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Original Article

Osteoporosis complication is a risk factor for frailty in females with type 2 diabetes mellitus

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Abstract. [Purpose] This study aimed to examine the effect of osteoporosis complications on the physical function, frailty in patients with type 2 diabetes mellitus. [Participants and Methods] The participants were 27 female type 2 diabetes mellitus patients aged ≥65 years. Of these, 14 patients had osteoporosis. In order to evaluate the physical function, we measured the lower limb muscle strength, handgrip, gait speed, etc. We performed statistical comparison of both the groups and examined the applicable number of items on the Linda Fried Frailty scale and the correlation by evaluating the physical function. [Results] The lower limb muscle strength of patients with osteoporosis and type 2 diabetes mellitus was significantly lower than that of type 2 diabetes mellitus patients without osteoporosis. Factors of the osteoporosis group that inversely correlated to the Linda Fried Frailty scale included lower limb muscle strength, handgrip, and gait speed. [Conclusion] We found that osteoporosis reduced lower limb muscle strength in type 2 diabetes mellitus patients and was correlated with frailty.
Key words: Type 2 diabetes mellitus, Osteoporosis, Physical function

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INTRODUCTION

Osteoporosis frequently occurs in patients with diabetes due to hypoinsulinemia and insulin resistance[1)]. In females, aging promotes accelerated muscle loss with diabetes. In particular, females with type 2 diabetes mellitus (T2DM) experience a decrease in muscle strength with reduction in vitamin D as osteoporosis progresses, and the decreased muscle strength remarkably impairs activities of daily living, including locomotive activity[2, 3)].

Exercise is the key in the treatment of T2DM. Chronic exercise intervention is effective for maintaining their physical function and quality of life[4)], as well as for glycemic control and improved insulin resistance[5)]. An effective exercise for T2DM patients with osteoporosis would be to gradually increase the exercise load, and by continuing, muscle strength and bone mineral density improved[6)]. However, if the effect of severity of osteoporosis on muscles and bones is not evaluated, there is a possibility of exercise-induced fracture in T2DM patients with osteoporosis[7)]. In elderly females with osteoporosis, the reported annual increase in the risk of physical frailty is 5%[8)]. However, the regulation of exercises in osteoporosis, fractures, aging muscle, and frailty is not yet fully understood. Few reports have studied effective exercises for T2DM, patients and have shown no association with physical function. Considering the negative effects of osteoporosis on physical function, we may assist T2DM patients with osteoporosis with standard exercises who may benefit from them.

This study aimed to clarify a difference of influence to give osteoporosis complication, frailty, physical function by

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extracting osteoporosis and a diagnosed case in female T2DM patients and comparing it with non-osteoporosis.

PARTICIPANTS AND METHODS

This cross-sectional study was approved by the Ethics Committee of the Ashiya municipal hospital under the number 112. The study protocol was approved by the institutional review boards of the Ashiya municipal hospital. The study procedures were performed as per the Declaration of Helsinki and the Good Clinical Practice guidelines.

Patients who were in hospital for the purpose of education of diabetes at our hospital from November 2016 to November 2017 were included in the current study. We initiated a research study on female T2DM patients aged ≥65 years. We classified all the female T2DM patients as those with osteoporosis (osteoporosis group) and those without osteoporosis (control group). Osteoporosis was diagnosed based on the set guidelines[9]. Osteoporosis is clinically diagnosed by two criteria. The first is the occurrence of a fragility fracture (hip fracture, osteopenia-associated vertebral, proximal humerus, pelvis, or other wrist fractures involving major bones) in one of the major bones and second is a DXA bone density test results with a T-score of −2.5 or less in the spine, hip, or wrist. For the present analysis, the inclusion criteria were as follows: (1) diagnosis of T2DM, (2) age ≥65 years, (3) female. The exclusion criteria were as follows: (1) history of stroke, dementia and (2) difficulty in walking.

In order to evaluate the physical function, we measured the lower limb muscle strength, handgrip, and gait speed. Lower limb muscle strength was assessed using a Hand-held dynamometer (HDD: ISOFORCE GT-300, OG Wellness Technologies Co., Japan) using a protocol previously used in patients. Patients are seated with the padded sensor of the HDD placed just above the knee. Maximal strength is indicated by the peak torque (Nm) obtained. We conducted 5-second isometric contractions twice and recorded the mean, value. Furthermore, the lower limb muscle strength of the right and left leg was compared, the stronger one was recorded. Handgrip was measured using an HDD with participants seated, their elbow by their side and flexed to right angles, and a neutral wrist position, with the HDD handle position and provision of support underneath the HDD. The handgrip of the left and right hand was measured twice using an HDD, and the mean was adopted. The gait speed was readily assessed in the clinical setting by measuring the time taken to walk a set distance, such as 10 meters, at usual pace.

