

Low muscle mass and risk of type 2 diabetes in middle-aged and older adults: findings from the KoGES

Jang Won Son¹ · Seong Su Lee¹ · Sung Rae Kim¹ · Soon Jib Yoo¹ ·
Bong Yun Cha² · Ho Young Son³ · Nam H. Cho⁴

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Abstract

Aims/hypothesis Asians have a propensity to develop type 2 diabetes with a lower BMI than Western populations. This discrepancy may be due to differences in body fat and muscle mass for a given BMI. However, unlike adiposity, it is unclear whether muscle mass affects the risk of type 2 diabetes in Asian populations.

Methods We conducted a 2-yearly prospective assessment of 6895 participants who were free of diabetes at the baseline examination as part of the Korean Genome Epidemiology Study. The muscle mass index (MMI) was defined as the weight-adjusted appendicular skeletal muscle mass. Using Cox regression models, we evaluated the association between MMI and the risk of developing type 2 diabetes across sex-specific tertiles of MMI. Low muscle mass was defined as the sex-specific lowest tertile of MMI. Main covariates included age, sex, urban or rural residence, family history of diabetes, hypertension, smoking status, education level, monthly income, physical activity, alcohol consumption and diet. In addition, body fat mass, waist

circumference and BMI were controlled as categorical variables. Obesity was defined as a BMI of ≥ 25 kg/m² or a waist circumference of ≥ 90 cm for men and ≥ 85 cm for women.

Results During a median follow-up of 9.06 years, 1336 participants developed type 2 diabetes. At baseline, the mean age was 52.1 years and the mean BMI was 24.4 kg/m². The mean MMI for men and women was 32.1% and 26.0%, respectively. There was an inverse association between MMI and the risk of type 2 diabetes. Multivariate-adjusted HRs for the risk of developing type 2 diabetes were 2.05 (95% CI 1.73, 2.43), 1.39 (95% CI 1.17, 1.66) and 1.0 from the lowest to highest sex-specific MMI tertile, with an HR of 1.35 (95% CI 1.26, 1.45) per SD decline in MMI. Further adjustments for fat mass, waist circumference and BMI as categorical variables did not modify the relationship (each $p < 0.01$). In BMI-stratified analyses, the population-attributable fraction of the lowest tertile of MMI for developing type 2 diabetes was increased by 11.9% in the non-obese group and 19.7% in the obese group.

Conclusions/interpretation Low muscle mass as defined by MMI was associated with an increased risk of type 2 diabetes, independent of general obesity, in middle-aged and older Korean adults.

✉ Nam H. Cho
chnaha@ajou.ac.kr

¹ Division of Endocrinology and Metabolism, Department of Internal Medicine, Bucheon St Mary's Hospital, College of Medicine, The Catholic University of Korea, Bucheon, Korea

² Division of Endocrinology and Metabolism, Department of Internal Medicine, Seoul St Mary's Hospital, College of Medicine, The Catholic University of Korea, Seoul, Korea

³ Division of Endocrinology and Metabolism, Department of Internal Medicine, Hallym University Medical Center, Hallym University College of Medicine, Seoul, Korea

⁴ Department of Preventive Medicine, Ajou University School of Medicine, 5 Wonchon-Dong, Youngtong-Gu, Suwon 443-721, Korea

Keywords BMI · Obesity · Skeletal muscle · Type 2 diabetes mellitus

Abbreviations

ASM	Appendicular skeletal muscle mass
BIA	Bioelectrical impedance analysis
DXA	Dual-energy x-ray absorptiometry
KoGES	Korean Genome Epidemiology Study
MF-BIA	Multifrequency bioelectrical impedance analysis
MMI	Muscle mass index

Introduction

There are ethnic differences in the association between obesity and the risk of type 2 diabetes. Compared with Western populations, Asians are considerably leaner and are more likely to develop diabetes with less weight gain and obesity [1, 2]. Thus, the BMI cut-off value for diagnosis of obesity for Asians has been adjusted to 27.5 kg/m² or even less, and further assessment of fat distribution has been encouraged [3]. However, there is ongoing debate regarding whether these measures for obesity are appropriate for individualised type 2 diabetes risk, especially regarding interethnic differences. This debate is related to differences in body composition, including fat and muscle mass, for a given BMI [4, 5].

