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# 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 worldwide[1], 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 adults[2]. 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 2010[3], along with an increase in diabetes prevalence in that population[4]. 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 adults[5]. The trend of increasing diabetes incidence in older adults accords with a previous report from the USA[6], 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.

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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[5,7,8]; 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[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[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 β-cell function (HOMA-β) was carried out as previously described[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[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[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[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 diabetic retinopathy (DR) was evaluated using seven standard photographs following the Early Treatment for Diabetic Retinopathy Study[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[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[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[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 by ASM divided by bodyweight (kg) as a percentage of bodyweight (ASM / weight), modified from

the study of Janssen *et al.*[20]. 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 $P < 0.050$.

## 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)-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 1.379–4.452, $P = 0.002$), 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*‡ | 25–39 years | 45–64 years | ≥75 years | *P*† | *P*‡ |
| Unweighted *n* | 67 | 496 | 127 | | | 5111 | 6036 | 955 | | |
| Age (years) | 35.1 (0.5) | 54.3 (0.3) | 79.2 (0.4) | <0.001 | <0.001 | 32.2 (0.1) | 52.7 (0.1) | 78.8 (0.1) | <0.001 | <0.001 |
| Women (%) | 29.4 (5.8) | 35.3 (2.4) | 65.7 (4.6) | <0.001 | <0.001 | 48.6 (0.7) | 51.2 (0.6) | 63.5 (1.7) | <0.001 | <0.001 |
| Height (cm) | 167.7 (1.5) | 163.7 (0.5) | 154.1 (0.8) | <0.001 | <0.001 | 167.0 (0.1) | 162.1 (0.1) | 153.3 (0.4) | <0.001 | <0.001 |
| Weight (kg) | 77.6 (2.1) | 68.2 (0.6) | 59.4 (0.9) | 0.495 | <0.001 | 65.2 (0.2) | 63.3 (0.1) | 54.0 (0.4) | <0.001 | <0.001 |
| BMI (kg/m$^2$) | 27.6 (0.6) | 25.4 (0.2) | 25.0 (0.3) | <0.001 | 0.296 | 23.2 (0.1) | 24.0 (0.0) | 22.9 (0.1) | <0.001 | <0.001 |
| WC (cm) | 89.8 (1.5) | 88.2 (0.5) | 88.4 (1.0) | 0.121 | 0.821 | 79.0 (0.2) | 82.5 (0.1) | 81.7 (0.4) | <0.001 | 0.040 |
| SBP (mmHg) | 121.7 (2.1) | 124.8 (0.9) | 133.1 (1.6) | <0.001 | <0.001 | 108.9 (0.2) | 120.0 (0.3) | 132.8 (0.7) | <0.001 | <0.001 |
| DBP (mmHg) | 82.4 (1.7) | 80.2 (0.5) | 74.0 (0.9) | <0.001 | <0.001 | 72.8 (0.2) | 78.1 (0.2) | 74.5 (0.4) | <0.001 | <0.001 |
| Hb (g/dL) | 15.2 (0.2) | 14.6 (0.1) | 13.6 (0.2) | 0.001 | <0.001 | 14.2 (0.0) | 14.1 (0.0) | 13.3 (0.1) | <0.001 | <0.001 |
| FPG (mg/dL) | 163.6 (7.0) | 147.5 (2.5) | 139.9 (3.4) | 0.584 | 0.073 | 90.1 (0.2) | 95.0 (0.2) | 95.7 (0.4) | <0.001 | 0.081 |
| Insulin (μIU/mL)§,¶ | 14.8 (1.3) | 12.0 (0.5) | 16.4 (1.5) | <0.001 | 0.001 | 10.1 (0.1) | 9.4 (0.1) | 9.4 (0.2) | <0.001 | 0.438 |
| HOMA-IR§,¶ | 5.8 (0.5) | 4.4 (0.2) | 5.9 (0.7) | <0.001 | 0.014 | 2.3 (0.0) | 2.2 (0.0) | 2.2 (0.0) | 0.446 | 0.486 |
| HOMA-β§,¶ | 65.0 (6.4) | 61.4 (3.0) | 83.3 (6.2) | 0.002 | <0.001 | 141.1 (1.4) | 112.3 (1.2) | 109.8 (2.4) | <0.001 | 0.064 |
| TC (mg/dL) | 204.3 (4.8) | 194.0 (2.3) | 197.8 (4.0) | 0.008 | 0.406 | 180.3 (0.6) | 195.1 (0.6) | 195.6 (1.6) | <0.001 | 0.782 |
| TG (mg/dL)§ | 260.0 (28.6) | 206.1 (10.6) | 157.2 (7.3) | 0.001 | 0.006 | 120.7 (1.6) | 145.1 (2.1) | 137.5 (3.1) | <0.001 | 0.555 |
| HDL (mg/dL)§ | 42.8 (0.9) | 43.8 (0.5) | 44.1 (1.1) | <0.001 | 0.937 | 49.2 (0.2) | 48.0 (0.2) | 45.8 (0.4) | <0.001 | <0.001 |
| LDL (mg/dL) | 115.3 (4.8) | 112.8 (2.2) | 122.5 (3.8) | 0.002 | 0.024 | 107.7 (0.5) | 119.4 (0.6) | 122.6 (1.3) | <0.001 | 0.031 |
| AST (IU/L)§ | 34.7 (3.1) | 27.7 (0.8) | 24.0 (1.2) | 0.137 | 0.004 | 20.4 (0.2) | 23.7 (0.2) | 22.9 (0.3) | <0.001 | 0.856 |
| ALT (IU/L)§ | 46.1 (4.8) | 30.7 (0.9) | 22.3 (1.6) | <0.001 | <0.001 | 22.3 (0.3) | 22.9 (0.3) | 17.2 (0.4) | <0.001 | <0.001 |
| Cr (mg/dL) | 0.83 (0.02) | 0.87 (0.01) | 0.89 (0.02) | 0.828 | 0.378 | 0.85 (0.01) | 0.84 (0.00) | 0.88 (0.01) | <0.001 | <0.001 |
| Onset of age (years) | 34.4 (0.5) | 52.8 (0.3) | 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) | 0.014 | 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; DMR, diabetic 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-

