

ONLINE APPENDIX

Additional details on methods

Study subjects The Korean Sarcopenic Obesity Study (KSOS) is an ongoing epidemiologic study supported by the Korea Science and Engineering Foundation. This prospective observational cohort was designed to examine prevalence of sarcopenia and sarcopenic obesity in Korean adults with or without diabetes and to evaluate their effects on metabolic disorders and health outcomes; details have been previously published (1). Participants were enrolled for the KSOS cohort between September 2007 and August 2009. Study participants included 446 well-functioning, community-dwelling healthy volunteers without diabetes recruited from residents of Seoul, Korea and 428 diabetic patients treated at the Diabetes Center of Korea University Guro Hospital. None of the participants had a history of cardiovascular disease (myocardial infarction, unstable angina, stroke or cardiovascular revascularization), stage 2 hypertension (resting blood pressure, $\geq 160/100$ mmHg), malignant disease or severe renal or hepatic disease. Finally, analysis was conducted on 810 subjects (414 patients with type 2 diabetes, 396 control subjects) who had complete data on body composition. In order to define the definition of sarcopenia, another 145 healthy subjects (aged 20-39 years; 145 subjects) were employed as a young reference group. Medical histories and lifestyle information were collected by personal interview using a detailed questionnaire on current medications, smoking status, alcohol drinking, and physical activity (2). All participants provided written informed consent, and the Korea University Institutional Review Board, in accordance with the Declaration of Helsinki of the World Medical Association approved this study protocol.

Clinical and laboratory measurements: All blood samples were obtained in the morning after a 12-hour overnight fast and were immediately stored at -80° C for subsequent assays. Serum triglycerides and HDL cholesterol were determined enzymatically using a chemistry analyzer (Hitachi 747; Tokyo, Japan). A glucose oxidase method was used to measure fasting plasma glucose (FPG). A1C was measured using high performance liquid chromatography (Bio-Rad Variant II).

Body composition: Body mass index (BMI) was calculated as $\text{weight}/\text{height}^2$ (kg/m^2) and waist circumference was measured at the midpoint between the lower border of the rib cage and the iliac crest. A whole body DXA scan was performed for each patient to measure total and regional lean mass (kg), total body fat (kg) and total body fat percentage (%) using fan-beam technology (Hologic Discovery A, Hologic; Bedford, MA, USA). Appendicular skeletal muscle mass (ASM (kg)) was defined as the sum of lean soft tissue masses for the arms and legs, following the method of Heymsfield et al (3). ASM adjusted by stature index ($\text{ASM}/\text{height}^2$) was also computed as described by Baumgartner et al (4). Total skeletal muscle mass (kg) was also obtained from ASM by using the predictive equation of Kim et al (5). As described by Janssen et al, skeletal muscle index (SMI (%)); total skeletal muscle mass (kg)/weight (kg) $\times 100$ was obtained by calculation of total skeletal muscle mass adjusted by weight (6).

Definition of sarcopenia: First, sarcopenia was defined as $\text{ASM}/\text{height}^2$ less than two

standard deviations (SD) below the sex-specific normal mean for the young reference group from the entire study population (4). Alternatively, relative low muscle mass (sarcopenia) was defined as SMI (%) less than two SD below the mean of the young reference group (6). We previously established cut-off values for sarcopenia of 7.40 kg/m² (ASM/height²) and 35.71% (SMI) in Korean men, defined as less than two SD below the sex-specific normal mean for the young reference group. For Korean women, the corresponding limits were 5.14 kg/m² (ASM/height²) and 30.70% (SMI) (1).

