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ORIGINAL ARTICLE

High prevalence and clinical impact of dynapenia and sarcopenia in Japanese patients with type 1 and type 2 diabetes: Findings from the Impact of Diabetes Mellitus on Dynapenia study

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ABSTRACT

Aims/Introduction: The present study aimed to clarify the prevalence and clinical characteristics of sarcopenia and dynapenia, which are muscle weakness with and without low muscle mass, respectively, in Japanese patients with type 1 diabetes mellitus and type 2 diabetes mellitus.

Materials and Methods: This cross-sectional study enrolled 1,328 participants with type 1 diabetes (n = 177), type 2 diabetes (n = 645) and without diabetes (n = 506). Sarcopenia was defined as a low grip strength and slow gait speed with low skeletal muscle mass index, whereas dynapenia was defined as low strengths of grip and knee extension with a normal skeletal muscle mass index. Participants without sarcopenia and dynapenia were defined as robust.

Results: Among participants aged ≥65 years, sarcopenia and dynapenia were observed in 12.2% and 0.5% of individuals without diabetes, 42.9% and 11.4% of type 1 diabetes patients, and 20.9% and 13.9% of type 2 diabetes patients. In both type 1 diabetes and type 2 diabetes patients, sarcopenic patients were significantly older and thinner, and showed a significantly higher rate of diabetic neuropathy than robust patients. In patients with type 1 diabetes and type 2 diabetes, dynapenic patients were older, and showed a higher rate of diabetic neuropathy and lower estimated glomerular filtration rate than robust patients. Patients complicated with sarcopenia and dynapenia showed a significantly lower physical quality of life and higher rate of incidental falls than robust patients.

Conclusions: Sarcopenia and dynapenia were more frequent in patients with type 1 diabetes and type 2 diabetes than in individuals without diabetes, which might contribute to their impaired quality of life and incidental falls.

INTRODUCTION

Aging-related muscle loss and weakness, known as sarcopenia[1,2], is currently recognized as a diabetic complication[3,4], and might contribute to incidental falls and frailty in patients with diabetes[5]. Sarcopenia was diagnosed as an aging-related muscle weakness accompanied with loss of muscle mass and physical performance by a recent revised consensus of the Asian Working Group for Sarcopenia (AWGS)[2]. In a previous study, the

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prevalence of sarcopenia according to the AWGS 2014 criteria[6] was reported to be 4–11% in general older adults[6], whereas a higher prevalence (14.8%) has been reported in patients with type 2 diabetes[7]. In addition, sarcopenia can increase the risk of mortality in type 2 diabetes mellitus[8]. However, the prevalence and clinical characteristics of sarcopenia have not been determined in patients with type 1 diabetes mellitus.

Manini *et al.*[9] proposed that an aging-related impairment of muscle strength without reducing muscle mass should be determined as dynapenia. As dynapenia is not associated with low muscle volume, it might be caused by different pathogenic factors from sarcopenia. Therefore, muscular weakness should be classified as sarcopenia and dynapenia separately according to the presence and absence of low skeletal muscle mass. A previous study showed that the decline in knee extension strength in the group with the highest quartile of glycated hemoglobin (HbA1c) seemed to start when the patients were aged in their 40s[10]. In addition, a longer duration of diabetes (≥6 years) and poor glycemic control (HbA1c >8.0%) were associated with even lower knee extension strength[4]. However, the detail of clinical characteristics of dynapenia with regard to the quality of life (QOL) and incidental falls in patients with type 1 diabetes and type 2 diabetes have not yet been evaluated.

Therefore, the present study intended to clarify the prevalence and clinical characteristics, especially the QOL and incidental falls, of sarcopenia and dynapenia in Japanese patients with type 1 diabetes and type 2 diabetes.

METHODS

Study design and participants

The present cross-sectional study was approved by the ethics committee of Tokushima University Hospital (approval #2281-9). This was a multi-institutional joint cross-sectional study of seven medical centers on the Impact of Diabetes Mellitus on Dynapenia (iDIAMOND) Study. We recruited individuals without diabetes from the community in the Harima region, Hyogo prefecture, and people who underwent health checkups in the Tokushima University Hospital (Tokushima, Japan) and Osaka Rosai Hospital (Osaka, Japan). The inclusion criteria were patients with type 1 diabetes and type 2 diabetes who were aged ≥30 years. Patients using steroids and those with stroke-induced quadriplegia, myopathy or mobility disability were excluded. In addition, individuals without diabetes aged ≥30 years were included as the control group. All participants gave written informed consent. In the present study, type 1 diabetes and type 2 diabetes was defined by a physician's diagnosis and medical chart review. Elderly adults were defined as those aged ≥65 years.

Assessments of bodyweight and composition

Bodyweight and skeletal muscle mass were measured using a multifrequency bioelectrical impedance analysis (In Body bioelectrical impedance analyzer; In Body Japan, Tokyo, Japan). Obesity was defined as a body mass index (BMI) of ≥25.0 kg/m^2, while underweight was defined as a BMI of <18.5 kg/m^2 according to the criteria of obesity reported by the Japan Society for the Study of Obesity. The skeletal muscle mass index (SMI) was calculated by dividing the total skeletal muscle mass of upper and lower limbs by the squared height[1,2].