**Table 2** | Risk factors for prediction of recent-onset diabetes mellitus

| | Total | | Men | | Women | |
|---|---|---|---|---|---|---|
| | Odds ratio† (95% CI) | *P*-value | Odds ratio† (95% CI) | *P*-value | Odds ratio† (95% CI) | *P*-value |
| Abdominal obesity | | | | | | |
| 45–64 years | 2.131 (1.711–2.654) | <0.001 | 2.122 (1.567–2.875) | <0.001 | 4.316 (2.864–6.505) | <0.001 |
| ≥75 years | 3.177 (2.096–4.815) | <0.001 | 2.958 (1.438–6.087) | 0.003 | 3.891 (2.091–7.241) | <0.001 |
| Sarcopenia | | | | | | |
| 45–64 years | 1.550 (1.222–1.966) | <0.001 | 1.719 (1.246–2.373) | 0.001 | 1.687 (1.168–2.435) | 0.005 |
| ≥75 years | 2.711 (1.673–4.395) | <0.001 | 3.496 (1.611–7.583) | 0.002 | 2.337 (1.261–4.329) | 0.007 |
| Hypertension | | | | | | |
| 45–64 years | 2.402 (1.908–3.024) | <0.001 | 2.143 (1.613–2.847) | <0.001 | 2.553 (1.786–3.647) | <0.001 |
| ≥75 years | 2.330 (1.405–3.865) | 0.001 | 2.103 (1.003–4.408) | 0.049 | 2.491 (1.187–5.229) | 0.016 |
| Low HDL cholesterolemia | | | | | | |
| 45–64 years | 1.446 (1.160–1.802) | 0.001 | 1.429 (1.089–1.877) | 0.010 | 2.117 (1.424–3.146) | <0.001 |
| ≥75 years | 1.469 (0.949–2.274) | 0.084 | 1.991 (1.024–3.874) | 0.043 | 1.212 (0.666–2.207) | 0.527 |
| Hypertriglyceridemia | | | | | | |
| 45–64 years | 2.237 (1.748–2.863) | <0.001 | 1.578 (1.150–2.165) | 0.005 | 3.068 (2.070–4.547) | <0.001 |
| ≥75 years | 1.460 (0.914–2.332) | 0.113 | 1.570 (0.745–3.307) | 0.637 | 1.485 (0.819–2.693) | 0.192 |
| HOMA-β‡ | | | | | | |
| 45–64 years | −7.960 (−8.935 to −6.985)§ | <0.001 | −7.970 (−9.307 to −6.634)§ | <0.001 | −7.826 (−9.214 to −6.438)§ | <0.001 |
| ≥75 years | −4.039 (−5.414 to −2.664)§ | <0.001 | −3.883 (−6.098 to −1.667)§ | 0.001 | −4.291 (−6.032 to −2.549)§ | <0.001 |
| Exercise¶ | | | | | | |
| 45–64 years | 1.042 (0.842–1.289) | 0.705 | 1.074 (0.810–1.425) | 0.619 | 0.994 (0.717–1.377) | 0.971 |
| ≥75 years | 1.105 (0.727–1.681) | 0.639 | 1.638 (0.810–3.312) | 0.170 | 0.874 (0.496–1.540) | 0.640 |

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.

quently 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.