Despite having a lower BMI, Asian populations are more prone to abdominal obesity and low muscle mass with increased insulin resistance. This phenotype has been associated with an increased risk of diabetes compared with Westerners of the same BMI range [4–6]. Environmental, genetic and intrauterine developmental factors are expected to be involved in ethnic variation in body composition [1, 2, 7]. Reduced beta cell functional capacity may also limit the potential to increase insulin secretion in response to decreased insulin sensitivity [8–10]. Therefore, when fat and caloric intake became excessive, a diminished skeletal muscle entrapment capacity may contribute to lower glucose utilisation states, leading to increased insulin resistance and beta cell exhaustion. These characteristics may partially explain the accelerated diabetes epidemic in Asians at lower degrees of obesity compared with Western populations after environmental perturbations, such as changes in diet and lifestyle.

Given this hypothesis, it is assumed that low muscle mass in addition to adiposity may have an impact on type 2 diabetes risk. Several recent studies have focused on the role of muscle mass in addition to adiposity in metabolic disorders, and inverse associations have been suggested between muscle mass and insulin resistance, the metabolic syndrome and diabetes risk [11–13]. However, previous studies regarding this issue were cross-sectional and focused on low muscle mass related to sarcopenia as part of the ageing process. No prospective studies have aimed to predict type 2 diabetes risk by assessing muscle mass; therefore, it cannot demonstrate that low muscle mass precedes rather than follow diabetes onset. To address this issue, we evaluated the association between low muscle mass and incidence of type 2 diabetes in middle-aged and older adults in the Korean Genome Epidemiology Study (KoGES), a large prospective population-based study.

Methods

Study population Participants in the present study were recruited from two population-based cohorts: the Ansong and

Ansan cohorts from the KoGES [10]. Eligibility criteria for the KoGES included age 40–69 years and residence within the survey area for 6 months or longer prior to enrolment. A total of 10,038 participants were included in the KoGES cohorts (5018 from a farming community for the Ansong cohort and 5020 from an industrial community for the Ansan cohort). Baseline examinations were performed in 2001 and 2002, and 2-yearly follow-up examinations continued through 2014. We excluded from the analysis participants with unknown glucose status ($n=91$), a previous history of diabetes ($n=572$) and incident diabetes at the baseline examination ($n=635$). After excluding these 1298 participants, 8740 participants underwent repeat examinations every 2 years. Informed written consent was obtained from all participants. Demographic information was collected at the baseline examination using a standard questionnaire that was administered during face-to-face interviews. The study protocol was approved by the Ethics Committee of the Korea Center for Disease Control and the Ajou University School of Medicine Institutional Review Board.

Diagnosis of type 2 diabetes For both baseline and 2-yearly follow-up evaluations, all participants underwent a 75 g OGTT after an overnight fast of at least 8 h, and biochemical assays were performed at a central laboratory (Seoul Clinical Laboratories, Seoul, Korea). A previous diagnosis of diabetes was identified by self-report, the use of oral hypoglycaemic agents and/or insulin, or OGTT results at baseline. At subsequent follow-up examinations, newly diagnosed type 2 diabetes was defined as a fasting glucose concentration of ≥ 7 mmol/l or a post-load glucose concentration of ≥ 11 mmol/l after a 75 g OGTT based on the WHO criteria [14].

