Poor glycemic control rather than types of diabetes is a risk factor for sarcopenia in diabetes mellitus: The MUSCLES-DM study

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ABSTRACT

Aims/Introduction: Though poor glycemic control and insulin treatment are reported to be associated with sarcopenia in type 2 diabetes, type 1 diabetes may be a stronger risk for sarcopenia. We therefore studied the effect of the type of diabetes, glycemic control, and insulin therapy on the prevalence and characteristics of sarcopenia.

Materials and Methods: A total of 812 Japanese patients with diabetes (type 1: n = 57; type 2: n = 755) were enrolled in this study. Sarcopenia was defined as low handgrip strength or slow gait speed and low appendicular skeletal muscle mass.

Results: Among participants aged ≥65 years, the sarcopenia prevalence rate was higher among patients with type 1 diabetes (20.0%) than among those with type 2 diabetes (8.1%). The prevalence rate of low handgrip strength was higher in type 1 diabetes (50.0%) than in type 2 diabetes (28.7%). In logistic regression analysis, type 1 diabetes was significantly associated with the prevalence of low handgrip strength. In logistic regression analysis, medication with insulin was significantly associated with the prevalence of sarcopenia; this association was not retained after adjusting for HbA1c.

Conclusions: The prevalence of sarcopenia in older adult patients was higher in those with type 1 diabetes than in those with type 2 diabetes. Among the components of sarcopenia, the difference was most prominent in the frequency of low handgrip strength. Poor glycemic control rather than type of diabetes or insulin treatment was revealed to be a primary risk factor for sarcopenia in diabetes mellitus.

INTRODUCTION

Sarcopenia is defined as the loss of skeletal muscle mass and strength and is a condition that commonly accompanies aging1. Sarcopenia is diagnosed based on (i) muscle strength, (ii) muscle quantity/quality, and (iii) physical performance according to the definition by the European Working Group on Sarcopenia in Older People (EWGSOP)2. Because of differences in body size and adiposity between Asian and Western populations, an Asian version of the definition of sarcopenia was required3, and the consensus of the Asian Working Group for Sarcopenia 2019 has been recommended in this regard4.

In addition to body size and adiposity, European and Asian populations have been reported to differ in clinical characteristics and pathogenesis of type 2 diabetes; insulin resistance is more pronounced in European populations while impaired insulin secretion contributes more prominently in Asian populations, including the Japanese populations5,6. Differences between European and Japanese populations were observed in the characteristics of type 1 diabetes as well. Patients with type
1 diabetes in Japan exhibit a thinner body and a higher frequency of complete loss of endogenous insulin compared to those in European countries.

Studies on sarcopenia in different populations are therefore important to clarify the factors contributing to sarcopenia to establish effective methods for its prevention and intervention.

We previously reported an increased prevalence of sarcopenia in Japanese patients with type 2 diabetes, and that glycemic control (HbA1c) was significantly associated with sarcopenia independent of other possible covariates. A subsequent longitudinal study indicated that improved glycemic control and insulin treatment were associated with improved muscle mass and gait speed. These data suggest that the characteristics of sarcopenia and its components may differ between type 1 diabetes (which is characterized by poor glycemic control and intensive insulin treatment) and type 2 diabetes. However, few studies have been reported on sarcopenia in patients with type 1 diabetes.

The present study was intended to reveal differences between type 1 and type 2 diabetes in the prevalence and factors contributing to sarcopenia with reference to insulin treatment and endogenous insulin secretion. It is hoped that these data will help to establish effective methods for prevention and intervention in sarcopenia.

MATERIALS AND METHODS
Study participants
In this study, we analyzed data from an ongoing multicenter study for clarifying evidence for sarcopenia in patients with diabetes mellitus (the MUSCLES-DM study)

Participants were recruited between May 2016 and December 2017 from three university hospitals (Kindai University, Osaka University, and Ehime University) and two general clinics (Fukuda Clinic and Katsuya Clinic). The inclusion criteria were as follows: patients with type 1 or type 2 diabetes who were aged ≥40 years at recruitment. We analyzed 812 patients (57 patients with type 1 diabetes and 755 patients with type 2 diabetes) who had complete data on measurements of physical performance required for the diagnosis of sarcopenia as well as clinical data including disease history, regular exercise habit, treatment regimens, and plasma levels of glycemic parameters.

