Journal of Bone and Mineral Metabolism (2019) 37:503–511
https://doi.org/10.1007/s00774-018-0948-6

ORIGINAL ARTICLE

Osteoporosis and vertebral fracture are associated with deterioration of activities of daily living and quality of life in patients with type 2 diabetes mellitus

Ippei Kanazawa[1] · Ayumu Takeno[1,2] · Ken-ichiro Tanaka[1,2] · Yuko Yamane[3] · Toshitsugu Sugimoto[1]

Received: 5 May 2018 / Accepted: 3 August 2018 / Published online: 6 September 2018

Abstract

Patients with type 2 diabetes mellitus (T2DM) have an increased risk of fragility fracture. However, whether diabetes-related osteoporosis independently contributes to the deterioration of activities of daily living (ADLs) and quality of life (QOL) is unclear. This cross-sectional study investigated the association between osteoporosis, ADLs, and QOL in 309 patients with T2DM. ADLs and QOL were assessed using Barthel Index (BI) and a SF-36 questionnaire. Multiple logistic regression analyses adjusted for age, gender, T2DM duration, body mass index, hemoglobin A1c, estimated GFR, diabetic neuropathy, retinopathy, nephropathy, cardiovascular disease, cerebrovascular disease, peripheral artery disease, and anti-diabetic treatments were conducted. The number of patients with osteoporosis or vertebral fracture was 166 (53.7%) and 118 (38.2%), respectively. Osteoporosis was significantly associated with lower general health (GH), social functioning (SF), and role emotional (RE) (OR 2.56, 1.79, and 1.92, respectively; all p values < 0.05 at least) and marginally associated with lower BI (OR 2.39, $p = 0.068$). Moreover, the presence of vertebral fracture grade 2 or 3 was significantly associated with lower BI, bodily pain (BP), GH, vitality, SF, and RE (OR 2.58, 2.01, 3.64, 1.99, 2.18, and 1.97, respectively; all p values < 0.05 at least). Osteoporosis and severe vertebral fracture were associated with the deterioration of ADLs and QOL independently of other diabetic complications. Therefore, the management of diabetes-related osteoporosis is an important strategy to avoid the deterioration of ADLs and QOL in T2DM.

Keywords Type 2 diabetes mellitus · Osteoporosis · Vertebral fracture · ADLs · QOL

Abbreviations

ADLs	Activities of daily living
BI	Barthel Index
BMD	Bone mineral density
BMI	Body mass index
BP	Bodily pain
eGFR	Estimated glomerular filtration rate
GH	General health
HbA1c	Hemoglobin A1c
MH	Mental health
PAD	Peripheral arery disease
PF	Physical functioning
RE	Role emotional
RP	Role physical
SF	Social functioning
QOL	Quality of life
T2DM	Type 2 diabetes mellitus
VT	Vitality
YAM	Young adult mean

Introduction

Accumulating evidence has shown that patients with type 2 diabetes mellitus (T2DM) have an increased risk of osteoporotic fractures [1–3]. The incidence of T2DM and osteoporosis is increased with aging of the population; therefore, these diseases have become a cause for concern worldwide. It has been shown that osteoporotic fractures such as hip and vertebral fractures increase mortality in the general population [4, 5] and that vertebral fractures are independently associated with all-cause mortality in patients with

✉ Ippei Kanazawa
ippei.k@med.shimane-u.ac.jp

[1] Department of Internal Medicine 1, Faculty of Medicine, Shimane University, 89-1 Enya-cho, Izumo 693-8501, Japan