Assessments of muscle strength and physical performance

The strengths of grip and knee extension were evaluated as indicators of muscle strength, and gait speed also was determined to evaluate physical performance. The maximum isometric grip strength in each hand was measured in a standing position (GRIP-D TKK5401; Takei, Niigata, Japan)[1,2,5]. The maximum isometric lower-extremity knee extension strength torque was determined using a hand-held dynamometer (μTas F-1; ANIMA, Tokyo, Japan)[11]. The participants sat on a bench and the force sensor was fixed firmly by a belt to the distal end of the tibia to a rigid bar. We multiplied the maximal isometric knee extension strength and the lever arm strength to calculate knee extension torque (Nm). The knee extension strength was evaluated by the knee extension strength torque divided by the bodyweight (Nm/kg)[12,13]. For the usual gait speed, participants were instructed to walk a distance of 10 m at a speed that was normal to them, and the length of time that it took to walk 4 m (3–7 m) was measured[1,2,5].

Definitions of sarcopenia and dynapenia

Sarcopenia was diagnosed according to the definition of the AWGS 2019 criteria[2], which involves a low grip strength, slow gait speed and low SMI (cut-off values shown in Table S1). Dynapenia was defined according to the previous proposal by Manini and Clark as a low grip and knee extension strength with normal SMI[9,13]. Participants who were not diagnosed with sarcopenia or dynapenia were categorized as robust.

Clinical data

The duration of diabetes, HbA1c value, ratio of urinary albumin to creatinine, estimated glomerular filtration rate (eGFR), diabetic neuropathy, diabetic retinopathy (including simple diabetic retinopathy, pre-proliferative diabetic retinopathy and proliferative diabetic retinopathy), and medicines for diabetes, hypertension and dyslipidemia were collected from the medical records or an interview survey. The eGFR was calculated using the following equation obtained from the Japanese Society of Nephrology: eGFR (male) = $194 \times Cr^{-1.094} \times age^{-0.287}$; eGFR (female) = $194 \times Cr^{-1.094} \times age^{-0.287} \times 0.739$[14]. We defined diabetic neuropathy according to the simplified diagnostic criteria of diabetic polyneuropathy proposed by the consensus of the Japanese study group of diabetic neuropathy. In this criteria, diabetic neuropathy was diagnosed when the patients matched two items out of three items, such as bilateral symptoms of extremities, decreased Achilles tendon reflex and shortened vibration sensory of lower extremities.

Assessments of the health-related QOL and physical activity

The health-related QOL of the surveyed participants was estimated using the Short-Form 8 Health Survey. The questionnaire consists of questions measuring the physical component summary and the mental component summary in relation to health concepts[15].

Physical activity was evaluated by a diagnostic survey with a short version of the International Physical Activity Questionnaire for each participant[16,17]. The weekly energy consumption (EC) expressed as kilocalories per week was calculated from the data collected from the questionnaires.

History of incidental falls

The history of incidental falls was obtained from a medical interview using the care prevention checklist, the reliability and validity of which have been evaluated in Japanese individuals[18]. Incidental fall was defined as one or more falls in the past year.[5]

Statistical analysis

The SPSS Statistics 22 software program (IBM Japan, Tokyo, Japan) was used to carry out the statistical analyses. All data are presented as the mean ± standard deviation. Intergroup comparisons (individuals without diabetes vs type 1 diabetes patients vs type 2 diabetes patients or robust vs sarcopenia vs dynapenia) were assessed using an unpaired one-way analysis of variance or an unpaired *t*-test (continuous variables), χ^2-test (categorical variables), analysis of covariance (adjusted analysis, continuous variables) and Mantel–Haenszel test (adjusted analysis, categorical variables). Multivariate logistic regression analyses were used to calculate the cross-sectional association of sarcopenia and dynapenia in type 1 diabetes or type 2 diabetes patients (input of covariates in type 1 diabetes and type 2 diabetes: age ≥65 years, female, BMI ≥25.0 kg/m^2 or BMI <18.5 kg/m^2, HbA1c ≥8.0%, diabetic neuropathy, eGFR <30 mL/min/1.73 m^2, EC of ≥3 Mets). The odds ratios (ORs) and 95% confidence intervals (CIs) were calculated using logistic regression models. Covariates in the multivariate logistic regression analyses were selected using a forced entry method. *P*-values of <0.05 were considered to show statistical significance.

RESULTS

Prevalence rate of sarcopenia and dynapenia

A total of 1,328 Japanese participants (individuals without diabetes, $n = 506$; type 1 diabetes patients, $n = 177$; type 2 diabetes patients, $n = 645$) were enrolled in the present study (Tables S2–S5). The prevalence rate of sarcopenia and dynapenia in individuals without diabetes and in type 1 diabetes and type 2 diabetes patients is shown in Figure 1.