All study procedures were approved by the ethics committees of the three universities, and all patients gave written informed consent.

Assessment of sarcopenia
Sarcopenia was diagnosed according to the revised definition of the Asian Working Group for Sarcopenia (AWGS2019), using the following parameters: low appendicular skeletal muscle mass (ASM) (men, <7.0 kg/m²; women, <5.7 kg/m²), low muscle strength (low handgrip strength: men, <28 kg; women, <18 kg), and low physical performance (slow gait speed, <1.0 m/s). Sarcopenia was diagnosed based on the presence of “low ASM + low muscle strength” or “low ASM + low physical performance.”

Assessment of ASM
The ASM was estimated using bioelectrical impedance analysis devices (MC780A; Tanita Co., Tokyo, Japan). The ASM was determined using the following formula.

\[ \text{ASM} = \text{appendicular lean mass (kg)} / \text{body height (m)}^2. \]

Measurement of handgrip strength
Handgrip strength of the dominant hand was measured using a standard digital grip dynamometer (Grip D; Takei Scientific Instruments Co., Ltd., Niigata, Japan). Measurements were taken twice in a sitting position with the arm positioned horizontally to the ground. The participants were instructed to adjust the handle of the dynamometer to be under the second phalanx of the fingers when gripped. The mean values of all the measurements were used for the analysis.

Measurement of usual gait speed
The usual gait speed was measured on a 2.44-m or 4-m walkway with a 1-m approach way using a digital timer. Measurements were taken twice, and the average value was used for the analysis.

Exercise habit
Presence of regular exercise habit (at least twice a week for 30 min for over a year) were investigated using a yes-no question.

Statistical analysis
All calculated values are presented as the mean ± standard deviation of frequency. We used the Mann–Whitney U-test to compare means for continuous variables, and Fisher’s exact test to compare proportions for categorical variables between the groups. Conditional logistic regression analysis was used to calculate odds ratios (ORs) and 95% confidence intervals (CIs) for the independent risk factors for sarcopenia and sarcopenia components.

Participants were grouped based on the following: age, <65 years and ≥65 years; sex, male and female; body mass index (BMI), <25 kg/m² and ≥25 kg/m²; or <18.5 kg/m² and ≥18.5 kg/m²; duration of diabetes, <20 years and ≥20 years; HbA1c, <8.0% and ≥8.0%; diabetic retinopathy stage, <pre-proliferative diabetic retinopathy (Pre-PDR) and ≥Pre-PDR; diabetic nephropathy stage, <III and ≥III; estimated glomerular filtration rate (eGFR), <60 mL/min/1.73 m² and ≥60 mL/min/1.73 m²; C-peptide, <0.6 ng/mL and ≥0.6 ng/mL; albumin (Alb); <4.0 g/dL and ≥4.0 g/dL; regular exercise habit, “Yes” and “No”; cardiovascular diseases, “Yes” and “No”; orthopedic diseases, “Yes” and “No”; antihyperglycemic drugs, and name of medicine “Yes” and “No.”
All statistical analyses were performed using JMP statistical software (JMP Pro version 14.0.0; SAS Institute, Cary, NC, USA). A P-value <0.05 was considered statistically significant.

RESULTS

Prevalence rate of sarcopenia and its components in type 1 and type 2 diabetes

The prevalence rate of sarcopenia and its components in patients with type 1 and type 2 diabetes is shown in Figure 1.

Among participants aged ≥65 years, the prevalence rate of sarcopenia was significantly higher in those with type 1 diabetes than in those with type 2 diabetes (20.0 vs 8.1%, \( P = 0.04 \)). As for sarcopenia components, the prevalence rate of low handgrip strength was significantly higher in patients with type 1 diabetes than in those with type 2 diabetes (26.7 vs 15.5%, \( P = 0.02 \)). In the <65 years group, there was no significant difference between patients with type 1 and type 2 diabetes in the prevalence of sarcopenia or its components.