[2] Masuda Red Cross Hospital, Masuda, Japan

[3] Yamane Hospital, Hamada, Japan

T2DM [6]. Moreover, osteoporotic fractures impair activities of daily living (ADLs) and the quality of life (QOL) [7]. Because hip fractures usually cause loss of function, many patients with hip fractures need long-term rehabilitation and institutionalization at a nursing home. Furthermore, vertebral fractures cause chronic back pain, loss of function, and multiple organ dysfunctions, including chronic obstructive pulmonary disease, myocardial infarction, congestive heart failure, and gastroesophageal reflux disease [8–10]. Therefore, osteoporosis affects not only the general population but also patients with T2DM. Patients with T2DM are at increased risk of diabetic micro- and macrovascular diseases and usually need to manage comorbidities such as hypertension and dyslipidaemia. Diabetic neuropathy, retinopathy, and nephropathy have a negative impact on ADLs and QOL in diabetic patients [11–13]. Moreover, cardio vascular and cerebrovascular diseases lead to hospitalization, deteriorate ADLs and QOL, and cause mortality [11–13]. Therefore, whether osteoporosis affects morbidity and health-related QOL in patients with T2DM needs to be clarified. However, to the best of our knowledge, no studies to date investigated whether diabetes-related osteoporosis is associated with ADLs and QOL in patients with T2DM. The present study evaluated the association of the prevalence of osteoporosis and vertebral fractures with ADLs and QOL scores in patients with T2DM.

Materials and methods

Subjects

This cross-sectional study evaluated 309 Japanese patients with T2DM (196 men and 113 postmenopausal women; mean age of 65.3 years). The subjects who visited Shimane University Hospital, Masuda Red Cross Hospital, and Yamane Hospital for treatment of T2DM were consecutively enrolled from 2014 to 2016. This study was approved by the institutional review boards of Shimane University Faculty of Medicine, Masuda Red Cross Hospital, and Yamane Hospital. All subjects agreed to participate in the study and provided informed consent. All women had been without spontaneous menses for more than 1 year. Patients with a history of injury-associated fractures, blindness, and end-stage renal disease [estimated glomerular filtration rate (eGFR) < 15 mL/min/1.73 m^2] were excluded. Upon enrolment in the study, the clinical characteristics of the patients were recorded with special attention to the history of macrovascular complications (cardiovascular disease, cerebrovascular disease, and peripheral artery disease [PAD]). The presence of cardiovascular disease, cerebrovascular disease, or PAD was defined by the history of myocardial infarction, percutaneous coronary intervention, symptomatic cerebral infarction, or arterial occlusive disease.

Collection of anthropometric and biochemical data

Body height (cm) was measured with a Martin metal anthropometer to the nearest 0.1 cm according to a standard technique, and body weight (kg) was measured using an electronic medical scale (precision of 0.05 kg) with the subject wearing light clothes. Body mass index (BMI) (kg/m^2) was calculated using the following formula: weight/(height in meters)^2. Hemoglobin A1c (HbA_{1c}) (NGSP) was determined using high-performance liquid chromatography at the central laboratories of our hospitals.

Assessment of diabetic microvascular complications

Diabetic neuropathy was diagnosed using the criteria proposed by the Diabetic Neuropathy Study Group in Japan [14]. The prerequisite conditions included (1) presence of T2DM and (2) exclusion of other possible neuropathies. In addition, any of the following criteria should be present: (1) sensory symptoms due to diabetic neuropathy, (2) bilaterally decreased or absence of ankle reflex, or (3) decreased vibratory sensation in bilateral medial malleoli. The presence of diabetic retinopathy was diagnosed by ophthalmologists. Diabetic nephropathy was diagnosed in cases in which albuminuria was found and non-diabetic kidney diseases were excluded [15]. Urinary albumin (uAlb) excretion for 24 h or albumin-to-creatinine ratio (ACR) in a random spot urine collection was used for the diagnosis of albuminuria (uAlb ≥ 30 mg/day or ACR ≥ 30 mg/g in two of three samples).