Among elderly participants aged ≥65 years, type 1 diabetes was associated with the highest prevalence rate of sarcopenia (Figure 1; vs non-diabetes, $P < 0.001$; vs type 2 diabetes mellitus, $P = 0.003$). Sarcopenia was also more frequently observed in elderly patients with type 2 diabetes than in individuals without diabetes ($P < 0.001$). In contrast, in these elderly participants, type 1 diabetes mellitus and type 2 diabetes mellitus were associated with an equally higher prevalence rate of dynapenia than in individuals without diabetes (Figure 1; type 1 diabetes patients vs individuals without diabetes, $P < 0.001$; type 2 diabetes patients vs individuals without diabetes, $P < 0.001$). In participants aged 50–64 years, type 2 diabetes patients also showed a significantly higher prevalence rate of dynapenia than in individuals without diabetes (type 2 diabetes patients vs individuals without diabetes, $P = 0.030$).

Among elderly participants aged ≥65 years, patients with type 1 diabetes showed a significantly higher rate of low SMI, grip strength and knee extension strength than type 2 diabetes patients and individuals without diabetes (low SMI: vs individuals without diabetes, $P < 0.001$; vs type 2 diabetes patients, $P = 0.043$; low grip strength: vs individuals without diabetes, $P < 0.001$; vs type 2 diabetes patients, $P = 0.026$; low knee extension strength: vs individuals without diabetes, $P < 0.001$; vs type 2 diabetes patients, $P = 0.008$). In elderly patients with type 2 diabetes, the prevalence rates of low SMI, grip strength and knee extension strength were significantly higher than those of individuals without diabetes (low SMI; $P < 0.001$, low grip strength; $P < 0.001$, low knee extension strength; $P < 0.001$). Patients who were aged 50–64 years with type 1 diabetes and type 2 diabetes showed a significantly higher rate of low grip strength and low knee extension strength than individuals without diabetes (low grip strength: type 1 diabetes patients, $P = 0.002$; type 2 diabetes patients, $P = 0.003$; low knee extension strength: type 1 diabetes patients and type 2 diabetes patients, $P < 0.001$).

Clinical characteristics of sarcopenia and dynapenia

The clinical characteristics of sarcopenia and dynapenia in individuals without diabetes, and patients with type 1 diabetes and type 2 diabetes are shown in Tables S3, 1 and 2, respectively.

Sarcopenic patients with type 1 diabetes and type 2 diabetes were significantly older (type 1 diabetes patients and type 2 diabetes patients, $P < 0.001$) and had significantly higher rates of BMI <18.5 kg/m^2 (type 1 diabetes and type 2 diabetes, $P < 0.001$) and diabetic neuropathy (type 1 diabetes, $P = 0.031$; type 2 diabetes, $P = 0.043$), and lower EC of ≥3 METs (type 1 diabetes patients, $P < 0.047$; type 2 diabetes patients, $P < 0.001$) than robust patients with type 1 diabetes and type 2 diabetes.

Dynapenic patients with type 1 diabetes and type 2 diabetes were older (type 1 diabetes patients, $P = 0.005$; type 2 diabetes patients, $P < 0.001$), and showed a higher rate of diabetic neuropathy (type 1 diabetes patients, $P = 0.001$; type 2 diabetes patients, $P < 0.001$) and eGFR <30 mL/min/1.73 m^2 (type 1 diabetes patients and type 2 diabetes patients, $P < 0.001$) than robust patients with type 1 diabetes and type 2 diabetes. In