Body composition and laboratory assessments All participants attended a community clinic for clinical assessments at each follow-up visit. BMI was calculated as weight in kg divided by the square of the height in metres, with participants in light clothing and barefoot. Lean body mass and body fat were assessed by multifrequency bioelectrical impedance analysis (MF-BIA; InBody 3.0, Biospace, Seoul, Korea). Unlike conventional bioelectrical impedance analysis (BIA) equipment that often takes only partial measurements and relies on formulas to estimate whole body composition, the MF-BIA technique assumes that the human body is composed of five interconnecting cylinders and takes direct impedance measurements from these bodily compartments. Using a tetrapolar eight-point tactile electrode system, measurements of impedance were taken at four specific frequencies (5, 50, 250 and 500 kHz) in five segments (right arm, left arm, trunk, right leg and left leg) and used to calculate a value for segmental lean body mass by determining the intracellular and extracellular water components of the total amount of water in the body. The MF-BIA machine can provide valid and accurate estimates of lean body mass and body fat that are closely

associated with those measured using dual-energy x-ray absorptiometry (DXA) across ranges of age, volume status and BMI [15–17]. The Asian Working Group of Sarcopenia supports using BIA for evaluation of body composition in community-based assessments because of its simplicity and portability [18].

Lean body mass was estimated by dividing the total amount of water in the body by 0.73, a formula that was validated in previous studies [15, 19]. At the limb level, lean body mass is synonymous with skeletal muscle mass, and the appendicular skeletal muscle mass (ASM) calculation was performed based on the sum of the lean body mass in all four limbs [20]. In our study, the muscle mass index (MMI) was derived by dividing ASM by weight in $\text{kg} \times 100$, which is suggested to be a better predictor of insulin resistance and diabetes risk than ASM or height-adjusted ASM [11, 13, 21–23].

Main covariates Covariates including baseline age, sex, urban or rural residence, family history of diabetes, hypertension, smoking status, education level, monthly income, physical activity, alcohol consumption and diet were evaluated based on self-reports. Physical activity was classified into two categories: none and regular exercise (≥ 1 session/week). A single exercise session was defined as exercising for at least 30 min. Total caloric intake was estimated from a food frequency questionnaire by trained dietitians [24]. Hypertension was defined as systolic BP of >140 mmHg, diastolic BP of >90 mmHg or the use of antihypertensive medication. Fat mass, BMI and waist circumference were also controlled for as categorical variables. Obesity was defined as a BMI of ≥ 25 kg/m^2 or a waist circumference of ≥ 90 cm for men and ≥ 85 cm for women [25, 26].

Statistical analysis All data were expressed as means and SD or as numbers and percentages. One-way ANOVA and linear-by-linear association tests were used for comparing baseline characteristics according to sex-specific tertiles of MMI.

We calculated the cumulative incidence of type 2 diabetes and HRs using multivariable-adjusted Cox proportional hazard regression models to assess the risk of developing diabetes according to sex-specific tertiles of MMI at baseline and as a continuous variable per 1 SD decline in MMI. Each participant was followed from the date of the baseline visit until the first follow-up visit at which diabetes was ascertained, the date of the last informative contact or the end date of the study. Incidence rates were calculated by dividing the number of incident cases by the number of person-years of follow-up in each MMI tertile.

Multivariable models were adjusted for the main covariates. Log-minus-log plots were produced for each variable to verify the assumption of proportional hazards. Colinearities between fat mass, BMI, or waist circumference and MMI

were assessed using variance inflation factors, with variance inflation factors of >10 indicating model instability. Statistical interaction effects by age, sex and menopause at baseline and the risk of diabetes associated with tertiles of MMI were assessed by including interaction terms in the models. As part of the sensitivity analysis, participants diagnosed with diabetes within the first 2 years of follow-up were excluded to limit the effect of reverse causation between low muscle mass and diabetes.

Cox regression models were modelled by jointly classifying participants by each sex-specific tertile for MMI at a given BMI to evaluate the predictive value of MMI in addition to BMI for diabetes risk. The population-attributable fraction was calculated as $p([\text{HR} - 1]/\text{HR})$, where p is the proportion of total cases in the population arising from the specified exposure category. All p values were based on two-sided tests, and $p < 0.05$ was taken to indicate statistical significance. Analyses were performed using SPSS version 18.0 (SPSS, Chicago, IL, USA).

