Difference between old and young adults in contribution of β-cell function and sarcopenia in developing diabetes mellitus

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ABSTRACT

Aims/Introduction: To investigate the difference in contributing factors in developing diabetes between old and young adults.

Materials and Methods: Subjects with recent-onset diabetes were selected from a nationwide survey data and classified according to age: elderly (age ≥75 years), middle-age (age 45–64 years) and young (age 25–39 years). The homeostasis model assessment of insulin resistance and β-cell function were calculated. Sarcopenia was assessed using dual-energy X-ray absorptiometry.

Results: The prevalence of recent-onset diabetes was 13.5%, 8.0%, and 1.4% in patients aged ≥75 years (unweighted n = 1,082), 45–64 years (unweighted n = 6,532), and 25–39 years (unweighted n = 5,178), respectively. Homeostasis model assessment of β-cell function along with homeostasis model assessment of insulin resistance showed increasing trends as onset age increased in recent-onset diabetes (P for trend < 0.001 in both). Elderly-onset diabetic patients had significantly higher homeostasis model assessment of β-cell function and homeostasis model assessment of insulin resistance compared with the middle-age-onset group (P < 0.001 and 0.014, respectively). Multivariate analysis showed that sarcopenia was significantly associated with recent-onset diabetes only in patients aged ≥75 years (odds ratio [OR] 2.478, 95% confidence interval [CI] 1.379–4.452) but not in patients aged 45–64 years. In the middle-age group, abdominal obesity (OR 2.933, 95% CI 2.086–4.122), hypertriglyceridemia (OR 1.529, 95% CI 1.078–2.169) and low high-density lipoprotein cholesterolemia (OR 1.930, 95% CI 1.383–2.695) were associated with recent-onset diabetes.

Conclusions: Elderly-onset diabetic patients had higher insulin resistance and relatively preserved β-cell function compared with middle-age-onset patients. Sarcopenia might play a more important role in developing diabetes in the elderly population.

INTRODUCTION

As life expectancy is being prolonged worldwide1, the prevalence of chronic diseases such as diabetes mellitus in the elderly population has been growing. In the USA, diabetes prevalence increased by 62% within a decade among older adults5. South Korea is one of the most rapidly aging countries in the world; the proportion of the elderly population aged ≥65 years in Korea has increased over the past 10 years from 7.2% of the total population in 2000 to 11.0% in 20105, along with an increase in diabetes prevalence in that population4. In recent years in Korea, the diabetes mellitus incidence in the population aged ≥70 years reached approximately 20 per 1,000 person-years, which was more than twice as high as that in young adults5. The trend of increasing diabetes incidence in older adults accords with a previous report from the USA6, and indicates that the increase in diabetes prevalence in the elderly population might be explained not only by the increasing elderly population, but also by other underlying differences between the elderly and the young in the risk for developing diabetes.
Type 2 diabetes mellitus is associated with a risk of atherosclerotic complications including coronary artery disease, cerebrovascular disease and peripheral artery disease, which are of great concern for public health.\textsuperscript{5,7,8,1} Increasing rates of diabetes in the elderly population could also increase the economic burden. Even though the prevalence and incidence of diabetes in the elderly population has been growing, very few studies have focused on the clinical characteristics of elderly-onset diabetes mellitus.

In the present study, we investigated the clinical characteristics of recent-onset diabetes in an elderly population, and also investigated the difference in contributing factors in developing diabetes between adults with elderly-onset and middle-age-onset diabetes. We analyzed data from the representative Korean National Health and Nutrition Examination Survey (KNHANES) 2008–2010.

**METHODS**

**Study population and database**

KNHANES is a nationwide, community-based, cross-sectional survey examining the general health and nutrition status of the non-institutionalized civilians of Korea. It has been carried out periodically since 1998, and annually since 2008 by the Division of Health and Nutritional Survey under the Korean Centers for Disease Control and Prevention, and details of the surveys have been described previously.\textsuperscript{9–11} Briefly, participants were selected by a stratified, multistage probability sampling design for the selection of household units. To ensure the results represent the entire Korean population, weights are assigned to each respondent.\textsuperscript{12}

The data we analyzed represent the recent years of the Korean population. The numbers of participants in the health examination in each KNHANES were as follows: 9,308 (response rate, 74.3\%) in 2008, 10,078 (response rate, 79.2\%) in 2009 and 8,473 (response rate, 77.5\%) in 2010. We included adults aged ≥25 years in the present study. All individuals voluntarily agreed to participate in this survey and provided informed consent. The KNHANES was approved by the ethics committee of the Korean Centers for Disease Control and Prevention (2008-04EXP-01-C, 2009-01CON-03-2C and 2010-02CON-21-C), and the study was carried out according to the Declaration of Helsinki guidelines 1995.