It is well known that sarcopenia increases the risk of diabetes[21]. Sarcopenia is associated with a decreased metabolic rate[22] and functional capacity[23], as well as increased insulin resistance itself[23–25]. The important role of muscle in insulin resistance has been confirmed by epidemiological[23,24] and experimental[25] data. Furthermore, the contribution of sarcopenia has been thought to be more prominent in elderly patients with diabetes[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[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[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 3** | Multivariate model for the prediction of recent-onset diabetes mellitus in participants aged 45–64 years and ≥75 years

| | 45–64 years | | ≥75 years | |
|---|---|---|---|---|
| | Odds ratio† (95% CI) | *P*-value | Odds ratio† (95% CI) | *P*-value |
| Model 1 | | | | |
| Abdominal obesity | 3.077 (2.311–4.097) | <0.001 | 2.735 (1.631–4.586) | <0.001 |
| Sarcopenia | 1.599 (1.160–2.203) | 0.004 | 2.557 (1.474–4.438) | 0.001 |
| Model 2 | | | | |
| Abdominal obesity | 2.863 (2.096–3.911) | <0.001 | 2.295 (1.343–3.923) | 0.003 |
| Sarcopenia | 1.433 (1.018–2.018) | 0.039 | 2.958 (1.622–5.395) | <0.001 |
| Hypertriglyceridemia | 2.092 (1.535–2.850) | <0.001 | 1.261 (0.674–2.359) | 0.467 |
| Model 3 | | | | |
| Abdominal obesity | 2.578 (1.874–3.547) | <0.001 | 2.153 (1.274–3.636) | 0.004 |
| Sarcopenia | 1.280 (0.903–1.814) | 0.166 | 2.814 (1.561–5.075) | 0.001 |
| Hypertriglyceridemia | 1.699 (1.232–2.343) | 0.001 | 1.072 (0.531–2.164) | 0.846 |
| Low HDL cholesterolemia | 1.766 (1.277–2.441) | 0.001 | 1.363 (0.716–2.594) | 0.344 |
| Hypertension | 2.197 (1.586–3.045) | <0.001 | 2.241 (1.301–3.860) | 0.004 |
| Model 4 | | | | |
| Abdominal obesity | 2.933 (2.086–4.122) | <0.001 | 2.396 (1.246–4.605) | 0.009 |
| Sarcopenia | 1.274 (0.894–1.815) | 0.180 | 2.478 (1.379–4.452) | 0.002 |
| Hypertriglyceridemia | 1.529 (1.078–2.169) | 0.017 | 1.173 (0.565–2.435) | 0.668 |
| Low HDL cholesterolemia | 1.930 (1.383–2.695) | <0.001 | 1.289 (0.629–2.638) | 0.487 |
| Hypertension | 2.125 (1.534–2.943) | <0.001 | 2.567 (1.475–4.470) | 0.001 |
| Exercise‡ | 1.135 (0.824–1.564) | 0.438 | 1.470 (0.808–2.677) | 0.207 |
| Sex§ | 1.569 (1.098–2.241) | 0.014 | 1.247 (0.593–2.620) | 0.560 |