Results

Study population A total of 3252 men and 3643 women were followed up for 12 years and evaluated for the incidence of type 2 diabetes. In this analysis, we excluded participants who were lost to follow-up after the first visit ($n = 1052$), those missing data on waist circumference ($n = 7$), those with a BMI of <18.5 kg/m^2 ($n = 142$) and those for whom data on BIA were invalid or missing at the baseline examination ($n = 644$). During a mean follow-up period of 9.06 years, 1336 (19.4%) new cases of type 2 diabetes were identified. The incidence rate of type 2 diabetes was 20.8% in men and 18.1% in women. At baseline, the mean age was 52.1 years and the mean BMI was 24.4 kg/m^2 . Participants were divided into three groups based on sex-specific MMI tertiles: $<30.94\%$, 30.94–33.11% and $\geq 33.11\%$ in men and $<24.96\%$, 24.96–26.95% and $\geq 26.95\%$ in women. As shown in Table 1, those in the lower MMI group were older and more likely to be urban residents, more likely to be obese and have a lower education level compared with those in the higher MMI group. There was a trend toward higher HbA_{1c} levels, higher fasting plasma glucose levels and higher post-load 2 h glucose levels toward the lower tertiles of MMI, whereas a family history of diabetes, total calorie consumption and physical activity were not significantly different across sex-specific MMI tertiles.

Low MMI and risk of type 2 diabetes Various Cox regression models were used to determine the risk of developing type 2 diabetes across the sex-specific tertiles of MMI (shown in Table 2). We found a graded increase in diabetes risk in the lower MMI groups. Those in the lower sex-specific MMI category had an approximately 2.5-fold increased risk of

Table 1 Baseline characteristics

Characteristics	MMI tertile			<i>p</i> for trend
	Lowest	Middle	Highest	
Age, years	53.8±8.9	50.7±8.3	49.7±8.2	<0.001
Weight, kg	66.3±10.5	63.6±9.4	59.9±8.3	<0.001
BMI, kg/m ²	26.6±2.9	24.6±2.3	22.6±2.2	<0.001
Waist circumference, cm	87.5±8.0	82.4±7.5	77.6±7.2	<0.001
Hypertension, <i>n</i> (%)	692 (30.1)	423 (18.4)	273 (11.9)	<0.001
Body fat, %	35.4±6.6	29.9±6.2	24.0±6.6	<0.001
MMI, %	26.3±3.3	28.8±3.1	31.7±3.5	<0.001
HbA _{1c} , mmol/mol	36.2±4.5	35.2±4.2	34.4±3.8	<0.001
HbA _{1c} , %	5.5±0.4	5.4±0.4	5.3±0.4	<0.001
Fasting plasma glucose, mmol/l	4.74±0.52	4.70±0.49	4.65±0.48	<0.001
2 h glucose, mmol/l	7.0±1.7	6.6±1.7	6.2±1.7	<0.001
Total energy intake, kJ	7767.1±2816.2	7819.4±2992.3	7911.9±2801.6	0.094
Protein, %	13.3±2.4	13.4±2.3	13.3±2.3	0.924
Fat %	13.6±5.4	14.2±5.3	14.3±5.3	<0.001
Carbohydrate, %	71.7±7.0	71.0±6.8	71.0±6.7	<0.001
Family history of diabetes, <i>n</i> (%)	223 (9.7)	265 (11.5)	255 (11.1)	0.128
Area (rural), <i>n</i> (%)	1086 (47.3)	1036 (45.1)	1230 (53.5)	<0.001
Smoking, <i>n</i> (%)				0.002
Never-smoker	1376 (60.9)	1373 (60.3)	1346 (59.6)	
Ex-smoker	407 (18.0)	364 (16.0)	293 (13.0)	
Current smoker	475 (21.0)	539 (23.7)	620 (27.4)	
Alcohol consumption (>251 kJ/day), <i>n</i> (%)	515 (22.9)	521 (23.3)	516 (23.1)	0.874
Regular exercise (≥1/week), <i>n</i> (%)	455 (19.8)	433 (18.8)	404 (17.6)	0.054
Monthly income, <i>n</i> (%)				<0.001
<1 million Korean Won	877 (46.2)	679 (37.5)	686 (38.0)	
1–2 million Korean Won	633 (33.3)	656 (36.2)	717 (39.7)	
>2 million Korean Won	389 (20.5)	476 (26.3)	401 (22.2)	
Education level, <i>n</i> (%)				<0.001
Elementary school or lower	893 (39.2)	639 (27.9)	568 (24.9)	
Middle to high school	1063 (46.7)	1332 (58.2)	1403 (61.6)	
High school graduate	322 (14.1)	318 (13.9)	307 (13.5)	