Among patients with type 1 diabetes, the prevalence rate of sarcopenia and low handgrip strength was higher in the age ≥65 years group than in the age <65 years group (Figure 1). Among patients with type 2 diabetes, the prevalence rates of low ASM, low handgrip strength, and slow gait speed were higher in the age ≥65 years group than in the age <65 years group (Figure 1).

Prevalence rate of sarcopenia and its components in patients with type 1 and type 2 diabetes according to insulin treatment and endogenous insulin secretion

Insulin treatment has been reported to affect sarcopenia and its components.10 We therefore stratified patients with type 2 diabetes according to insulin treatment and endogenous insulin secretory capacity. The prevalence rates of low handgrip strength and slow gait speed were significantly higher in patients with type 2 diabetes under insulin treatment than in those without insulin treatment (low handgrip strength: 31.7% vs 22.5%, \( P = 0.0097 \); slow gait speed: 31.2% vs 23.7%, \( P = 0.035 \)) (Figure S1). A higher tendency of sarcopenia and low ASM were observed in patients with type 2 diabetes under insulin treatment than in those without insulin treatment. The prevalence of sarcopenia and its components in patients with type 1 diabetes was comparable to that in those with type 2 diabetes with insulin treatment (Figure S2).

When patients with type 2 diabetes were stratified into three groups according to tertiles of fasting C-peptide levels, sarcopenia was most frequent in the lowest tertile of the fasting C-peptide groups (\( P = 0.0003 \)). Among the sarcopenia components, low ASM and low handgrip strength were most frequently observed in the lowest tertile of C-peptide groups (\( P < 0.0001 \) and \( P = 0.0064 \), respectively) (Figure S3). The prevalence of sarcopenia and its components in patients with type 1 diabetes was comparable to that in those with type 2 diabetes in the lowest tertile of C-peptide groups (Figure S4).

Figure 1 | Prevalence rate of sarcopenia and its components in patients with type 1 and type 2 diabetes. Study participants were subdivided by type of diabetes (type 1 and type 2) and age (cutoff at 65 years, which is a criterion to define older people). Age < 65 years: type 1: \( n = 27 \), type 2: \( n = 160 \); age ≥65 years: type 1: \( n = 30 \), type 2: \( n = 595 \). Statistical significance was assessed by Fisher’s exact test. * \( P < 0.05 \), ** \( P < 0.01 \), *** \( P < 0.001 \). ASM, appendicular skeletal muscle mass; T1D, type 1 diabetes; T2D, type 2 diabetes.
Logistic regression analysis for the risk of sarcopenia and its components

To identify the clinical parameters associated with a risk of sarcopenia and its components, logistic regression analysis was performed with clinical parameters which showed significant differences between those with and without sarcopenia and its components (Table S1). Under adjusted conditions, factors significantly associated with the prevalence of sarcopenia included age ≥ 65 years, BMI ≥ 25 kg/m², BMI < 18.5 kg/m², Alb < 4.0 g/dL, and medication with insulin. Factors significantly associated with the prevalence of low ASM included age ≥ 65 years, BMI ≥ 25 kg/m², BMI < 18.5 kg/m², and medication with insulin (Table S2). Factors significantly associated with the prevalence of low handgrip were type 1 diabetes, age ≥ 65 years, female sex, BMI ≥ 25 kg/m², BMI < 18.5 kg/m², retinopathy stage ≥ Pre-PDR, nephropathy stage ≥ III, regular exercise habit “No”, HbA1c ≥ 8.0%, Alb < 4.0 g/dL, and medication with insulin (Table S2). Factors significantly associated with the prevalence of slow gait speed were age ≥ 65 years, female sex, BMI ≥ 25 kg/m², no regular exercise habit “No” habit, cardiovascular diseases, HbA1c ≥ 8.0%, Alb < 4.0 g/dL, and medication with insulin (Table S2).