Statistical analysis: Data are expressed as means \pm SD or median [inter-quartile range]. Discrete variables are presented as percentage. Differences in baseline characteristics and body composition indices according to diabetes status were tested using the independent two-sample *t*-test or Wilcoxon's rank-sum test and Pearson's chi-square test. The Analysis of covariance (ANCOVA) method was used to compare body composition between subjects with and without type 2 diabetes after adjusting for confounding factors. Prevalence of sarcopenia was compared in those with type 2 diabetes versus those without diabetes using Pearson's chi-square test. Simple logistic regression analysis was used to examine the independent influence of type 2 diabetes on sarcopenia and the odds ratio (OR) was computed. In addition, adjustment for potential confounders such as age and gender was performed using multiple logistic regression analysis (model 1); plus BMI (model 2); plus smoking, alcohol drinking, and physical activity (model 3); plus antihypertensive agent, lipid lowering agent, systolic and diastolic blood pressure, total cholesterol, triglyceride, and HDL-cholesterol (model 4). All statistical outcomes based on two-sided tests were obtained from SPSS for Windows (Version 12.0, SPSS Inc., Chicago, IL, USA). The *P*-value <0.05 was regarded as statistically significant.

References

1. **Kim TN, Yang SJ, Yoo HJ, Lim KI, Kang HJ, Song W, Seo JA, Kim SG, Kim NH, Baik SH, Choi DS, Choi KM.** Prevalence of sarcopenia and sarcopenic obesity in Korean adults: the Korean sarcopenic obesity study. *Int J Obes (Lond)* 2009;33:885-892
2. **Salti I, Benard E, Detournay B, Bianchi-Biscay M, Le Brigand C, Voinet C, Jabbar A.** A population-based study of diabetes and its characteristics during the fasting month of Ramadan in 13 countries: results of the epidemiology of diabetes and Ramadan 1422/2001 (EPIDIAR) study. *Diabetes Care* 2004;27:2306-2311
3. **Heymsfield SB, Smith R, Aulet M, Bensen B, Lichtman S, Wang J, Pierson RN, Jr.** Appendicular skeletal muscle mass: measurement by dual-photon absorptiometry. *Am J Clin Nutr* 1990;52:214-218
4. **Baumgartner RN, Koehler KM, Gallagher D, Romero L, Heymsfield SB, Ross RR, Garry PJ, Lindeman RD.** Epidemiology of sarcopenia among the elderly in New Mexico. *Am J Epidemiol* 1998;147:755-763
5. **Kim J, Wang Z, Heymsfield SB, Baumgartner RN, Gallagher D.** Total-body skeletal muscle mass: estimation by a new dual-energy X-ray absorptiometry method. *Am J Clin Nutr* 2002;76:378-383
6. **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

Supplementary Table 1. Clinical, metabolic and anthropometric characteristics of study subjects