**Measurement of metabolic parameters**

Anthropometric measurements were recorded by well-trained examiners in the same manner in each study. Weight was measured to the nearest 0.1 kg using a calibrated balance-beam scale (Giant-150N; Hana, Seoul, Korea). Venous blood samples were drawn after a 12-h overnight fast, and plasma was separated immediately by centrifugation. The plasma glucose and lipid concentrations were measured enzymatically in a central laboratory using the Hitachi Automatic Analyzer 7600 (Hitachi, Tokyo, Japan). Fasting insulin levels were measured using immunoradiometric assays (INS-IRMA; BioSource, Nivelles, Belgium). The homeostasis model assessment of insulin resistance (HOMA-IR) and \(\beta\)-cell function (HOMA-\(\beta\)) was carried out as previously described.\textsuperscript{13} To confirm and compare the accuracy and consistency of each survey, all biochemical measurements were double checked on another day, and at least 40 samples were selected to be measured using the standard method according to the Clinical and Laboratory Standards Institute guidelines. The details of the measurement of metabolic parameters have been described previously.\textsuperscript{9,10}

Cases of diabetes mellitus were defined as subjects who used antidiabetic medication including insulin at the time of the survey or had 8-h fasting plasma glucose levels that were ≥7 mmol/L. The criterion for abdominal obesity in men and women was waist circumference (WC) ≥90 cm and ≥80 cm, respectively, using the International Obesity Task Force criteria for the Asian-Pacific population.\textsuperscript{14} Hypertriglyceridemia was defined as a triglyceride level ≥1.69 mmol/L after at least 12 h of fasting, a low high-density lipoprotein (HDL) cholesterol level was defined as <1.03 mmol/L in men and <1.28 mmol/L in women according to the National Cholesterol Education Program criteria,\textsuperscript{15} and hypertension was defined as blood pressure ≥140/90 mmHg or use of antihypertensive medication.

The presence of albuminuria was defined as a spot urine albumin/creatinine ratio of ≥30 μg/mg. The level of diabetetic retinopathy (DR) was evaluated using seven standard photographs following the Early Treatment for Diabetic Retinopathy Study,\textsuperscript{16} after pharmacological pupil dilatation. Eyes were graded based on the worse eye according to the Early Treatment for Diabetic Retinopathy Study severity scale, and categorized as no DR or any DR as described previously.\textsuperscript{17}

Daily activity and exercise were assessed by self-administered questionnaires. We defined subjects who exercised regularly as those who carried out vigorous exercise ≥20 min/day and ≥3 days/week or moderate-intensity exercise ≥30 min/day and ≥5 days/week.\textsuperscript{18}

To compare the differences in the risk factors for developing diabetes mellitus according to age, we selected patients with recent-onset diabetes, defined as those who have diabetes for <5 years according to self-administered questionnaires or newly detected diabetic patients in the KNHANES. We classified them according to age: elderly (age ≥75 years), middle age (45–64 years) and young (25–39 years); age-gaps between groups were made for clear discrimination of characteristics among age groups. Age-matched non-diabetic subjects were used to compare clinical characteristics of young and old adults.

**Measurement of body composition and definition of sarcopenia**

Whole-body dual-energy X-ray absorptiometry (Discovery W; Hologic, Waltham, MA, USA) was carried out for each participant to measure whole-body, and regional body fat and muscle mass in each compartment, including the arms, legs and trunk, following the manufacturer’s protocol as described.\textsuperscript{19} Appendicular skeletal muscle mass (ASM) was calculated as the sum of lean muscle mass in the bilateral upper and lower limbs.

Sarcopenia was defined as ASM divided by bodyweight (kg) as a percentage of bodyweight (ASM / weight), modified from...
the study of Janssen et al. Sarcopenia was classified as class I or class II, defined as ASM/weight 1–2 or ≥2 standard deviations, respectively, below the gender-specific mean for healthy young adults. Data from healthy men and women aged 20–39 years were used as reference values. The cut-off values for class I sarcopenia were 32.2% for men and 25.6% for women. For class II sarcopenia, the cut-off values were 29.1% for men and 23.0% for women.

Statistical analysis
All statistical analyses were carried out using SPSS (version 18; IBM SPSS Statistics; IBM Corp., Armonk, NY, USA) with complex-samples analysis procedures. We used KNHANES stratification variables and sampling weights designated by the Korean Centers for Disease Control and Prevention, which were based on the sample design of each survey year. Data are presented as percentage (standard error [SE]) for nominal data or means ± SE for continuous variables. The statistical significance of differences between the groups was evaluated using logistic regression analysis for categorical variables and a general linear model for continuous variables. The odds ratio (OR) and 95% confidence interval (CI) predicting diabetes were obtained from multivariate logistic regression models after controlling for age and HOMA-β. Significance was defined as \( P < 0.05 \).

RESULTS
Clinical characteristics of the study participants
We classified all participants according to age: ≥75 years, 45–64 years and 25–39 years. The prevalence of recent-onset diabetes was 13.5% (SE, 1.3%), 8.0% (SE, 0.4%), and 1.4% (SE, 0.2%) in participants aged ≥75 years, 45–64 years and 25–39 years, respectively; and the mean duration of diabetes was 1.4 years (SE, 0.1 years; Table 1). Although there was a higher percentage of women (63.5% [SE, 1.7%]) in participants aged ≥75 years, there was no difference in the prevalence of recent-onset diabetes according to sex in this age group (12.8% [SE, 1.9%] in men and 13.9% [SE, 1.7%] in women, \( P = 0.650 \)).