Logistic regression analysis for sarcopenia and its components focused on the type of diabetes

The clinical characteristics of patients with type 1 and type 2 diabetes are shown in Table 1. In comparison with patients with type 2 diabetes, patients with type 1 diabetes were younger (P < 0.001), more frequently female (P = 0.01), had lower BMI (P = 0.01), lower rate of obesity (BMI ≥ 25.0 kg/m²) (P = 0.04), higher rate of underweight (BMI < 18.5 kg/m²) (P = 0.01), regular exercise habit “No” (P = 0.01), less cardiovascular complications (P = 0.0002), less orthopedic complications (P = 0.001), lower HbA1c level (P < 0.001), higher rate of HbA1c ≥ 8.0% (P = 0.002), lower C-peptide (P < 0.001), and lower Alb (P < 0.0001). In the analysis of medication for hyperglycemia, patients with type 1 diabetes had a higher insulin prescription rate and lower prescription rate of medication other than insulin in comparison with patients with type 2 diabetes.

Table 1 | Clinical characteristics of patients with type 1 diabetes and type 2 diabetes

|                      | Type 1 diabetes | Type 2 diabetes | P       |
|----------------------|-----------------|-----------------|---------|
| Age (years)          | 62.7 ± 12.3     | 699 ± 9.0       | <0.001  |
| Female sex (%)       | 57.9            | 400             | 0.01    |
| BMI (kg/m²)          | 23.4 ± 4.6      | 247 ± 4.0       | 0.01    |
| BMI ≥ 25.0 kg/m² (%) | 28.1            | 428             | 0.04    |
| BMI < 18.5 kg/m² (%) | 12.3            | 40              | 0.01    |
| Duration of diabetes (years) | 18.6 ± 12.9 | 15.6 ± 10.1   | 0.19    |
| Retinopathy, PDR or post-PC | 15.8         | 12.8           | 0.54    |
| Nephropathy, stage ≥ III (%) | 10.5     | 8.6            | 0.62    |
| Regular exercise habit (%) | 35.1         | 54.3           | 0.01    |
| Cardiovascular complications (%) | 12.3    | 35.0           | <0.001  |
| Orthopedic complications (%) | 10.5    | 30.7           | <0.001  |
| Plasma markers       |                 |                 |         |
| HbA1c (%)            | 8.0 ± 1.3       | 7.4 ± 1.3       | <0.001  |
| HbA1c ≥ 8.0% (%)     | 43.9            | 243             | 0.002   |
| C-peptide (ng/mL)*   | 0.09 ± 0.45     | 1.61 ± 1.29     | <0.001  |
| eGFR (ml/min/1.73 m²) | 68.6 ± 19.4   | 638 ± 192       | 0.0547  |
| Albumin (mg/dL)      | 3.97 ± 0.34     | 4.23 ± 0.39     | <0.001  |
| Medication of hyperglycemia |         |                 |         |
| Sulfonylureas (%)    | 0.0             | 27.0            | <0.001  |
| Biguanides (%)       | 0.0             | 37.0            | <0.001  |
| Alpha-glucosidase inhibitor (%) | 3.5   | 14.0           | 0.02    |
| Thiazolidinediones (%) | 0.0       | 14.8           | <0.001  |
| Glinides (%)         | 0.0             | 9.1             | 0.01    |
| DPP-4 inhibitors (%) | 7.0             | 60.0            | <0.001  |
| GLP-1 analogs (%)    | 0.0             | 5.3             | 0.10    |
| SGLT-2 inhibitors (%) | 1.8          | 13.1            | 0.006   |
| Insulin (%)          | 100.0           | 28.9            | <0.001  |

Values are shown as the mean ± standard deviation or frequency. Statistical significance was assessed by Mann–Whitney U test or Chi-squared test.