Parameter	Men		P-value	Women		P-value
	With diabetes (n = 218)	Without diabetes (n = 152)		With diabetes (n = 196)	Without diabetes (n = 244)	
Age (years)	58.5 ± 9.3	58.1 ± 10.5	0.761	59.3 ± 8.5	58.2 ± 9.1	0.174
Height (cm)	167.3 ± 5.4	168.2 ± 6.1	0.128	154.9 ± 5.7	155.5 ± 5.1	0.281
Weight (kg)	69.6 ± 9.8	70.7 ± 9.9	0.305	60.3 ± 9.5	58.8 ± 8.5	0.085
BMI (kg/m ²)	24.8 ± 2.9	24.9 ± 2.7	0.751	25.0 ± 3.4	24.3 ± 3.4	0.025
Waist circumference (cm)	87.9 ± 7.1	88.8 ± 7.1	0.240	84.2 ± 7.9	83.0 ± 7.8	0.121
Systolic BP (mmHg)	127.5 ± 14.7	126.6 ± 12.2	0.543	127.2 ± 16.4	123.2 ± 13.3	0.006
Diastolic BP (mmHg)	81.1 ± 10.6	83.5 ± 9.8	0.033	78.4 ± 10.0	79.3 ± 9.9	0.345
Total cholesterol (mmol/L)	3.2[2.6, 4.0]	4.7[4.1, 5.1]	<0.001	3.4[2.7, 4.0]	4.9[4.4, 5.5]	<0.001
Triglyceride (mmol/L)	1.2[0.7, 1.8]	1.4[1.0, 2.0]	0.003	1.1[0.8, 1.7]	1.2[0.9, 1.7]	0.215
HDL cholesterol (mmol/L)	0.9[0.7, 1.1]	1.2[1.0, 1.5]	<0.001	1.0[0.8, 1.2]	1.4[1.2, 1.7]	<0.001
LDL cholesterol (mmol/L)	1.6[1.1, 2.2]	2.6[2.0, 3.0]	<0.001	1.7[1.3, 2.3]	2.7[2.3, 3.3]	<0.001
Fasting glucose (mmol/L)	6.1 ± 2.1	5.6 ± 1.3	0.006	6.0 ± 1.9	5.3 ± 0.8	<0.001
HbA1c (%)	7.1 ± 0.8	-	-	7.3 ± 1.0	-	-
Smoking (current, %)	35.3	24.3	0.030	5.6	1.6	0.032
Alcohol drinking (%)	82.6	79.6	0.499	17.9	25.4	0.064
Antihypertensive agent (%)	50.0	25.7	<0.001	56.6	20.5	<0.001
Lipid lowering agent (%)	40.8	5.3	<0.001	54.1	6.1	<0.001
Hypoglycemic agent (%)						
Insulin/Sulfonylurea/Metformin/TZD	14.2/60.1/71.1/13.3	-	-	20.9/53.1/78.1/7.7	-	-
Physical activity (%)						
Sedentary or light/Moderate/Heavy or vigorous	74.8/22.5/2.8	81.0/18.4/0.7	0.206	84.7/11.7/3.6	85.7/13.5/0.8	0.116

Dual Energy X-ray Absorptiometry (DXA)

Total body fat percentage	22.3 ± 0.2	20.7 ± 0.3	0.001	30.4 ± 0.3	30.1 ± 0.3	0.599
Total body fat mass (kg)	16.0 ± 0.2	15.0 ± 0.2	0.004	18.9 ± 0.2	18.5 ± 0.2	0.331
Total lean body mass (kg)	51.6 ± 0.3	53.5 ± 0.4	0.006	39.2 ± 0.3	39.6 ± 0.2	0.449
ASM (kg)	24.9 ± 0.5	25.7 ± 0.6	0.409	17.8 ± 0.2	18.4 ± 0.2	0.042
ASM/height ² (kg/m ²)	8.9 ± 0.1	9.0 ± 0.2	0.688	7.4 ± 0.1	7.6 ± 0.1	0.024
SMI (%)	40.1 ± 0.2	42.0 ± 0.3	<0.001	33.8 ± 0.2	34.8 ± 0.2	0.018

ASM, Appendicular Skeletal Muscle; BMI, Body mass index; BP, Blood pressure; HDL, High-density lipoprotein; LDL, Low-density lipoprotein; SMI, Skeletal Muscle mass Index; Thiazolidinediones, TZD

Upper panel: Data are presented as mean ± SD, median [inter-quartile range] or (%) as appropriate. Clinical and metabolic characteristics of study subjects. *P*-values represent overall differences across groups for each gender as determined by the independent two-sample *t* test or Wilcoxon's rank-sum test for continuous variables and Pearson's chi-square test for categorical variables. **Low panel:** Data are presented as mean ± standard error. Body compositional parameters across category of type 2 diabetes for each gender. *P*-values represent the differences between the two groups for each gender as determined by Analysis of Covariance (ANCOVA). Covariates in this analysis included age, BMI, physical activity, smoking, alcohol drinking, antihypertensive agent, lipid lowering agent, systolic and diastolic blood pressure, total cholesterol, HDL-cholesterol, triglyceride, and fasting blood glucose levels.