In non-diabetic participants, blood pressure, WC, and serum creatinine, triglyceride and low-density lipoprotein (LDL)-c-cholesterol levels tended to increase, and body mass index (BMI) and HDL-cholesterol levels tended to decrease with increasing age (Table 1). HOMA-β was significantly decreased as age increased (\( P \) for trend <0.001); however, there was no difference in HOMA-IR across the age groups in non-diabetic participants (\( P = 0.446 \)).

In participants with recent-onset diabetes, the same trends found in non-diabetic participants were observed for BMI, blood pressure, and HDL- and LDL-cholesterol levels according to age group (Table 1). However, HOMA-β along with HOMA-IR showed an increasing trend as onset age increased in recent-onset diabetes (\( P \) for trend = 0.002 and <0.001, respectively; Table 1). Elderly-onset diabetic patients had significantly higher HOMA-β and HOMA-IR compared with the middle-age-onset diabetic group (\( P < 0.001 \) and 0.014, respectively). There was no difference in BMI and WC between elderly-onset and middle-age-onset diabetic groups (Table 1).

Among the participants with recent-onset diabetes, the prevalence of DR was 8.7% (SE, 3.4%) and 6.9% (SE, 1.4%) in elderly-onset and middle-age-onset diabetic patients, respectively (\( P \) for group difference = 0.393). Albuminuria was more frequently found in elderly-onset diabetic patients compared with middle-age-onset patients, but the difference was not statistically significant (\( P = 0.078 \); Table 1). The prevalence of DR and albuminuria in young-onset diabetic patients was relatively high compared with the other groups (Table 1), but a statistically significant difference was found only for albuminuria (\( P = 0.025 \) and 0.419 for albuminuria and DR, respectively).

Risk factors for prediction of recent-onset diabetes mellitus according to age
We compared the association between recent-onset diabetes and diabetic risk factors, such as abdominal obesity, sarcopenia, hypertension, low HDL cholesterolemia and hypertriglyceridemia, according to age group. Because the unweighted number of participants in the young-onset diabetic group was too small to analyze the association between diabetes and metabolic risk factors, and there was a consistent trend in metabolic risk factors according to age, further analysis to characterize elderly-onset diabetes was carried out only in participants aged 45–64 years and ≥75 years.

Abdominal obesity, sarcopenia and hypertension were found more frequently in participants aged 45–64 years and ≥75 years with recent-onset diabetes compared with their respective control groups (Table 2). The association between sarcopenia and diabetes was more prominent in participants aged ≥75 years (age-adjusted OR 2.711, 95% CI 1.673–4.395, \( P < 0.001 \)) compared with that in participants aged 45–64 years (age-adjusted OR 1.550, 95% CI 1.222–1.966, \( P < 0.001 \)), which was also observed in a sex-stratified analysis (Table 2). By contrast, low HDL cholesterolemia and hypertriglyceridemia were significantly associated with recent-onset diabetes only in those aged 45–64 years (age-adjusted \( P = 0.001 \) and <0.001, respectively; Table 2). However, HOMA-β was significantly decreased in participants with recent-onset diabetes in both age groups (age-adjusted \( P < 0.001 \)).

Next, we carried out multivariate logistic analysis including age, sex, abdominal obesity, sarcopenia, hypertension, low HDL cholesterolemia, hypertriglyceridemia, exercise and HOMA-β to investigate the relative contribution of these metabolic risk factors to the prevalence of recent-onset diabetes mellitus in each age group. In the multivariate analysis, sarcopenia was significantly associated with diabetes only in participants aged ≥75 years (OR 2.478, 95% CI 1.379–4.542, \( P = 0.002 \)), but not in participants aged 45–64 years (OR 1.274, 95% CI 0.894–1.815, \( P = 0.180 \); Table 3). Abdominal obesity was also associated with recent-onset diabetes in the elderly group (OR 2.396,
Table 1 | Anthropometric and biochemical parameters of all study participants