Data are expressed as means ±SD unless otherwise indicated

Statistical significance for linear-by-linear association between categorical variables was calculated using the χ^2 test for trend. MMI = ASM divided by body weight in kg. Sex-specific MMI tertiles in men: Lowest, <30.94 (%); Middle, 30.94–33.11 (%); Highest, ≥33.11 (%). Sex-specific MMI tertiles in women: Lowest, <24.96 (%); Middle, 24.96–26.95 (%); Highest, ≥26.95 (%)

developing diabetes compared with those in the higher category (32.1 vs 13.0 events per 1000 person-years; HR 2.55 [95% CI 2.21, 2.93]). The age- and sex-adjusted HRs from lowest to highest MMI tertiles were 2.38 (95% CI 2.06, 2.74), 1.54 (95% CI 1.33, 1.79) and 1.0 ($p < 0.001$). Further adjustment for urban or rural residency, family history of diabetes, hypertension, physical activity, smoking, alcohol consumption, education level and total caloric intake only slightly attenuated the HR. In this multivariable-adjusted model, compared with those with the highest MMI, the HR for diabetes for those with the lowest MMI was 2.05 (95% CI 1.73, 2.43)

and the HR increase per each SD decline was 1.35 (95% CI 1.26, 1.45). There were no interaction effects between MMI and sex ($p = 0.708$), age group (dichotomised at 65 years old) in men ($p = 0.191$) and women ($p = 0.599$), and menopause status ($p = 0.298$) on incident diabetes risk. Changes in body weight or MMI during the follow-up period had minimal effects on the HR between baseline MMI and incident diabetes risk (data not shown).

This inverse association between MMI and type 2 diabetes risk remained strong even after additional adjustments for body fat according to the sex-specific median values of fat

Table 2 HRs for incident type 2 diabetes according to sex-specific MMI stratified group

Variable	MMI tertile			<i>p</i> for trend	Per 1 SD decline in MMI
	Lowest	Middle	Highest		
Total participants					
Events/person-year, <i>n</i> (%)	630 (27.4)	422 (18.4)	284 (12.4)		
Incident cases of DM/1000 persons	32.1	20.0	13.0		
Unadjusted HR	2.55 (2.21, 2.93)	1.56 (1.34, 1.81)	1.00	<0.001	1.19 (1.14, 1.25)
Age-/sex-adjusted HR	2.38 (2.06, 2.74)	1.54 (1.33, 1.79)	1.00	<0.001	1.44 (1.36, 1.53)
Multivariable-adjusted HR ^a	2.05 (1.73, 2.43)	1.39 (1.17, 1.66)	1.00	<0.001	1.35 (1.26, 1.45)
Excluding those who diagnosed within the first 2 years of follow-up					
Event/person-year, <i>n</i> (%)	491 (22.7)	333 (15.1)	218 (9.8)		
Incident cases of DM/1000 persons	25.3	15.9	10.1		
Unadjusted HR	2.67 (2.27, 3.13)	1.62 (1.37, 1.92)	1.00	<0.001	1.21 (1.15, 1.26)
Age-/sex-adjusted HR	2.51 (2.14, 2.95)	1.61 (1.35, 1.91)	1.00	<0.001	1.46 (1.37, 1.56)
Multivariable-adjusted HR ^a	2.08 (1.72, 2.52)	1.42 (1.16, 1.73)	1.00	<0.001	1.36 (1.26, 1.47)