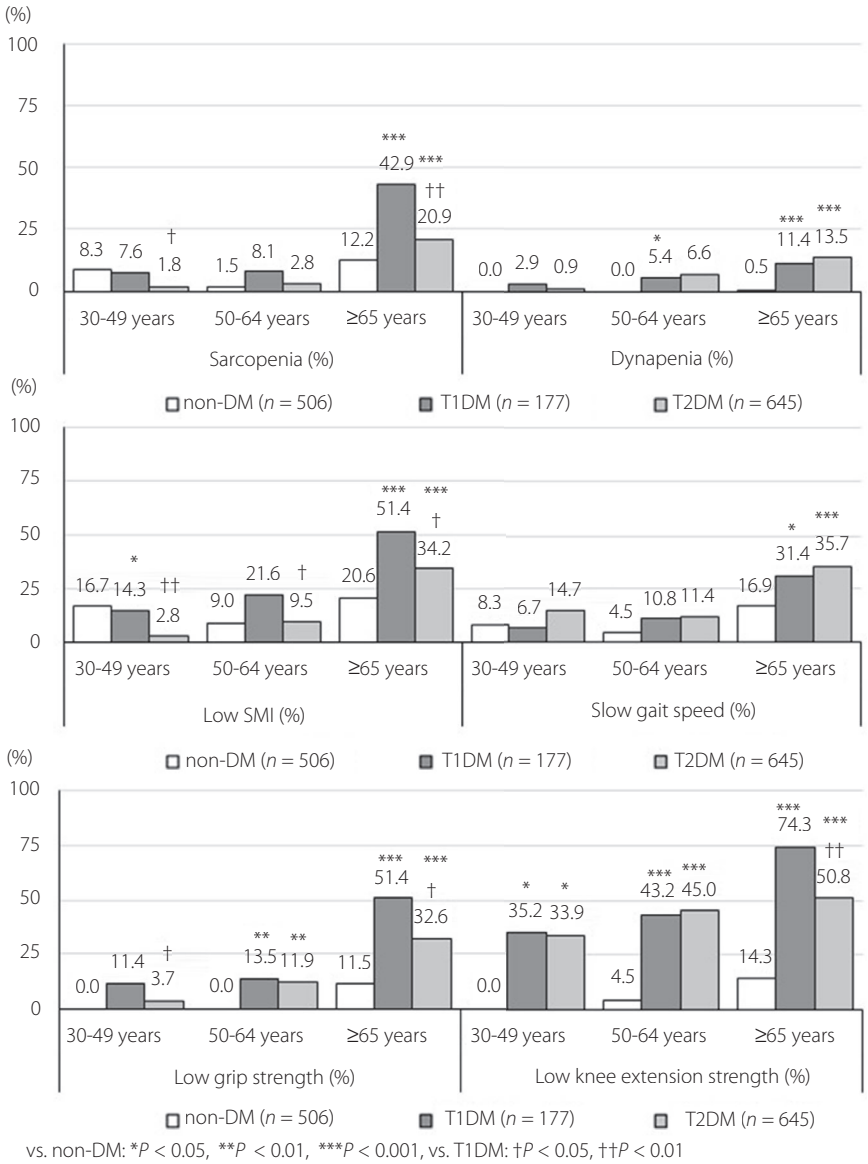

Figure 1 | Prevalence rate of sarcopenia and dynapenia, and these components in individuals without diabetes (non-DM), and patients with type 1 diabetes (T1DM) and type 2 diabetes (T2DM; vs non-DM $*P < 0.05$, $**P < 0.01$, $***P < 0.001$, vs T1DM $^{\dagger}P < 0.05$, $^{\dagger\dagger}P < 0.01$. DM, diabetes mellitus; SMI, skeletal muscle mass index.

addition, dynapenic patients showed a higher rate of BMI ≥25.0 than robust and sarcopenic patients with type 2 diabetes.

Health-related QOL of sarcopenia and dynapenia

Sarcopenic patients with type 1 diabetes and type 2 diabetes have a significantly lower physical QOL than robust patients with type 1 diabetes and type 2 diabetes (type 1 diabetes patients, $P < 0.001$; type 2 diabetes patients, $P = 0.018$; Tables 1 and 2). Dynapenic patients with type 1 diabetes and type 2 diabetes had a lower physical QOL (type 1 diabetes and type 2 diabetes, $P < 0.001$) than robust patients with type 1 diabetes and type 2 diabetes (Tables 1,2).

The analysis of covariance adjusted by age ≥65 years showed that sarcopenia and dynapenia were associated with a lower physical QOL than a robust status (type 1 diabetes, with sarcopenia: $P = 0.015$, with dynapenia: $P = 0.001$; type 2 diabetes, with sarcopenia: $P = 0.036$, with dynapenia: $P < 0.001$; Figure 2). In contrast, neither sarcopenia nor dynapenia affected the mental QOL in patients with type 1 diabetes and type 2 diabetes compared with robust patients.

Table 1 | Clinical characteristics of the study patients with type 1 diabetes according to the presence of sarcopenia and dynapenia

Type 1 diabetes patients (n = 177)	Robust (n = 142)	Sarcopenia (n = 26)	P-value robust vs sarcopenia	Dynapenia (n = 9)	P-value robust vs dynapenia	P-value sarcopenia vs dynapenia
Age (years)	46.2 ± 11.8	61.2 ± 16.3	<0.001	60.3 ± 17.1	0.005	0.982
Female (%)	62.7	69.2	0.792	77.8	0.361	0.490
BMI (kg/m^2)	23.3 ± 3.7	20.8 ± 2.9	0.004	23.9 ± 3.0	0.882	0.072
BMI ≥25.0 kg/m^2 (%)	22.5	11.5	0.095	33.3	0.423	0.058
BMI <18.5 kg/m^2 (%)	3.5	26.9	<0.001	0	0.610	0.113
Duration of diabetes (years)	19.3 ± 11.6	16.1 ± 14.0	0.423	19.7 ± 7.3	0.995	0.716
HbA1c (%)	8.1 ± 1.9	7.8 ± 1.8	0.839	7.6 ± 0.7	0.744	0.943
HbA1c ≥8.0% (%)	39.7	29.2	0.274	22.2	0.089	0.330
Urinary albumin/creatinine ratio (mg/gCr)	81.1 ± 343.1	92.3 ± 192.0	0.990	57.2 ± 126.5	0.980	0.968
eGFR (mL/min/1.73 m^2)	84.4 ± 21.2	71.3 ± 24.2	0.019	62.1 ± 34.6	0.012	0.544
Diabetic neuropathy (%)	25.8	46.2	0.048	85.7	0.011	0.235
Diabetic retinopathy, PPDR and PDR (%)	14.6	30.8	0.036	44.4	0.119	0.886
eGFR <30 mL/min/1.73 m^2 (%)	1.4	3.9	0.398	22.2	<0.001	0.090
Sitting (h/day)	5.4 ± 3.9	5.3 ± 3.0	0.993	8.0 ± 4.7	0.119	0.164
EC of ≥3 Mets (kcal/day)	183 ± 226	76 ± 124	0.047	65 ± 115	0.233	0.991
Physical QOL (score)	48.6 ± 7.8	39.5 ± 12.8	<0.001	36.2 ± 15.0	<0.001	0.618
Mental QOL (score)	46.3 ± 10.6	44.3 ± 8.1	0.642	44.1 ± 12.1	0.809	0.642
Incidental fall, ≥1 times (%)	7.0	30.8	<0.001	44.4	0.004	0.886