*n = 54 and 572 for type 1 and type 2 diabetes, respectively. BMI, body mass index; DPP4, dipeptidyl peptidase 4; eGFR, estimated glomerular filtration rate; GLP-1, glucagon-like peptide 1; HbA1c, glycated hemoglobin; SGLT-2, sodium-glucose co-transporter 2.
Because many factors differed significantly between the type 1 and type 2 diabetes groups (Table 1), logistic regression analyses were carried out to clarify whether the difference in sarcopenia and its components between type 1 and type 2 diabetes groups was independent of these factors (Table 2). When BMI, regular exercise habit, cardiovascular complications, C-peptide, or medication for diabetes except insulin were added to age and sex as adjustment factors, type 1 diabetes remained significantly associated with the increased prevalence of low handgrip strength; this indicated that type 1 diabetes is a risk factor for low handgrip strength independent of these confounding factors. When HbA1c, Alb, or medication with insulin were added to age and sex as adjustment factors, the significant association of type 1 diabetes with the prevalence of low handgrip was not retained.

**Logistic regression analysis for sarcopenia and its components focused on medication for diabetes**

As sarcopenia and its components were significantly more frequent in patients with insulin treatment than in those without insulin treatment (Table S2), logistic regression analysis was carried out to clarify whether the difference in sarcopenia and its components between patients treated with and without insulin was independent of the other covariates (Table S3). The significant association between insulin treatment and the increased prevalence of sarcopenia and all components of sarcopenia was retained even after adjusting for age and sex. When type of diabetes or C-peptide was added as an adjustment factor, insulin treatment remained significantly associated with the increased prevalence of low handgrip strength and slow gait speed, but its significant association with the prevalence of sarcopenia and low SMI was not retained. When HbA1c was added as an adjustment factor, the significant associations with the prevalence of sarcopenia and its components were not retained.

**Logistic regression analysis for sarcopenia and its components focused on HbA1c**

The significant associations of type 1 diabetes with the prevalence of low handgrip and the prevalence of sarcopenia and its components were not retained, when HbA1c was added to age and sex as adjustment factors (Table 2). Moreover, HbA1c is a significant factor for the prevalence of low handgrip strength and slow gait speed (Table S2). When medication with insulin was added to age and sex as adjustment factors, the significant association with HbA1c was not retained, but the significant associations with the prevalence of low handgrip strength were retained when any factor was added to age and sex as adjustment factor (Table 3).

**DISCUSSION**

In this cross-sectional study, differences in the prevalence rates of sarcopenia and its components were observed between patients with type 1 and type 2 diabetes. The prevalence of sarcopenia and low handgrip strength in older adult patients with type 1 diabetes was significantly higher than that in older adult patients with type 2 diabetes (2.5 times and 1.7 times, respectively).

We also found that age ≥ 65 years, BMI < 18.5 kg/m², Alb < 4.0 g/dL, and medication with insulin were risk factors for sarcopenia, and that BMI ≥ 25 kg/m² was a protective factor for sarcopenia under-age- and sex-adjusted conditions (Table S2). These findings are in line with previous studies which reported that aging, obesity, underweight, and low albumin are factors associated with sarcopenia in patients with diabetes, as well as healthy subjects.²,¹²,¹³

We previously reported that in MUSCLES-DM study participants, insulin treatment was associated with sarcopenia as per a cross-sectional study,¹⁴ while as per a longitudinal study, insulin treatment attenuated the progression of sarcopenia in patients with type 2 diabetes.¹⁰,¹⁵,¹⁶ This suggests that insulin treatment itself may not adversely affect sarcopenia and other factors participating in sarcopenia. To clarify the contribution of insulin...
treatment to sarcopenia, we studied patients with type 1 and type 2 diabetes with and without insulin treatment. Sarcopenia and its components were more frequent in type 1 diabetes and type 2 diabetes with insulin treatment than in type 2 diabetes without insulin treatment, indicating that insulin treatment is a risk factor for sarcopenia regardless of the type of diabetes. In logistic regression analysis, significant differences were not retained when diabetes type, HbA1c, or C-peptide was adjusted (Table S3), indicating that these factors contribute to the significant association between sarcopenia and insulin treatment. These data suggest that the higher frequency of sarcopenia and its components in patients with insulin treatment is due to poor glycemic control reflected by high HbA1c which is often observed in type 1 diabetes patients with low C-peptide. This can explain the apparent discrepancy between the cross-sectional study which reported a risk of sarcopenia with insulin treatment and the longitudinal studies which reported an attenuation of sarcopenia with insulin treatment. Insulin treatment per se may not have adverse effects on sarcopenia but may be beneficial when glycemic control is improved by insulin treatment, as observed in the longitudinal studies. Although type 1 diabetes is characterized by very low C-peptide levels and treatment with insulin, the results of the present study suggest that better glycemic control achieved by intensive insulin therapy may protect patients with type 1 diabetes against sarcopenia as in the case of other chronic complications. A longitudinal study of type 1 diabetes and sarcopenia with reference to glycemic control will clarify this aspect; such a study is now ongoing as part of the MUSCLES-DM study.