| Age groups | Participants with DM | Participants without DM |
|------------|----------------------|-------------------------|
|            | 25–39 years | 45–64 years | ≥75 years | P† | P‡ |
|            | Unweighted n |            |            |    |    |
| Age (years) | 67 | 496 | 127 | <0.001 | <0.001 |
| Women (%)   | 35.1 (0.5) | 54.3 (0.3) | 79.2 (0.4) | <0.001 | <0.001 |
| Height (cm) | 167.7 (1.5) | 163.7 (0.5) | 154.1 (0.8) | <0.001 | <0.001 |
| Weight (kg) | 77.6 (2.1) | 68.2 (0.6) | 59.9 (0.9) | 0.495 | 0.495 |
| BMI (kg/m²) | 27.6 (0.6) | 25.4 (0.2) | 25.0 (0.3) | <0.001 | 0.296 |
| WC (cm)     | 89.8 (1.5) | 88.2 (0.5) | 88.4 (1.0) | 0.121 | 0.821 |
| SBP (mmHg)  | 121.7 (2.1) | 124.8 (0.9) | 133.1 (1.6) | <0.001 | 0.001 |
| DBP (mmHg)  | 82.4 (1.7) | 80.2 (0.5) | 74.0 (0.9) | <0.001 | <0.001 |
| Hb (g/dL)   | 15.2 (0.2) | 14.6 (0.1) | 13.6 (0.2) | 0.001 | 0.001 |
| FPG (mg/dL) | 163.6 (7.0) | 147.5 (2.5) | 139.9 (3.4) | 0.584 | 0.073 |
| Insulin (μU/mL) | 148.4 (1.3) | 120.5 (0.2) | 164.1 (1.5) | <0.001 | 0.001 |
| HOMA-IR (%) | 5.8 (0.5) | 4.4 (0.2) | 5.9 (0.7) | <0.001 | 0.014 |
| HOMA-β (%)  | 65.0 (6.4) | 61.4 (3.0) | 83.3 (6.2) | 0.002 | <0.001 |
| TC (mg/dL)  | 204.3 (4.8) | 194.0 (2.3) | 197.8 (4.0) | 0.008 | 0.406 |
| TG (mg/dL)  | 260.0 (28.6) | 206.1 (10.6) | 157.2 (7.3) | 0.001 | 0.006 |
| HDL (mg/dL) | 42.9 (0.9) | 43.8 (0.5) | 44.1 (1.1) | <0.001 | 0.976 |
| LDL (mg/dL) | 115.3 (4.8) | 112.8 (2.2) | 122.5 (3.8) | 0.002 | 0.024 |
| AST (IU/L)  | 34.7 (3.1) | 27.7 (0.8) | 24.0 (1.2) | 0.137 | 0.004 |
| ALT (IU/L)  | 46.1 (4.8) | 30.7 (0.9) | 22.3 (1.6) | <0.001 | 0.001 |
| Cr (mg/dL)  | 0.83 (0.02) | 0.87 (0.01) | 0.89 (0.02) | 0.828 | 0.378 |
| Onset of age (years) | 34.4 (0.5) | 52.8 (0.8) | 77.6 (0.5) | <0.001 | <0.001 |
| DM duration (years) | 0.7 (0.2) | 1.5 (0.1) | 1.5 (0.2) | 0.001 | 0.665 |
| DM medication (%) | 20.5 (5.6) | 48.8 (2.4) | 54.3 (4.9) | <0.001 | 0.324 |
| Insulin use (%) | 16.9 (14.9) | 3.5 (1.1) | 4.8 (2.5) | 0.110 | 0.586 |
| DMR (%) | 11.1 (5.7) | 6.9 (1.4) | 8.7 (3.4) | 0.624 | 0.393 |
| Albuminuria (%) | 9.6 (4.2) | 2.3 (0.7) | 5.9 (2.8) | 0.001 | 0.078 |

Values are presented as means or proportion (standard error). †Difference among all age groups from the general linear model for continuous variables or logistic regression analysis for categorical variables. ‡Difference between middle-age-onset group and elderly-onset group from the general linear model for continuous variables or logistic regression analysis for categorical variables. §These variables were log transformed before analyses. ¶Insulin users were excluded for the analysis. ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMI, body mass index; Cr, creatinine; DBP, diastolic blood pressure; DM, diabetes mellitus; DMAR, diabetes retinopathy; FPG, fasting plasma glucose; Hb, hemoglobin; HDL, high-density lipoprotein cholesterol; HOMA-β, homeostasis model assessment of β-cell function; HOMA-IR, homeostasis model assessment of insulin resistance; LDL, LDL cholesterol; SBP, systolic blood pressure; TC, total cholesterol; TG, triglyceride; WC, waist circumference.

95% CI 1.246–4.605, P = 0.009). For participants aged 45–64 years, abdominal obesity (OR 2.933, 95% CI 2.086–4.122, P < 0.001), hypertriglyceridemia (OR 1.529, 95% CI 1.078–2.169, P = 0.017), low HDL cholesterolemia (OR 1.930, 95% CI 1.383–2.695, P < 0.001), hypertension (OR 2.125, 95% CI, 1.534–2.943, P < 0.001) and male sex (OR 1.569, 95% CI 1.098–2.241, P = 0.014) were significantly associated with recent-onset diabetes mellitus.

Body composition analysis using whole-body dual-energy X-ray absorptiometry showed that total percent body fat increased and total lean body mass decreased as age increased in both diabetic (P for trend < 0.001 in both) and non-diabetic subjects (P for trend < 0.001 in both; Table 4). The prevalence of sarcopenia was increased as age increased regardless of the presence of diabetes. Sarcopenia prevalence in the diabetic participants was 66.0% (SE, 5.3%) and 40.8% (SE, 2.8%) in the elderly-onset and middle-age-onset groups, respectively (P for group difference < 0.001), whereas the prevalence in the non-diabetic participants was 41.7% (SE, 2.4%) and 29.7% (SE, 1.0%) in participants aged ≥75 years and 45–64 years, respectively (P for group difference < 0.001).