Data are shown as the mean ± standard deviation. BMI, body mass index; EC, energy consumption; eGFR, estimated glomerular filtration rate; HbA1c, glycated hemoglobin; PDR, proliferative diabetic retinopathy; PPDR, pre-proliferative diabetic retinopathy; QOL, quality of life.

Incidental falls of sarcopenia and dynapenia

Sarcopenic patients with type 1 diabetes and type 2 diabetes showed a higher rate of incidental falls (type 1 diabetes, $P < 0.001$; type 2 diabetes, $P < 0.001$) than robust patients (Tables 1,2). Dynapenic patients with type 1 diabetes and type 2 diabetes also showed a higher rate of incidental falls (type 1 diabetes patients , $P = 0.004$; type 2 diabetes patients, $P < 0.001$) than robust patients (Tables 1,2).

The analysis using the Mantel–Haenszel test adjusted by age ≥65 years showed that dynapenic patients with type 1 diabetes were associated with a higher rate of incidental falls than a robust status (dynapenia with adjusted age ≥65 years, $P = 0.026$; Figure 2). In patients with type 2 diabetes, sarcopenia and dynapenia were associated with a higher rate of incidental fall than a robust status (with sarcopenia: $P < 0.001$, with dynapenia: $P < 0.001$).

ORs for the risk of sarcopenia and dynapenia

The ORs, determined by a multivariate logistic regression analysis, of clinical parameters related to sarcopenia and dynapenia in patients with type 1 diabetes and type 2 diabetes are shown in Table 3.

In patients with type 1 diabetes and type 2 diabetes, age ≥65 years and BMI <18.5 kg/m^2 were significantly associated with the prevalence of sarcopenia. In addition, HbA1c ≥8.0% and EC of ≥3 Mets (kcal/day) was significantly associated with the prevalence of sarcopenia in patients with type 2 diabetes.

In patients with type 1 diabetes, diabetic neuropathy was significantly associated with the prevalence of dynapenia. In patients with type 2 diabetes, female, participants aged ≥65 years, BMI ≥25.0 kg/m^2, diabetic neuropathy, eGFR <30 mL/min/1.73 m^2 and EC of ≥3 Mets (kcal/day) were significantly associated with the prevalence of dynapenia.

DISCUSSION

In the present multicenter cross-sectional iDIAMOND study, the prevalence and clinical characteristics, involving the QOL and incidental falls, of sarcopenia and dynapenia were investigated in Japanese individuals without diabetes and patients with type 1 diabetes and type 2 diabetes. We used the new AWGS 2019 criteria to describe the prevalence of diabetes-related sarcopenia in patients with type 1 diabetes and type 2 diabetes compared with individuals without diabetes. The present findings provide basic epidemiological data comparing the prevalence of sarcopenia in type 1 diabetes patients and type 2 diabetes patients in an Asian population.

We showed for the first time that the prevalence of sarcopenia in patients with type 1 diabetes was significantly higher than that in patients with type 2 diabetes and individuals without diabetes among elderly adults, according to the newly established criteria of sarcopenia for an Asian population[2] (Figure 1). Sarcopenia is reported to be associated with aging, an underweight status (e.g., malnutrition and low protein intake) and chronic disease, including diabetes[1]. Indeed, older age and underweight status were associated with sarcopenia in all

Table 2 | Clinical characteristics of the study patients with type 2 diabetes mellitus according to the presence of sarcopenia and dynapenia