The high prevalence of sarcopenia in type 1 diabetes patients was due to the high prevalence of weak handgrip under age- and sex-adjusted conditions (Table 2). Weak handgrip was reported to be associated with poor prognosis and mortality in older adults. Logistic regression analyses were carried out to clarify the factors contributing to the positive association between type 1 diabetes and low handgrip strength (Table 2). The results showed that the positive association was independent of BMI, regular exercise habit, cardiovascular complications, orthopedic complications, C-peptide, and medication with drugs except insulin. In contrast, the significant association was not retained when HbA1c, Alb, or medication with insulin was added as an adjustment factor, suggesting the possibility that improvement in HbA1c and serum albumin contribute to strong handgrip strength. Significant associations were reported between the incidence of type 2 diabetes and handgrip strength; improvement in HbA1c was reported to be associated with improved ASM and gait speed in patients with type 2 diabetes. The present study suggests the need for a longitudinal study to investigate whether improved glycemic control contributes to better handgrip strength in both type 1 and type 2 diabetes.

The present study identified factors contributing to differences in the prevalence of sarcopenia between patients with type 1 and type 2 diabetes in the Japanese population. Although an association between lean body mass and high HbA1c has been reported in type 1 diabetes in the European population, it is not fully understood whether similar results can be obtained in Western countries like the one in this study.

There were several limitations to this study. First, we could not infer causality because of the cross-sectional study design. Second, we could not examine the associations between type 1/type 2 diabetes and sarcopenia and its components due to the small number of patients with type 1 diabetes (n = 57) (compared to the number of patients with type 2 diabetes [n = 755]). Type 1 diabetes was not significantly associated with sarcopenia or its components in the unadjusted model (Table S2). There were significant differences in age and sex between type 1 and type 2 diabetes patients (Table 1). This difference may be due to the age- and sex-adjusted conditions. Third, we estimated the ASM using bioelectrical impedance analysis devices, and did not use dual-energy X-ray absorptiometry. However, in bioelectrical impedance analysis devices, devices have been reported to correlate strongly with dual-energy X-ray absorptiometry. Additionally, bioelectrical impedance analysis devices have been recognized in the European Working Group on Sarcopenia in Older People and the Asian Working Group for Sarcopenia.

In summary, the prevalence of sarcopenia in older adult patients with type 1 diabetes was higher than that in older adult patients with type 2 diabetes. Above all, there was a distinct difference in the frequency of low handgrip strength between the two groups. Our results indicated that poor glycemic control rather than the type of diabetes or insulin treatment is a primary risk factor for sarcopenia in diabetes mellitus. A longitudinal study is needed to clarify whether type 1 diabetes mellitus