In the elderly-onset diabetic group, the advanced stage of sarcopenia (classified as class II) was found more frequently than the milder form (class I); the class II sarcopenia prevalence was 35.6% (SE, 6.5%), and that of class I was 30.4% (SE, 4.9%). The difference in sarcopenia prevalence between the elderly-onset and middle-age-onset diabetic groups was found only for sarcopenia class II (P < 0.001), but not for sarcopenia class I (P = 0.913; Table 4). In participants aged ≥75 years, there was no difference in the sarcopenia class I prevalence between diabetic (30.4% [SE, 4.9%]) and non-diabetic participants (30.9% [SE, 2.2%]; P = 0.926), but sarcopenia class II was more fre-
It is well known that sarcopenia increases the risk of diabetes\textsuperscript{21}. Sarcopenia is associated with a decreased metabolic rate\textsuperscript{22} and functional capacity\textsuperscript{23}, as well as increased insulin resistance itself\textsuperscript{23-25}. The important role of muscle in insulin resistance has been confirmed by epidemiological\textsuperscript{23,24} and experimental\textsuperscript{25} data. Furthermore, the contribution of sarcopenia has been thought to be more prominent in elderly patients with diabetes\textsuperscript{21}, which is in accord with the present study. We showed that the association between diabetes and sarcopenia in a multivariate model was significant only in the elderly group, but not in the middle-age group. The independent association between sarcopenia and diabetes in the elderly population might be explained by an accelerated loss of skeletal muscle with aging in elderly diabetic patients compared with age-matched non-diabetic subjects\textsuperscript{26}. In the present study, a markedly higher difference in the prevalence of sarcopenia class II rather than class I between diabetic and non-diabetic participants was found in the elderly group. Regarding pancreatic β-cell function, it is well-known that the proliferative and regenerative capacity of β-cells deteriorates with aging\textsuperscript{27}, which agrees with our findings in non-diabetic participants. However, in recent-onset diabetic patients, the elderly-onset group had significantly higher HOMA-β compared with the middle-age-onset group, although pancreatic β-

![Table 2 | Risk factors for prediction of recent-onset diabetes mellitus](http://onlinelibrary.wiley.com/journal/jdi)

|                        | Total       | Men         | Women        |
|------------------------|-------------|-------------|--------------|
| **Abdominal obesity**  |             |             |              |
| 45–64 years            | 2.131 (1.711–2.654) | <0.001 | 2.122 (1.567–2.875) | <0.001 |
| ≥75 years              | 3.177 (2.096–4.815) | <0.001 | 2.958 (1.438–6.087) | 0.003  |
| **Sarcopenia**         |             |             |              |
| 45–64 years            | 1.550 (1.222–1.966) | <0.001 | 1.719 (1.246–2.373) | 0.001  |
| ≥75 years              | 2.711 (1.673–4.395) | <0.001 | 3.496 (1.611–7.583) | 0.002  |
| **Hypertension**       |             |             |              |
| 45–64 years            | 2.402 (1.908–3.024) | <0.001 | 2.143 (1.613–2.847) | <0.001 |
| ≥75 years              | 2.330 (1.405–3.865) | 0.001 | 2.103 (1.003–4.408) | 0.049  |
| **Low HDL cholesterolia** |             |             |              |
| 45–64 years            | 1.446 (1.160–1.802) | 0.001 | 1.429 (1.089–1.877) | 0.010  |
| ≥75 years              | 1.469 (0.949–2.274) | 0.084 | 1.991 (1.024–3.874) | 0.043  |
| **Hypertriglyceridemia** |             |             |              |
| 45–64 years            | 2.237 (1.748–2.863) | <0.001 | 1.578 (1.150–2.165) | 0.005  |
| ≥75 years              | 1.460 (0.914–2.332) | 0.113 | 1.570 (0.745–3.307) | 0.637  |
| **HOMA-β**             |             |             |              |
| 45–64 years            | –7.960 (–8.935 to –6.985) | <0.001 | –7.970 (–9.307 to –6.634) | <0.001 |
| ≥75 years              | –4.039 (–5.414 to –2.664) | <0.001 | –3.883 (–6.098 to –1.667) | <0.001 |
| **Exercise**           |             |             |              |
| 45–64 years            | 1.042 (0.842–1.289) | 0.705 | 1.074 (0.810–1.425) | 0.619  |
| ≥75 years              | 1.105 (0.727–1.681) | 0.639 | 1.638 (0.810–3.312) | 0.170  |

Homeostasis model assessment of β-cell function (HOMA-β) was log transformed before analyses. †Logistic regression analysis for presence of diabetes mellitus adjusted for age. ‡Insulin users were excluded for the analysis. §Regression coefficients for log transformed HOMA-β. Vigorous exercise ≥20 min/day and ≥3 days/week or moderate-intensity exercise ≥30 min/day and ≥5 days/week. CI, confidence interval; HDL, high-density lipoprotein.

It is well known that sarcopenia increases the risk of diabetes\textsuperscript{21}. Sarcopenia is associated with a decreased metabolic rate\textsuperscript{22} and functional capacity\textsuperscript{23}, as well as increased insulin resistance itself\textsuperscript{23-25}. The important role of muscle in insulin resistance has been confirmed by epidemiological\textsuperscript{23,24} and experimental\textsuperscript{25} data. Furthermore, the contribution of sarcopenia has been thought to be more prominent in elderly patients with diabetes\textsuperscript{21}, which is in accord with the present study. We showed that the association between diabetes and sarcopenia in a multivariate model was significant only in the elderly group, but not in the middle-age group. The independent association between sarcopenia and diabetes in the elderly population might be explained by an accelerated loss of skeletal muscle with aging in elderly diabetic patients compared with age-matched non-diabetic subjects\textsuperscript{26}. In the present study, a markedly higher difference in the prevalence of sarcopenia class II rather than class I between diabetic and non-diabetic participants was found in the elderly group. Regarding pancreatic β-cell function, it is well-known that the proliferative and regenerative capacity of β-cells deteriorates with aging\textsuperscript{27}, which agrees with our findings in non-diabetic participants. However, in recent-onset diabetic patients, the elderly-onset group had significantly higher HOMA-β compared with the middle-age-onset group, although pancreatic β-

sequently found in those with recent-onset diabetes (35.6% [SE, 6.5%]) compared with non-diabetic participants (10.8% [SE, 1.5%], \(P < 0.001\)).