Type 2 diabetes patients (n = 645)	Robust (n = 510)	Sarcopenia (n = 76)	P-value robust vs sarcopenia	Dynapenia (n = 59)	P-value robust vs dynapenia	P-value sarcopenia vs dynapenia
Age (years)	60.4 ± 11.5	72.4 ± 7.9	<0.001	69.8 ± 9.1	<0.001	0.359
Female (%)	37.3	38.2	0.879	61.0	0.001	0.015
BMI (kg/m^2)	26.6 ± 5.0	21.3 ± 3.4	<0.001	27.7 ± 4.6	0.202	<0.001
BMI ≥25.0 kg/m^2 (%)	59.0	10.5	<0.001	72.9	0.037	<0.001
BMI <18.5 kg/m^2 (%)	2.4	15.8	<0.001	0	0.239	0.001
Duration of diabetes (years)	10.7 ± 8.8	16.6 ± 11.5	<0.001	15.1 ± 10.3	0.002	0.642
HbA1c (%)	8.9 ± 2.3	9.2 ± 2.4	0.563	8.3 ± 2.0	0.091	0.046
HbA1c ≥8.0% (%)	56.6	66.7	0.125	44.8	0.070	0.012
Urinary albumin/creatinine ratio (mg/gCr)	165.9 ± 768.2	109.2 ± 238.0	0.873	418.6 ± 1172.7	0.102	0.127
eGFR (mL/min/1.73 m^2)	75.0 ± 23.8	73.3 ± 24.8	0.825	58.7 ± 24.5	<0.001	0.001
Diabetic neuropathy (%)	45.5	58.1	0.043	69.5	<0.001	0.166
Diabetic retinopathy, PPDR and PDR (%)	14.9	22.4	0.087	35.6	<0.001	0.090
eGFR <30 mL/min/1.73 m^2 (%)	2.0	4.0	0.273	15.3	<0.001	0.022
Sitting (h/day)	6.7 ± 4.3	7.7 ± 4.4	0.139	8.7 ± 5.4	0.004	0.448
EC of ≥3 Mets (kcal/day)	189 ± 214	88 ± 106	<0.001	85 ± 138	0.001	0.997
Physical QOL (score)	45.0 ± 9.1	41.7 ± 10.7	0.018	33.2 ± 11.4	<0.001	<0.001
Mental QOL (score)	47.6 ± 8.8	47.0 ± 8.1	0.854	48.3 ± 9.0	0.860	0.707
Incidental fall, ≥1 times (%)	7.7	30.3	<0.001	49.2	<0.001	0.025

BMI, body mass index; EC, energy consumption; eGFR, estimated glomerular filtration rate; HbA1c, glycated hemoglobin; PDR, proliferative diabetic retinopathy; PPDR, pre-proliferative diabetic retinopathy; QOL, quality of life. Data are shown as the mean value ± standard deviation.

groups in the present study (Table 2). Chronic hyperglycemia (HbA1c >8.0%), but not diabetic microangiopathy, was also associated with the prevalence of sarcopenia in patients with type 2 diabetes (Table 3), which was comparable to the finding of a previous study[19]. However, the HbA1c level was not associated with the highest prevalence of sarcopenia in patients with type 1 diabetes (Table 3). As the pathophysiology of type 1 diabetes, such as depleted endogenous insulin secretion, increased glucose fluctuation and increased incidence of hypoglycemia, is markedly different from that of type 2 diabetes, other risk factors might contribute to the development of sarcopenia in these patients. O'Neill *et al.*[20] recently reported that FoxO transcription factors mediate the majority of transcriptional changes in response to increasing protein degradation and muscle atrophy in a streptozotocin-induced rodent model of type 1 diabetes. Therefore, markedly decreased endogenous insulin signaling might impair skeletal muscle mass and strength in patients with type 1 diabetes.

Type 2 diabetes-related sarcopenia has been the focus of previous diabetes treatment practices. Future clinical practices should consider treatment focusing on sarcopenia in type 1 diabetes patients as well as type 2 diabetes patients. Furthermore, our new results are expected to help healthcare professionals who treat elderly patients with type 1 diabetes and type 2 diabetes to diagnose sarcopenia at early stage, and to prevent developing frailty and physical disturbance. We also stimulate the activity of research in the field of diabetes-associated sarcopenia to prevent and slow adverse health outcomes that incur a heavy burden for patients and healthcare systems.

The prevalence of sarcopenia in the present study – 12.2% in individuals without diabetes and 20.9% in type 2 diabetes – appears to be higher than those reported in previous studies, 4–11% in older adults and 14.8% in type 2 diabetes patients. As we defined sarcopenia according to the new definition of AWGS 2019 in which the threshold of grip strength and gait speed were set at lower levels compared with the previous definition of AWGS 2014, the prevalence of sarcopenia might be estimated to be higher in these new criteria than the previous criteria. Indeed, the prevalence rate of sarcopenia determined by the criteria of AWGS 2014 was 10.3% in individuals without diabetes and 16.9% in type 2 diabetes patients, those data were equal to previous studies.

We also found for the first time that the prevalence of dynapenia in elderly patients with type 1 diabetes and type 2 diabetes was equally higher than that in individuals without diabetes, as shown in Figure 1. Furthermore, the prevalence of dynapenia in patients with type 2 diabetes was significantly higher than that in individuals without diabetes, even those who were aged <65 years. In patients with type 1 diabetes and type 2 diabetes, the skeletal muscle mass, which was low, decreased with age, and the low grip and knee extension strength showed a progressive decline before the age of 65 years (Figure 1). As dynapenia was associated with microangiopathy, but not with high glycated hemoglobin (Table 3), muscle weakness might have occurred due to a defect in the micro-environmental condition involving innervation and circulation, but not hyperglycemia itself, in these patients. Indeed, the severity of diabetic neuropathy has been shown to be