Supplementary Table 2. Clinical, anthropometric and metabolic characteristics of young Korean men and women (n = 145)

	Men (n=54)	Women (n=91)	<i>P</i>
Age (years)	33.9 ± 5.2	31.2 ± 6.6	0.014
Height (cm)	175.1 ± 5.9	160.2 ± 5.2	<0.001
Weight (kg)	80.5 ± 13.9	57.6 ± 10.8	<0.001
BMI (kg/m ²)	26.2 ± 3.1	22.4 ± 4.0	<0.001
Waist circumference (cm)	92.0 ± 9.1	80.0 ± 10.0	<0.001
Systolic BP (mmHg)	123.6 ± 12.2	110.2 ± 11.8	<0.001
Diastolic BP (mmHg)	81.2 ± 9.6	71.7 ± 8.2	<0.001
Total cholesterol (mmol/L)	4.8 (4.2, 5.3)	4.3 (3.8, 4.7)	0.011
Triglyceride (mmol/L)	1.7 (1.2, 3.0)	0.8 (0.6, 1.1)	<0.001
HDL cholesterol (mmol/L)	1.3 (1.1, 1.5)	1.5 (1.3, 1.8)	<0.001
LDL cholesterol (mmol/L)	2.5 (1.9, 3.1)	2.2 (1.9, 2.7)	0.179
Fasting glucose (mmol/L)	5.2 ± 0.6	4.9 ± 0.4	<0.001
Dual energy X-ray Absorptiometry			
Total body fat percentage (%)	22.8 ± 5.6	28.3 ± 6.4	<0.001
Total body fat mass (kg)	19.0 ± 7.9	17.1 ± 6.6	0.0128
Total lean body mass (kg)	58.7 ± 7.4	39.3 ± 5.2	<0.001
ASM (kg)	29.9 ± 3.4	18.7 ± 3.2	<0.001
ASM/height ² (kg/m ²)	9.8 ± 1.2	7.3 ± 1.1	<0.001
SMI (%)	43.6 ± 3.9	37.7 ± 3.5	<0.001
ASM/height² 2SD cut-point value	7.40 kg/m²	5.14 kg/m²	
SMI 2SD cut-point value	35.71%	30.70%	

Supplemental Table 3. Prevalence (%) of sarcopenia using ASM/height² and SMI methods

Indices of Sarcopenia	ASM/height ² below 2 SD (Baumgartner et al.)			SMI below 2 SD (Janssen et al.)		
	With diabetes	Without diabetes	<i>P</i> -value	With diabetes	Without diabetes	<i>P</i> -value
Total (n = 810)	5.3	2.0	0.010	15.7	6.9	<0.001
Men (n = 370)	10.1	4.6	0.039	10.1	3.3	0.010
40-59 years (n = 191)	2.5	2.7	0.634	2.5	1.4	0.505
≥ 60 years (n = 179)	19.0	6.3	0.011	19.0	5.1	0.005
Women (n = 440)	0	0.4	0.555	21.9	9.0	<0.001
40-59 years (n = 219)	0	0	-	16.7	4.1	0.002
≥ 60 years (n = 221)	0	0.8	0.548	27.0	14.0	0.013

ASM, appendicular skeletal muscle; SMI, skeletal muscle index; SD, standard deviation
P-values represent overall differences across groups, as determined by Pearson's chi-square test.

Supplemental Table 4. Logistic regression analysis of presence of sarcopenia as the dependent variable

Independent variable:	OR (95% CI)	P-value
Type 2 diabetes		
Unadjusted	2.538 (1.583 – 4.070)	<0.001
Model 1	2.976 (1.816 – 4.879)	<0.001
Model 2	3.200 (1.834 – 5.583)	<0.001
Model 3	3.199 (1.822 – 5.615)	<0.001
Model 4	3.069 (1.422 – 6.621)	0.004

Data are odds ratio (OR) (95% confidence interval (CI)).

Model 1: adjustment for age and gender. Model 2: Model 1 + adjustments for BMI. Model 3: Model 2 + adjustment for smoking, alcohol drinking, and physical activity. Model 4: Model 3 + adjustment for antihypertensive agent, lipid lowering agent, systolic and diastolic blood pressure, total cholesterol, triglyceride, and HDL-cholesterol.

*Sarcopenia was defined using SMI below 2SD of young reference group.