**DISCUSSION**

In the present study, we compared the clinical characteristics between elderly-onset and middle age-onset diabetic patients, and found that elderly-onset diabetic patients had higher insulin resistance and relatively preserved β-cell function compared with middle-age-onset patients. Although their insulin resistance was higher, the BMI and WC of elderly-onset participants were not different from middle-age-onset diabetic participants. Furthermore, their serum triglyceride level was significantly lower compared with middle-age-onset diabetic patients. Body composition analysis showed that there was no difference in fat mass between the two groups. However, elderly-onset diabetic patients had significantly lower skeletal muscle mass compared with the middle-age-onset group, and the sarcopenia prevalence was also significantly higher in the elderly-onset group. The presence of sarcopenia was a significant risk factor for diabetes in both age groups (45–64 years and ≥75 years); however, multivariate analysis adjusted for other metabolic risk factors showed that it was an independent risk factor only in participants aged ≥75 years.
Table 3 | Multivariate model for the prediction of recent-onset diabetes mellitus in participants aged 45–64 years and ≥75 years

| Age groups | Participants with recent-onset DM | Participants without DM |
|------------|----------------------------------|-------------------------|
|            | 25–39 years | 45–64 years | ≥75 years | P† | P‡ |
| Unweighted n | 67 | 496 | 127 | 5111 | 6036 | 955 |
| Total body fat percentage (%) | 28.6 (1.2) | 27.2 (0.4) | 33.0 (0.9) | <0.001 | <0.001 |
| Total body fat mass (kg) | 22.0 (1.2) | 18.5 (0.3) | 19.6 (0.7) | 0.010 | 0.181 |
| Total lean body mass (kg) | 54.3 (1.7) | 49.4 (0.6) | 39.3 (0.8) | 0.001 | 0.001 |
| ASM (kg) | 23.5 (0.8) | 21.1 (0.3) | 15.8 (0.4) | <0.001 | <0.001 |
| ASM/weight (%) | 30.7 (0.7) | 30.6 (0.2) | 26.7 (0.5) | <0.001 | <0.001 |

Values are presented as means or proportion (standard error). †Difference among age groups from general linear model for continuous variables or logistic regression analysis for categorical variables. ‡Difference between middle-age group and elderly-onset group from general linear model for continuous variables or logistic regression analysis for categorical variables. ASM, appendicular skeletal muscle mass; DM, diabetes mellitus.

Table 4 | Body composition parameters according to age of diabetic study participants

| Age groups | Participants with recent-onset DM | Participants without DM |
|------------|----------------------------------|-------------------------|
|            | 25–39 years | 45–64 years | ≥75 years | P† | P‡ |
| Abdominal obesity | 3.077 (2.311–4.097) | 1.599 (1.160–2.203) | 2.626 (1.397–4.157) | <0.001 | 0.004 |
| Sarcopenia | 1.280 (0.903–1.814) | 1.699 (1.232–2.343) | 1.766 (1.277–2.441) | <0.001 | <0.001 |
| Abdominal obesity | 2.933 (2.086–4.122) | 1.274 (0.894–1.815) | 1.599 (1.098–2.241) | <0.001 | 0.014 |
| Sarcopenia | 1.280 (0.903–1.814) | 1.699 (1.232–2.343) | 1.766 (1.277–2.441) | <0.001 | <0.001 |

Logistic regression analysis for presence of diabetes mellitus adjusting age and log transformed homeostasis model assessment of β-cell function.

Logistic regression analysis for presence of diabetes mellitus adjusting age and log transformed homeostasis model assessment of β-cell function.

Age groups

- 25–39 years
- 45–64 years
- ≥75 years

Participants with recent-onset DM

- Unweighted n: 67
- Total body fat percentage (%): 28.6 (1.2), 27.2 (0.4), 33.0 (0.9)
- Total body fat mass (kg): 22.0 (1.2), 18.5 (0.3), 19.6 (0.7)
- Total lean body mass (kg): 54.3 (1.7), 49.4 (0.6), 39.3 (0.8)
- ASM (kg): 23.5 (0.8), 21.1 (0.3), 15.8 (0.4)
- ASM/weight (%): 30.7 (0.7), 30.6 (0.2), 26.7 (0.5)

Participants without DM

- Unweighted n: 5111
- Total body fat percentage (%): 26.7 (0.2), 28.1 (0.2), 29.3 (0.4)
- Total body fat mass (kg): 17.3 (0.1), 17.5 (0.1), 15.9 (0.3)
- Total lean body mass (kg): 47.4 (0.2), 45.2 (0.1), 37.7 (0.3)
- ASM (kg): 20.7 (0.1), 19.2 (0.1), 15.5 (0.2)
- ASM/weight (%): 31.4 (0.1), 30.1 (0.1), 28.7 (0.2)

Considering the contribution of sarcopenia to the risk of diabetes mellitus in the elderly population, increasing muscle mass can be important for prevention or management of diabetes, and resistance training has been reported to be effective for that purpose in elderly subjects. Furthermore, resistance training...
can be superior to aerobic exercise because of its safety for subjects with cardiovascular disease\textsuperscript{30,31}, which is frequently found in elderly subjects.