related to muscular weakness in a previous study[11]. In addition, prolonged chronic hyperglycemia accumulates advanced glycation end-products in several tissues, which induces diabetic angiopathy through chronic inflammation and oxidative stress[21]. We previously showed that accumulated advanced glycation end-products, determined by skin autofluorescence, was negatively associated with low knee extension strength in patients with type 1 diabetes and type 2 diabetes[22,23]. In recent studies, obesity was considered to be the cause of sarcopenia[6]. An obesity status was significantly and independently associated with the risk of dynapenia in patients with type 2 diabetes in the present study (Table 3). In this study, however, sarcopenic obesity was observed in just 2.5% of elderly patients with type 2 diabetes (date not shown). In contrast, dynapenic obesity was more common (6.7%) than sarcopenic obesity in patients with type 2 diabetes, so future research on dynapenic obesity will be of interest. Elderly obese patients with type 2 diabetes might thus be at a higher risk of dynapenia, but not sarcopenic obesity. A heavy bodyweight can cause sustained overload on the muscle and increase or maintain its volume. However, we did not evaluate the intramuscular fat, body fat mass by site or adipokine levels; thus, the detailed mechanism underlying the development of dynapenia could not be clarified in the present study.

Finally, this study showed that diabetes patients with sarcopenia and dynapenia have a lower physical QOL and higher rate of incidental falls than robust patients. Sarcopenia has been reported to be associated with a low physical QOL in the general elderly population[24]. In the present study, sarcopenic patients also showed a lower physical QOL than robust patients with type 1 diabetes and type 2 diabetes mellitus (Figure 2). Thus, sarcopenia impairs the physical QOL, regardless of concomitant diabetes. In addition, a low muscle strength was identified as a discriminator of risk for mobility disability, whereas muscle mass measures were not good discriminators of mortality, incidental falls, mobility disability or instrumental activities of daily living disability[25]. Thus, muscle weakness might be a major cause of a poor physical QOL and high risk of incidental falls. In addition, as a result of an analysis of covariance adjusted by older age in the present study,

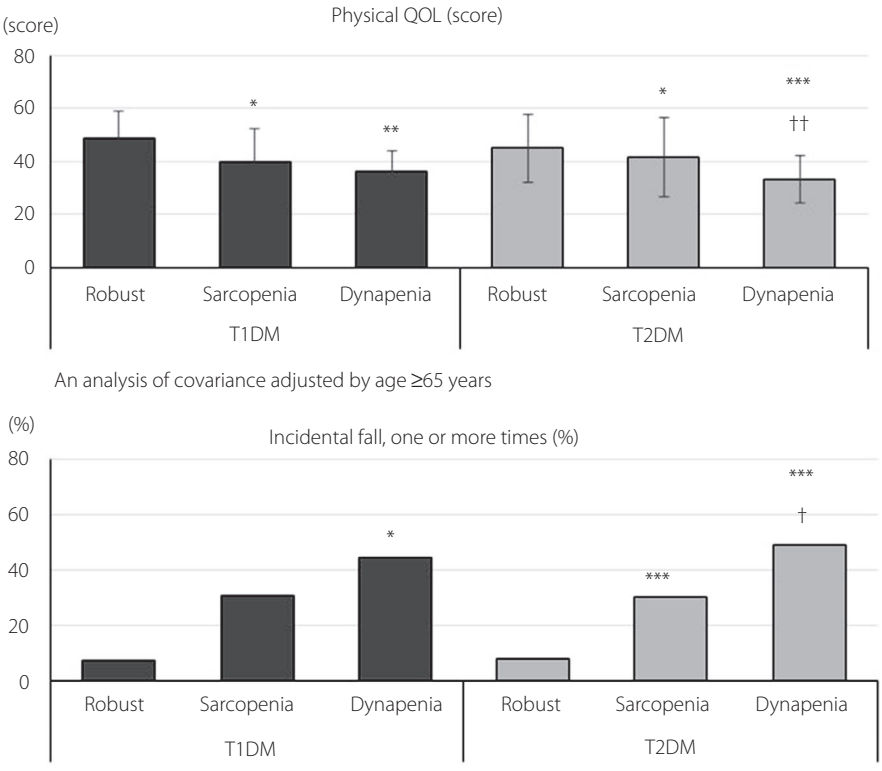

Figure 2 | Physical quality of life and incidental fall in the sarcopenic and dynapenic patients with type 1 diabetes (T1DM) and type 2 diabetes (T2DM). An analysis of the Mantel–Haenszel test adjusted by age ≥65 years. Both versus robust; *$P < 0.05$, **$P < 0.01$, ***$P < 0.001$, vs sarcopenia $^{\dagger}P < 0.05$, $^{\dagger\dagger}P < 0.01$. QOL, quality of life.