The muscle mass of the body segments was measured with a bioelectrical impedance (BIA: Inbody770, FUJITEX Co., Japan) device in terms of the skeletal muscle mass index (SMI). SMI was calculated as the bilateral mean with the upper and lower limbs (kg/m^2)[10].

We assessed frailty using the Linda Fried Frailty scale (LFS). The LFS was classified using a validated scale (0–5) that included weakness, weight loss, exhaustion, low physical activity, and slowed walking speed. Patients were asked to evaluate the current physical function on a scale of 0–5. Of the five criteria, individuals who met none of the criteria were regarded as not frailty, people with one or two positive criteria were considered to be prefrailty, and three or more are considered frailty. This categorization correlates with adverse health outcome as shown by Fried et al[11].

As other evaluations, we assessed homeostasis model assessment of insulin resistance (HOMA-IR), HbA1c.

Data are presented as mean ± standard deviation, values, unless otherwise specified. All the statistical analyses were performed with R software (R 2.8.1). The normality of the distribution of the variables was evaluated using the Shapiro-Wilk test. The comparison between the two groups of quantitative variables was performed with the nonparametric Mann-Whitney U-test.

Spearman rank correlation was used to determine the relationship between the applicable number of the items on the LFS and the relationship with the physical function in each group. A p-value of <0.05 was considered statistically significant.

RESULTS

The participant's physical characteristics and each parameter of T2DM are shown in Table 1. A total of 27 females with T2DM were included in this study. The osteoporosis group had 14 patients (76.9 ± 7.4 years), while the control group included 13 cases (73.4 ± 8.5 years).

Table 2 shows the results of the Mann-Whitney U-test with respect to lower limb muscle strength, handgrip, gait speed, upper SMI, lower SMI, HOMA-IR, fasting blood sugar level, and LFS. Lower limb muscle strength was significantly lower in the osteoporosis group than in the control group (p=0.03). HOMA-IR was significantly higher in the osteoporosis group than in the control group (p=0.02).

Table 3 shows the association between the LFS and physical function. The factors in the osteoporosis group that inversely correlated to LFS included knee extension muscle strength (r= −0.85, p=0.002) and handgrip (r= −0.64, p=0.04), and gait speed (r= −0.73, p=0.02). There were no significant correlations between LFS and physical function in the control group.

DISCUSSION

This study aimed to clarify the kind of symptoms in terms of the physical functions observed in females with osteoporosis and T2DM. In the osteoporosis group, the lower limb muscular strength was significantly lower than that in the control

Table 1. Baseline characteristics of participants

	Osteoporosis (n=14)	Control (n=13)	p value
Age (years)	77.5 (63–91)	74 (60–88)	0.75
Body mass index (kg/m^2)	23.9 (14.7–34.5)	24.9 (15.7–29.6)	0.16
FBS (mg/dl)	184.5 (115–299)	155 (74–284)	0.12

Values are expressed as median (min–max). *p<0.05.
Osteoporosis: female T2DM of osteoporosis; Control: female T2DM of non-osteoporosis; FBS: Fasting blood sugar level.

Table 2. The difference in outcomes between female T2DM patients with and without osteoporosis

	Osteoporosis (n=14)	Control (n=13)	p value
Lower limb muscle strength (nm)	54.2 (32.9–171.6)	83.4 (46.2–107.8)	0.03*
Handgrip (kgf)	19.2 (13.8–38.8)	23.8 (9.8–34.2)	0.26
Gait speed (m/s)	1.0 (0.4–1.6)	1.3 (1.0–1.5)	0.09
Upper SMI (kg/m^2)	0.8 (0.6–1.0)	0.7 (0.6–0.8)	0.05
Lower SMI (kg/m^2)	5.1 (3.7–6.1)	4.9 (4.0–5.9)	0.78
HOMA-IR	2.0 (0.9–6.0)	1.1 (0.3–3.4)	0.02*
HbA1c (%)	8.35 (7.6–12.1)	8.5 (6.8–12.9)	0.41
FBS (mg/dl)	184.5 (115–299)	155 (74–284)	0.12
LFS (points)	2 (1–4)	1 (0–3)	0.92

Values are expressed as median (min–max). *p<0.05.
Osteoporosis: female T2DM of osteoporosis; Control: female T2DM of non-osteoporosis; SMI: Skeltal muscle index; HOMA-IR: Homeostasis model assessment of insulin resistance; FBS: Fasting blood sugar level; LFS: the Linda Fried Frailty scale.