| Table 3 | Adjusted odds ratios and 95% confidence intervals (CIs) of HbA1c ≥ 8.0% and HbA1c < 8.0% according to sarcopenia and its components |
|---------|---------------------------------------------------------------|
| Adjusted factors | Sarcopenia | Low ASM | Low handgrip strength | Slow gait speed |
| | OR (95% CI) | P | OR (95% CI) | P | OR (95% CI) | P | OR (95% CI) | P |
| None | 1.62 (0.93–2.83) | 0.09 | 1.19 (0.76–1.85) | 0.05 | 1.81 (1.29–2.56) | <0.001 | 1.46 (1.03–2.07) | 0.03 |
| Age, Sex | 1.75 (0.99–3.07) | 0.05 | 1.26 (0.80–1.97) | 0.02 | 2.05 (1.42–2.95) | <0.001 | 1.53 (1.07–2.19) | 0.02 |
| Age, Sex, Diabetes type | 1.65 (0.93–2.93) | 0.09 | 1.20 (0.76–1.89) | 0.07 | 1.96 (1.36–2.83) | <0.001 | 1.54 (1.07–2.20) | 0.01 |
| Age, Sex, C-peptide | 1.89 (0.93–3.84) | 0.08 | 1.08 (0.61–1.90) | 0.06 | 2.57 (1.63–4.05) | <0.001 | 1.89 (1.24–2.90) | 0.003 |
| Age, Sex, Medication with insulin | 1.43 (0.77–2.67) | 0.26 | 1.02 (0.62–1.68) | 0.63 | 1.74 (1.17–2.61) | 0.006 | 1.39 (0.94–2.06) | 0.10 |

ASM, appendicular skeletal muscle mass; CI, confidence interval; HbA1c, glycated hemoglobin; OR, odds ratio.
remains as a risk factor for sarcopenia in patients with adequate glycemic control.

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DISCLOSURE
The authors declare no conflict of interest. Approval of the research protocol: The research protocol was approved by the ethics committees of Kindai University (28–079, 11 October, 2016), Osaka University (667, 7 June, 2016), and Ehime University (28–2, 29 June, 2016). Informed consent: All patients gave written informed consent. Registry and the registration no. of the study/trial: N/A. Animal studies: N/A.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Figure S1 | Prevalence rate of sarcopenia and its components in patients with type 2 diabetes with and without insulin treatment. Closed bar: type 2 diabetes with insulin treatment (n = 218), open bar: type 2 diabetes without insulin treatment (n = 537). Statistical significance was assessed by Fisher’s exact test. * P < 0.05, ** P < 0.01

Figure S2 | Prevalence rate of sarcopenia and its components in patients with type 1 diabetes and type 2 diabetes with and without insulin treatment. Closed bar: type 1 diabetes (n = 57), hashed bar: type 2 diabetes with insulin (n = 218), open bar: type 2 diabetes without insulin (n = 537). Statistical significance was assessed by Fisher’s exact test. * P < 0.05. T1D, type 1 diabetes; T2D, type 2 diabetes

Figure S3 | Prevalence rate of sarcopenia and its components in patients with type 2 diabetes with reference to endogenous insulin secretory capacity. Study participants were divided into three groups according to the tertiles of fasting C-peptide levels. Q1/3 (closed bar): 0.0–0.9 ng/mL (n = 190), Q2/3 (hashed bar): 1.0–1.6 ng/mL (n = 188), Q3/3 (open bar): 1.7–8.1 ng/mL (n = 194). Statistical significance was assessed by Fisher’s exact test. ** P < 0.01, *** P < 0.0001

Figure S4 | Prevalence rate of sarcopenia and its components in patients with type 1 diabetes (closed bar: n = 57) and type 2 diabetes divided into three groups according to the tertiles of fasting C-peptide levels. Closed bar: type 1 diabetes (n = 57). Patients with type 2 diabetes were divided into three groups according to the tertiles of fasting C-peptide levels. Q1/3 (dark hashed bar): 0.0–0.9 ng/mL (n = 190), Q2/3 (light hashed bar): 1.0–1.6 ng/mL (n = 188), Q3/3 (open bar): 1.7–8.1 ng/mL (n = 194). Statistical significance was assessed by Fisher’s exact test. ** P < 0.01, *** P < 0.0001. T1D, type 1 diabetes; T2D, type 2 diabetes

Table S1 | A. Clinical characteristics of patients with type 1 diabetes with and without sarcopenia and its components
B. Clinical characteristics of patients with type 2 diabetes with and without sarcopenia and its components

Table S2 | Logistic regression analysis for sarcopenia and its components.

Table S3 | Adjusted odds ratios and 95% confidence intervals (CIs) of medication with insulin for sarcopenia and its components.