^a Multivariable adjustment for age, rural or urban area, family history of diabetes (at least one diabetic first-degree relative), hypertension, smoking (never, former or current smoker), alcohol consumption (>251 kJ per day), education level (less than elementary school, middle to high school, or high school graduate), physical activity (≥ 1 /week), monthly income (<1 million, 1–2 million or >2 million Korean Won) and total caloric intake.

DM, diabetes mellitus

mass. Similarly, adding a category for currently recommended cut-offs for BMI or waist circumference to the multivariable-adjusted model did not modify the significance of these results (Fig. 1). All analyses were repeated after excluding participants who were diagnosed with diabetes within the first 2 years of follow-up, and the results were similar to the overall results (Table 2, Fig. 1).

We further examined the joint effects of general obesity and low muscle mass (shown in Fig. 2) and found no colinearity between BMI and MMI in men or women. The reference group consisted of those with a BMI of <25 kg/m² and a MMI in the third tertile. Compared with the reference group, the diabetes HR for individuals with a high BMI and low MMI was 2.35 (95% CI 1.94, 2.84). Even among obese individuals, those with higher MMIs had a lower risk of diabetes compared with those with lower MMIs at a given level of BMI (HR for the lowest tertile vs the highest tertile of MMI 1.42 [95% CI 1.03, 1.95]). At a given level of BMI, the population-attributable fraction of the lowest tertile of MMI for incident type 2 diabetes was increased by 11.9% in the non-obese group and by 19.7% in the obese group.

Discussion

This prospective, community-based study is the first to investigate the association between muscle mass and type 2 diabetes risk in an Asian population. In this study, we found that low MMI (as assessed by weight-adjusted ASM) was strongly associated with diabetes incidence in middle-aged and older

adults. After adjustment for obesity measures, the association between MMI and diabetes was attenuated but remained significant.

Using two composite measures, the BMI-associated risk waned with MMI; despite this, for a given BMI, low MMI individuals had an increased diabetes risk. Of note, for those in the non-obese group who had lower BMIs (<25 kg/m²), the risk of diabetes was increased by 95% in those in the lowest compared with those in the highest sex-specific tertile for MMI. A similar pattern was demonstrated for diabetes risk in the obese group, suggesting that sufficient muscle mass may confer a protective effect in those with a high BMI. These findings show that skeletal muscle mass measurement may contribute important information beyond BMI for reclassifying the risk of type 2 diabetes in Asian populations, even those with a low BMI. However, we did not assess diabetes risk in relation to visceral adiposity, which may not be measured adequately by waist circumference. Our results do not preclude the possibility that the associations observed were due to ectopic fat distribution.

The recent interest in age-related body composition changes has highlighted the possibility that a decline in skeletal muscle mass may have an impact on metabolic disorders and physical disabilities. Results of previous studies into the relationship between low muscle mass and metabolic disorders are mixed, and causality has yet to be demonstrated. The Health, Aging, and Body Composition Study, which included 2675 elderly adults, found that type 2 diabetes was associated with reduced muscle strength and excessive loss of skeletal muscle mass over a 6 year follow-up period [27]. Additional