The prevalence of diabetic complications in recent-onset diabetic patients in the present study was similar to a previous study of newly detected diabetic patients in Korea\textsuperscript{32}. The risk of diabetic nephropathy and DR is known to increase with age, even in elderly diabetic patients\textsuperscript{33–35}. In the present study, the prevalence of albuminuria and DR in elderly-onset diabetic patients was higher compared with that of middle-age-onset patients, despite a lack of statistical significance. Considering that elderly patients with diabetes are prone to rapidly progressive nephropathy\textsuperscript{34}, and that retinopathy progressed more rapidly during the first year of aggressive insulin therapy in elderly patients with baseline retinopathy\textsuperscript{36}, screening for diabetic nephropathy and retinopathy at the time of diabetes diagnosis should be carried out in elderly patients.

The main limitation of the present study was that as KNHANES is a cross-sectional evaluation of the health and nutritional status of Koreans, the findings of this study should be interpreted with caution regarding causal relationships. Further large-scale replication studies with a prospective design are warranted to confirm our findings. Second, we defined recent-onset diabetes according to self-administered questionnaires, which can result in misclassification of study participants due to recall bias. Furthermore, the relatively small number of unweighted subjects weakened the statistical power of the present results. However, the serially increasing or decreasing trends of clinical characteristics in subjects with recent-onset diabetes according to age group reflect that the present study design might be acceptable to characterize elderly-onset compared with middle-age-onset diabetes. In addition, the prevalence of diabetic complications in recent-onset diabetic patients in our study was similar to a previous study in Korea\textsuperscript{32}, which reflects that the classification of recent-onset diabetes in our study was acceptable considering that the prevalence of diabetic complications is increasing as disease duration increases. Furthermore, the prevalence of DR was less than that of a previous report of the entire diabetic patients in KNHANES regardless of disease duration, that is, 15.8% in KNHANES\textsuperscript{17}.

In summary, elderly-onset diabetic patients had more preserved $\beta$-cell function, but nevertheless were insulin resistant and had a more severe form of sarcopenia compared with middle-age-onset diabetic patients. The present study showed that sarcopenia was an independent risk factor contributing to the development of diabetes in an elderly population. Proper lifestyle management combined with resistance training should be recommended to reduce the burden of sarcopenia and diabetes, especially in an elderly population. Further investigation is required to elucidate the causal relationship between sarcopenia and the development of type 2 diabetes in older adults.

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**DISCLOSURE**

The authors declare no conflict of interest.