†Logistic regression analysis for presence of diabetes mellitus adjusting age and log transformed homeostasis model assessment of β-cell function. ‡Vigorous exercise ≥20 min/day and ≥3 days/week or moderate-intensity exercise ≥30 min/day and ≥5 days/week. §Reference sex: women. CI, confidence interval; HDL, high-density lipoprotein.

**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*‡ | 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 | 26.7 (0.2) | 28.1 (0.2) | 29.3 (0.4) | <0.001 | 0.007 |
| Total body fat mass (kg) | 22.0 (1.2) | 18.5 (0.3) | 19.6 (0.7) | 0.010 | 0.181 | 17.3 (0.1) | 17.5 (0.1) | 15.9 (0.3) | <0.001 | <0.001 |
| Total lean body mass (kg) | 54.3 (1.7) | 49.4 (0.6) | 39.3 (0.8) | <0.001 | <0.001 | 47.4 (0.2) | 45.2 (0.1) | 37.7 (0.3) | <0.001 | <0.001 |
| ASM (kg) | 23.5 (0.8) | 21.1 (0.3) | 15.8 (0.4) | <0.001 | <0.001 | 20.7 (0.1) | 19.2 (0.1) | 15.5 (0.2) | <0.001 | <0.001 |
| ASM/weight (%) | 30.7 (0.7) | 30.6 (0.2) | 26.7 (0.5) | <0.001 | <0.001 | 31.4 (0.1) | 30.1 (0.1) | 28.7 (0.2) | <0.001 | <0.001 |
| Sarcopenia | | | | | | | | | | |
| Total | 40.6 (7.9) | 40.8 (2.8) | 66.0 (5.3) | 0.001 | <0.001 | 20.6 (0.9) | 29.7 (1.0) | 41.7 (2.4) | <0.001 | <0.001 |
| Class I | 28.6 (7.6) | 31.0 (2.6) | 30.4 (4.9) | 0.959 | 0.913 | 18.1 (0.8) | 24.7 (0.9) | 30.9 (2.2) | <0.001 | 0.004 |
| Class II | 12.0 (5.8) | 9.8 (2.1) | 35.6 (6.5) | <0.001 | <0.001 | 2.5 (0.3) | 5.0 (0.5) | 10.8 (1.5) | <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.

cell dysfunction is an important risk factor for diabetes in all age groups. These findings might also reflect that in the elderly population, insulin resistance rather than β-cell dysfunction might be more important in the development of diabetes mellitus compared with the middle-aged participants.

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[28,29]. Furthermore, resistance training

can be superior to aerobic exercise because of its safety for subjects with cardiovascular disease[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[32]. The risk of diabetic nephropathy and DR is known to increase with age, even in elderly diabetic patients[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[34], and that retinopathy progressed more rapidly during the first year of aggressive insulin therapy in elderly patients with baseline retinopathy[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[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[17].

In summary, elderly-onset diabetic patients had more preserved β-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.

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