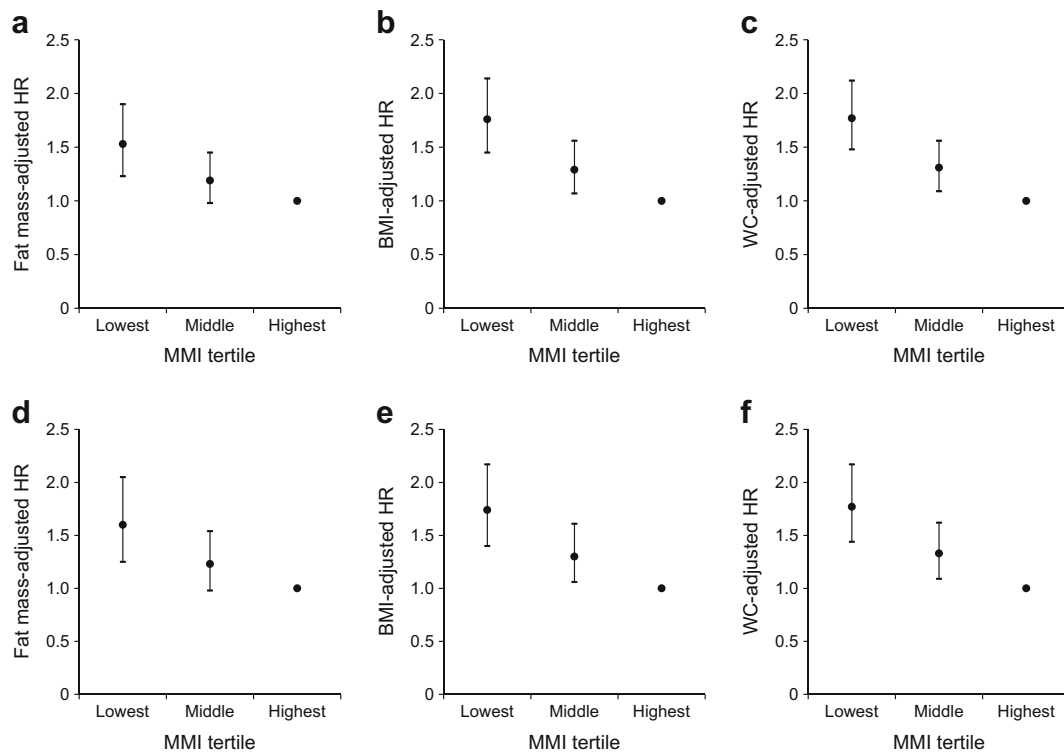


Fig. 1 Adjusted HRs for incident type 2 diabetes according to sex-specific tertiles of MMI. Adjustment variables for multivariable-adjusted HRs included main covariates, body fat or obesity as categorical variables. HRs (95% CI) adjusted by (a) fat mass, (b) BMI and (c) waist

circumference (WC) across tertiles of MMI in all participants. (d–f) The same analyses excluding participants diagnosed with diabetes within the first 2 years of follow-up

research based on 810 participants in the Korean Sarcopenic Obesity Study reported that sarcopenia prevalence was higher in diabetic patients than in the control group [28]. These findings indicate that type 2 diabetes is associated with an increased sarcopenia risk. However, it is unclear whether low muscle mass can cause type 2 diabetes.

Although a lack of muscle mass is postulated to contribute to insulin resistance and glucose intolerance, few studies have investigated the effects of low muscle mass on the risk of type

2 diabetes. Similar to our findings, the National Health and Nutrition Examination Survey III found that low muscle mass was strongly associated with insulin resistance, dysglycaemia and prediabetes, suggesting reverse causality [12, 13]. These studies and our data make important contributions toward understanding the physiological role of low muscle mass and its metabolic consequences.