Table 3 | Odds ratios of sarcopenia and dynapenia complications in type 1 diabetes and type 2 diabetes patients

	Type 1 diabetes patients			Type 2 diabetes patients		
	Sarcopenia			Sarcopenia		
	Multivariate			Multivariate		
	ORs	95% CIs	*P*-value	ORs	95% CIs	*P*-value
Age ≥65 years	5.283	1.713–16.290	0.004	13.067	5.432–31.432	<0.001
Female	0.646	0.209–1.997	0.448	0.609	0.338–1.098	0.099
BMI <18.5 kg/m^2	21.062	3.573–124.139	0.001	6.007	2.144–16.833	0.001
HbA1c ≥8.0%	0.784	0.251–2.455	0.676	2.044	1.141–3.662	0.016
Diabetic neuropathy	1.695	0.571–5.033	0.342	0.972	0.549–1.721	0.922
eGFR <30 mL/min/1.73 m^2	0.628	0.060–6.553	0.698	0.801	0.209–3.067	0.746
EC of ≥3 Mets (kcal/day)	0.997	0.993–1.001	0.136	0.995	0.993–0.998	<0.001
	Type 1 diabetes patients			Type 2 diabetes patients		
	Dynapenia			Dynapenia		
	Multivariate			Multivariate		
	ORs	95% CIs	*P*-value	ORs	95% CIs	*P*-value
Age ≥65 years	1.494	0.204–10.941	0.693	4.699	2.310–9.558	<0.001
Female	8.193	0.309–217.489	0.209	3.015	1.603–5.672	0.001
BMI ≥25.0 kg/m^2	0.870	0.042–18.047	0.929	3.645	1.847–7.195	<0.001
HbA1c ≥8.0%	0.481	0.055–4.214	0.508	0.666	0.359–1.235	0.197
Diabetic neuropathy	18.050	1.359–239.777	0.028	2.529	1.310–4.880	0.006
eGFR <30 mL/min/1.73 m^2	33.912	0.760–1512.575	0.069	4.130	1.448–11.782	0.008
EC of ≥3 Mets (kcal/day)	0.997	0.987–1.008	0.606	0.997	0.994–0.999	0.015

BMI, body mass index, CIs, confidence intervals, EC, energy consumption, eGFR, estimated glomerular filtration rate, HbA1c, glycated hemoglobin, ORs, odds ratios.

dynapenia showed a lower physical QOL than robust patients with type 1 diabetes and type 2 diabetes. Furthermore, as a result of the Mantel–Haenszel test adjusted by elderly in the present study, dynapenia represented a higher rate of incidental falls than robust in patients with type 1 diabetes] and type 2 diabetes (Figure 2). As both type 1 diabetes and type 2 diabetes patients are associated with an impaired bone structure quality, which is related to an increased fracture rate and delayed fracture healing[26–28], it is necessary to consider methods of preventing incidental falls in patients with type 1 diabetes and type 2 diabetes. In contrast, patients with type 1 diabetes and type 2 diabetes who had a history of incidental falls showed a higher rate of diabetic neuropathy and advanced retinopathy than patients with non-incidental falls (date were not shown). Therefore, dynapenia itself, as well as associated clinical features, such as aging and diabetic micro-angiopathy, might contribute to incidental falls. To clarify the influence of sarcopenia and dynapenia on physical QOL and incidental falls in patients with diabetes, further prospective studies will be necessary.

Several limitations associated with the present study warrant mention. First, it was impossible to infer causality because of the cross-sectional design. Second, we estimated the muscle mass using BIA-based measurements, not dual-energy X-ray absorptiometry. However, BIA measurements have been reported to be strongly correlated with dual-energy X-ray absorptiometry among older individuals[29], and the recent criteria of sarcopenia in the European Working Group on Sarcopenia in Older People 2[1] and AWGS 2019[2] allow us to use the BIA method as well as the dual-energy X-ray absorptiometry method clinically. Third, clinical characteristics, such as age, sex and BMI, were inconsistent among individuals without diabetes, type 1 diabetes patients and type 2 diabetes patients. Fourth, how reliably we captured the history of fall events in the present study was unclear. In addition, the clinical relevance of falls that occurred in the past to the current presence of sarcopenia or dynapenia was unclear – usually the temporality is reversed. Finally, the number of patients with type 1 diabetes who had dynapenia was relatively small.

In conclusion, sarcopenia and dynapenia were frequently observed in patients with type 1 diabetes and type 2 diabetes compared with individuals without diabetes, and were associated with poor physical QOL and high incidental falls, especially dynapenia.

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DISCLOSURE

The authors declare no conflict of interest.

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SUPPORTING INFORMATION

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

Table S1 | Cut-off values of a low skeletal muscle mass index, low grip strength, and slow gait speed according to the definitions of sarcopenia and dynapenia.

Table S2 | Clinical characteristics of all participants (S2–1), and participants aged 30–49 years (S2–2), 50–64 years old (S2–3) and ≥65 years (S2-4) among individuals without diabetes, type 1 diabetes patients and type 2 diabetes patients.

Table S3 | Medications of the study patients with type 1 diabetes according to the presence of sarcopenia and dynapenia.

Table S4 | Medications of the study patients with type 2 diabetes according to the presence of sarcopenia and dynapenia.

Table S5 | Numbers of enrolled participants without diabetes, and with type 1 diabetes and type 2 diabetes in each medical center and community center.