**REFERENCES**

1. World Population Prospects: The 2012 Revision, Key Findings and Advance Tables United Nations, Department of Economic and Social Affairs, Population Division, 2013.
2. Sloan FA, Bethel MA, Ruiz D Jr, et al. The growing burden of diabetes mellitus in the US elderly population. *Arch Intern Med* 2008; 168: 192–199; discussion 199.
3. Population Projections for Korea: 2010–2040 Statistics Korea, 2011.
4. Koo BK, Kim EK, Choi H, et al. Decreasing trends of the prevalence of diabetes and obesity in Korean women aged 30–59 years over the past decade: results from the Korean national health and nutrition examination survey, 2001–2010. *Diabetes Care* 2013; 36: e95–e96.
5. Koo BK, Lee CH, Yang BR, et al. The incidence and prevalence of diabetes mellitus and related atherosclerotic complications in Korea: a National Health Insurance Database Study. *PLoS ONE* 2014; 9: e110650.
6. McBean AM, Li S, Gilbertson DT, et al. Differences in diabetes prevalence, incidence, and mortality among the elderly of four racial/ethnic groups: whites, blacks, Hispanics, and Asians. *Diabetes Care* 2004; 27: 2317–2324.
7. Roh E, Ko S-H, Kwon H-S, et al. Prevalence and management of dyslipidemia in Korea: Korea National Health and Nutrition Examination Survey during 1998 to 2010. *Diabetes Metab J* 2013; 37: 433–449.
8. Kim CS, Ko S-H, Kwon H-S, et al. Prevalence, awareness, and management of obesity in Korea: data from the Korea national health and nutrition examination survey (1998–2011). *Diabetes Metab J* 2014; 38: 35–43.
9. Lim S, Shin H, Song JH, et al. Increasing prevalence of metabolic syndrome in Korea: the Korean National Health and Nutrition Examination Survey for 1998–2007. *Diabetes Care* 2011; 34: 1323–1328.
10. Choi YJ, Kim HC, Kim HM, et al. Prevalence and management of diabetes in Korean adults: Korea National Health and Nutrition Examination Surveys 1998–2005. *Diabetes Care* 2009; 32: 2016–2020.
11. Lee WK, Kong KA, Park H. Effect of preexisting musculoskeletal diseases on the 1-year incidence of fall-related injuries. *J Prev Med Public Health* 2012; 45: 283–290.
12. Brogan D. Software for Sample Survey Data, Misuse of Standard Packages. In: Peter Armitage, Theodore Colton (eds). *Encyclopedia of Biostatistics*. New York: John Wiley and Sons, 1998; 5: 4167–4174.
13. Matthews DR, Hosker JP, Rudenski AS, et al. Homeostasis model assessment: insulin resistance and beta-cell function from fasting plasma glucose and insulin concentrations in man. *Diabetologia* 1985; 28: 412–419.
14. World Health Organisation IAIfSoo, International Obesity TaskForce. The Asia-Pacific Perspective: Redefining Obesity
and its Treatment. Sydney, NSW: Health Communications; 2000.
15. Grundy SM, Cleeman JI, Daniels SR, et al. Diagnosis and management of the metabolic syndrome: an American Heart Association/National Heart, Lung, and Blood Institute Scientific Statement. Circulation 2005; 112: 2735–2752.
16. Diabetic retinopathy study. Report Number 6. Design, methods, and baseline results. Report Number 7. A modification of the Airlie House classification of diabetic retinopathy. Prepared by the Diabetic Retinopathy. Invest Ophthalmol Vis Sci 1981; 21: 1–226.
17. Lee SW, Youm Y, Lee WJ, et al. Prevalence and risk factors for diabetic retinopathy: the Korea National Health and Nutrition Examination Survey 2008-2011. Invest Ophthalmol Vis Sci 2013; 54: 6827–6833.
18. Haskell WL, Lee IM, Pate RR, et al. Physical activity and public health: updated recommendation for adults from the American College of Sports Medicine and the American Heart Association. Circulation 2007; 116: 1081–1093.
19. Janssen I, Heymsfield SB, Ross R. Low relative skeletal muscle mass (sarcopenia) in older persons is associated with functional impairment and physical disability. J Am Geriatr Soc 2002; 50: 889–896.
20. Kim TN, Park MS, Yang SJ, et al. Total-body skeletal muscle mass: estimation by a new dual-energy X-ray absorptiometry method. Am J Clin Nutr 2002; 76: 378–383.
21. Jee D, Lee WK, Kang S. Prevalence and risk factors for diabetic retinopathy: the Korea National Health and Nutrition Examination Survey 2008-2011. Invest Ophthalmol Vis Sci 2013; 54: 6827–6833.
22. Grundy SM, Cleeman JI, Daniels SR, et al. Diagnosis and management of the metabolic syndrome: an American Heart Association/National Heart, Lung, and Blood Institute Scientific Statement. Circulation 2005; 112: 2735–2752.
23. Lim S, Kim JH, Yoon JW, et al. Sarcopenic obesity: prevalence and association with metabolic syndrome in the Korean Longitudinal Study on Health and Aging (KLoSHA). Diabetes Care 2010; 33: 1652–1654.
24. Lee SW, Youm Y, Lee WJ, et al. Appendicular skeletal muscle mass and insulin resistance in an elderly korean population: the korean social life, health and aging project-health examination cohort. Diabetes Metab J 2015; 39: 37–45.
25. Skov-Jensen C, Skovbro M, Flint A, et al. Contraction-mediated glucose uptake is increased in men with impaired glucose tolerance. Appl Physiol Nutr Metab 2007; 32: 115–124.
26. Park SW, Goodpaster BH, Strotmeyer ES, et al. Accelerated loss of skeletal muscle strength in older adults with type 2 diabetes: the health, aging, and body composition study. Diabetes Care 2007; 30: 1507–1512.
27. Dunstan DW, Daly RM, Owen N, et al. High-intensity resistance training improves glycemic control in older patients with type 2 diabetes. Diabetes Care 2002; 25: 1729–1736.
28. Willey KA, Singh MA. Battling insulin resistance in elderly obese people with type 2 diabetes: bring on the heavy weights. Diabetes Care 2003; 26: 1580–1588.
29. Janssen I, Heymsfield SB, Ross R. Low relative skeletal muscle mass (sarcopenia) in older persons is associated with functional impairment and physical disability. J Am Geriatr Soc 2002; 50: 889–896.
30. Kim JH, Kwon HS, Park YM, et al. Prevalence and associated factors of diabetic retinopathy in rural Korea: the Chungju metabolic disease cohort study. J Korean Med Sci 2011; 26: 1068–1073.
31. Kim JH, Kwon HS, Park YM, et al. Prevalence and associated factors of diabetic retinopathy in rural Korea: the Chungju metabolic disease cohort study. J Korean Med Sci 2011; 26: 1068–1073.
32. Retnakaran R, Cull CA, Thorne KJ, et al. Risk factors for renal dysfunction in type 2 diabetes: U.K. Prospective Diabetes Study 74. Diabetes 2006; 55: 1832–1839.
33. Huang ES, Latierarong N, Liu Y, et al. Rates of complications and mortality in older patients with diabetes mellitus: the diabetes and aging study. JAMA Intern Med 2014; 174: 251–258.
34. Hornick T, Aron DC. Preventing and managing diabetic complications in elderly patients. Cleveol Clin J Med 2008; 75: 153–158.
35. Tovi J, Ingemansson SO, Engfeldt P. Insulin treatment of elderly type 2 diabetic patients: effects on retinopathy. Diabetes Metab J 1998; 24: 442–447.