Substantial evidence supports the biological plausibility of an inverse association between low muscle mass and diabetes risk. Primarily, skeletal muscle is a metabolically active organ that accounts for 30% of the resting metabolic rate and contributes to glucose metabolism under insulin-stimulated conditions by disposing of glucose, storing glycogen and potentially engaging in crosstalk with adipose tissue [29–32]. Therefore, low muscle mass as a result of genetic or environmental factors contributes to a lower glucose reservoir status, resulting in ectopic fat accumulation in muscle and increased insulin resistance when excessive fat and calories are consumed by individuals with a sedentary lifestyle [1, 2]. Consequently, low muscle mass either alone or in conjunction with increased fat deposition is hypothesised to promote beta cell exhaustion, resulting in early beta cell failure. The lower muscle mass and beta cell functional capacity of Asians compared with other populations may contribute to ethnic differences in the risk of diabetes. Several studies on the aetiology of insulin resistance in skeletal muscle have

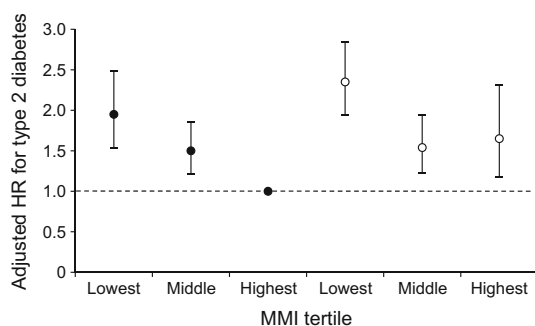


Fig. 2 Joint association of BMI and MMI with the incidence of type 2 diabetes. HRs (95% CI) after adjustment for age, rural or urban area, family history of diabetes, hypertension, smoking, alcohol drinking, education level, physical activity, monthly income and total caloric intake. The reference group (dashed line) consisted of individuals with a BMI of <math><25\text{ kg/m}^2</math> and an MMI in the highest tertile. Black circles, BMI <math><25\text{ kg/m}^2</math>; white circles, BMI $\geq 25\text{ kg/m}^2$

revealed the influence of numerous related factors, including mitochondrial dysfunction and potential crosstalk between skeletal muscle and adipose tissue [33–35].

Potential limitations should be noted. BIA analysis is a useful non-invasive method for assessing skeletal muscle mass in a large population-based study, but several factors (mainly related to hydration status) can affect BIA results, including age, obesity, consumption of food or beverages, and intensity of exercise [36, 37]. In older adults, BIA can overestimate body fat possibly because of variations in fat-free mass mineralisation during normal ageing [38]. This potential measurement error might have affected our observations. To reduce the possibility of measurement errors, participants fasted before the BIA assessment and hydration status was carefully monitored. Regarding the accuracy of BIA in the assessment of ASM, we found that the correlation coefficient between MF-BIA and DXA measures was 0.981, with an SE of estimation of 2.07 kg. These results suggest that the MF-BIA provided a reasonable estimate of ASM in our study. We classified physical activity into none or regular exercise, but this represents a broad range, and bias due to misclassification of physical activity needs to be considered. It is possible that residual confounding effects related to type, duration and intensity of physical activity attenuated the level of statistical significance of our findings. In addition, there may be relatively large differences in body composition even within Asian populations, such as those in South or East Asia. Therefore, our results are limited to a single ethnic group, and it is difficult to generalise our findings to larger populations. Ideally, further studies should include participants from many Asian ethnicities and should aim to generate cut-off values for low muscle mass in relation to metabolic risk.

In conclusion, our findings show that low muscle mass is an independent risk factor for type 2 diabetes in middle-aged and older Korean adults. This finding underscores the importance of examining muscle mass during risk assessments for type 2 diabetes in Asians with lower degrees of obesity.

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Data availability The data that support the findings of this study are available from the corresponding author (Nam H. Cho) upon reasonable request.

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Contribution statement NHC and JWS conceived and designed the study, analysed and interpreted the data, wrote the manuscript, contributed to discussions, and reviewed and edited the manuscript. SSL, SRK, SJY, BYC and HYS contributed to the study conception and design, contributed to data interpretation and discussion, and reviewed and edited the manuscript. All authors approved the final manuscript. NHC was the principal investigator and is responsible for the integrity of the work as a whole.

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