Table 3. The association between LFS and physical function

	Osteoporosis (n=14)		Control (n=13)	
	ρ	p	ρ	p
Lower limb muscle strength (Nm)	–0.6	0.04*	–0.5	0.33
Handgrip (kgf)	–0.9	0.002**	0.1	0.94
Gait speed (m/s)	–0.7	0.02*	–0.6	0.21
Upper smi (kg/m^2)	0.2	0.6	0.1	0.83
Lower smi (kg/m^2)	–0.5	0.25	0.5	0.36

Correlation coefficient (r). *p<0.05, **p<0.01.
LFS: the Linda Fried Frailty scale; Osteoporosis: female T2DM of osteoporosis; Control: female T2DM of non-osteoporosis; SMI: Skeltal muscle index.

group. With respect to this, Srikanthan et al. found that a decrease in muscle mass caused deterioration in insulin resistance and subsequent diabetes[12]. Moreover, diabetes with sarcopenia can cause abnormal bone metabolism and muscle strength loss simultaneously[13]. Further, reduced leg muscle mass was an independent risk factor for acute osteoporotic vertebral fracture in the multivariate analysis[14]. In the present study, HOMA-IR of the osteoporosis group was significantly higher than that of the non-osteoporosis group. In addition, lower limb muscle strength significantly decreased. Thus, female T2DM patients with osteoporosis and high insulin resistance are more likely to experience a decrease in lower limb muscle strength than T2DM patients without osteoporosis. These results show that osteoporosis might reduce lower limb muscle strength in female T2DM patients.

The lower limb muscle strength, handgrip, and gait speed in the osteoporosis group showed a negative correlation with frailty. Osteoporosis is a chronic inflammatory disorder[14], and chronic inflammation is related to fatty infiltration of the bone marrow and muscle[2]. A previous research had reported that osteosarcopenia progression is closely associated with decreasing muscle mass and bone density[15]. Bone and muscle loss may also be closely linked to the risk of frailty, as shown in a 2015 study conducted in China[16]. Further, mechanical stress changes, such as immobilization and lack of gravity, greatly influence both muscle and bone[17]. These findings suggest that the presence of interactions between muscles and bones, could be very important for understanding exercise of sarco-osteoporosis. In addition, assessment by handgrip strength, as a com-

ponent of frailty[11], is reported to be an important tool for health professionals and researchers. A study conducted with data from the Women's Health and Aging Study[18] showed that the risk of disability in instrumental activities of daily living and becoming frailty were 1.35 times higher, for each unit of 0.50 kgf decreasing handgrip. Additionally, it has been suggested that decreased gait speed correlates with frailty as bone mass decreases[19]. Based on these findings, chronic inflammation due to osteoporosis progressed to the lower handgrip strength and lower limb muscle strength. Moreover, it also affected the gait speed. It is conceivable that osteoporosis is not only associated with decreased lower limb muscle strength, but can also contribute to frailty. On the other hand, insulin resistance could be the factor why the control group did not correlate with frailty. Insulin resistance or insulin depletion may be an important factor in the progression of frailty in diabetes patients as insulin is a well-known anabolic hormone in muscles[20]. It seemed that the control group had no correlation with flail because HOMA-R was low.

The limitations of this study included the fact that it was a cross-sectional study; the sample size of people with T2DM was relatively small. In the future, we plan to measure the osteoporosis of such T2DM group in order to investigate clinical applications.

Thus, we performed a propensity-matched analysis using a T2DM patient to compare the outcome in the osteoporosis group and the non-osteoporosis group. The osteoporosis group had significantly decreased lower limb muscle strength than the non-osteoporosis group. Moreover, the lower limb muscle strength, handgrip, and gait speed of the osteoporosis group was associated with frailty.

These findings suggest that lower limb muscle exercise, such as walking, have the potential to be an innovative treatment for female T2DM patients with osteoporosis.

Conflict of interest

None.

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