± 5.8	31.6 ± 5.6	0.397			
	Gait speed(m/s)	1.26 ± 0.3	1.25 ± 0.3	1.14 ± 0.3	<0.001	0.999	<0.001	<0.001
	SPPB total score	10.9 ± 1.31	11.1 ± 1.27	10.8 ± 1.52	0.156			
	TUG test(s)	9.96 ± 2.30	9.83 ± 1.89	10.70 ± 2.78	0.003	0.999	0.027	0.003
	Abnormal Gait Speed (%)	7 (3.6%)	6 (3.1%)	18 (9.4%)	0.010	0.785	0.022	0.011
	Abnormal SPPB test (%)	29 (15.1%)	19 (9.9%)	28 (14.7%)	0.257			
	Abnormal TUG test (%)	9 (4.7%)	5 (2.6%)	17 (8.9%)	0.022	0.280	0.101	0.008
	K-ADL (score)	7.15 ± 0.5	7.08 ± 0.3	7.17 ± 0.62	0.509			
	K-IADL (score)	10.29 ± 0.9	10.28 ± 1.1	10.40 ± 1.5	0.792			

Women	Number (%)	218 (33.3%)	218 (33.3%)	218 (33.3%)				
	Age	75.7 ± 4.1	76.0 ± 3.9	75.9 ± 3.8	0.631			
	Sarcopenia							
	AWGS (%)	22 (10.1%)	18 (8.3%)	16 (7.3%)	0.579			
	KGS (%)	14 (6.4%)	13 (6.0%)	7 (3.2%)	0.263			
	FNIH (%)	15 (6.9%)	26 (11.9%)	19 (8.7%)	0.181			
	Muscle mass and function							
	MMI (kg/m^2)	5.7 ± 0.7	5.8 ± 0.7	6.1 ± 0.7	<0.001	0.122	<0.001	0.001
	HGS (kg)	20.5 ± 4.0	20.4 ± 4.0	21.1 ± 4.01	0.174			
	Gait speed(m/s)	1.11 ± 0.3	1.09 ± 0.2	1.05 ± 0.2	0.040	0.999	0.013	0.138
	SPPB total score	10.48 ± 1.9	10.45 ± 1.7	10.19 ± 1.7	0.031	0.999	0.047	0.103
	TUG test (s)	10.70 ± 2.9	10.85 ± 3.0	11.02 ± 2.9	0.409			
	Abnormal Gait Speed (%)	25 (11.5%)	24 (11.0%)	24 (11.0%)	0.985			
	Abnormal SPPB test (%)	49 (22.5%)	51 (23.4%)	60 (27.5%)	0.426			
	Abnormal TUG test (%)	24 (11.0%)	20 (9.2%)	21 (9.6%)	0.801			
	K-ADL (score)	7.17 ± 0.5	7.15 ± 0.4	7.18 ± 0.5	0.533			
	K-IADL (score)	10.37 ± 1.3	10.24 ± 0.9	10.32 ± 1.0	0.860			

Abnormal gait speed, ≤0.8m/s; Abnormal SPPB test, ≤9; abnormal TUG test, ≥14 seconds.

MMI, muscle mass index defined as appendicular skeletal muscle mass (ASM) in kilograms divided by the square of height; HGS, hand grip strength; SPPB, short physical performance battery; TUG test, timed up and go test; AWGS,

Asian working group for sarcopenia; KGS, Korean Geriatric Society; FNIH, Foundation for the National Institutes of Health. P^a: P for ANOVA in normally distributed data, P for Kruskal–Wallis in non–normally distributed data. P^b: HOMA–IR lowest 1/3 vs middle 1/3, P^c: HOMA–IR lowest 1/3 vs highest 1/3, P^d: HOMA–IR middle 1/3 vs highest 1/3. Data are mean ± SD in case of normal distribution, otherwise median (range: 95% CI). In normally distributed data Tukey' s method was used for post–hoc analysis. In non–normally distributed data, P for Mann–Whitney multiplied by 3, to adjust for multiple comparisons, was used for post–hoc analysis.