Diagnosis of osteoporosis and vertebral fractures

Osteoporosis was diagnosed in cases in which the patients met the diagnostic criteria for primary osteoporosis established by the Committee of the Japanese Society for Bone and Mineral Research [16] or had taken medications for osteoporosis. The diagnostic criteria were (1) presence of a fragility fracture in vertebrae or the proximal femur, (2) presence of other fragility fractures with a BMD < 80% of young adult mean (YAM), and (3) BMD was ≤ 70% or ≤ − 2.5 SD of YAM.

For the assessment of vertebral fractures, lateral radiographic images of the thoracic and lumbar spine were acquired at the same week of data collection for all subjects. The anterior, central, and posterior heights of each of the 13 vertebral bodies from T4 to L4 were measured. A vertebral fracture was diagnosed in cases in which at least one of three height measurements along the length of the same vertebra had decreased by > 20% compared to the height of the

nearest uncompressed vertebral body [17]. Vertebral fracture was graded using Genant semiquantitative criteria. VFs were classified as follows: grade 1, reduction of 20–25%; grade 2, reduction of 25–40%; and grade 3, reduction of > 40%.

Assessment of ADLs and QOL

The Barthel Index (BI) questionnaire [18] was used to estimate functional disability by quantifying the patients' performance in ten activities of daily life. These activities were grouped by self-care and mobility restriction (feeding, bathing, grooming, dressing, defecation, bladder function, ability to use the toilet, transfer, mobility and climbing stairs). The score ranged from 0 to 100, and the highest score indicated the best function. In this study, the BI cut-off was set at 99 because most patients achieved full scores.

QOL was measured using a 36-item questionnaire (SF-36v2) [19, 20]. SF-36v2 is widely used to assess physical and mental well-being at the individual and social levels. Eight derived subscales correspond to eight health concepts: physical functioning (PF), role functioning physical (RP), bodily pain (BP), general health (GH), vitality (VT), social functioning (SF), role functioning emotional (RE), and mental health (MH). Each subscale ranged from 0 to 100, with higher scores indicating better QOL. A score of 50 corresponded to the mean score for a normal control population. In this study, the median of each score was used as a cut-off value.

Statistical analysis

Data were expressed as mean ± standard deviation. Statistical analysis of differences among the groups was conducted using an unpaired *t* test, χ^2 tests, and the Jonckheere–Terpstra trend test. The association of the presence of osteoporosis and vertebral fractures with ADLs and QOL was analyzed using multivariate logistic regression analysis. All analyses were performed using software StatView (Abacus Concepts, Berkeley, CA, USA) and SPSS (SPSS Japan Inc., Tokyo, Japan). $p < 0.05$ was considered statistically significant.

Results

Baseline characteristics

The patient baseline characteristics are shown in Table 1. The study sample had a mean diabetes duration of 12.2 years, mean BMI of 25.2 kg/m^2, mean HbA_{1c} of 9.5%, and mean eGFR of 76.4 mL/min/1.73 m^2. Of the 309 evaluated patients, 166 (53.7%) had osteoporosis, 49 (15.9%) had grade 1 vertebral fracture, and 69 (22.3%) had grade-2 or -3 vertebral fracture. The number of subjects with proximal femur, radius, foot, and clinical vertebral fracture was 4, 4, 2, and 2, respectively. The number of patients with diabetic neuropathy, retinopathy, nephropathy, cardiovascular disease, cerebrovascular disease, and PAD was 233, 115, 130, 39, 30, and 8, respectively. The number of patients who had been using insulin, GLP-1 receptor agonists, and oral hypoglycaemic agents was 85, 8, and 195, respectively.

Table 1 Baseline characteristics of subjects

Number of subjects (M/F)	309 (196/113)
Age (years)	65.3 ± 11.8
Duration of diabetes (years)	12.2 ± 9.4
Body height (cm)	159.9 ± 9.5
Body weight (kg)	64.4 ± 14.8
Body mass index (kg/m^2)	25.2 ± 5.3
Serum creatinine (mg/dL)	0.83 ± 0.45
Estimated GFR (mL/min/1.73 m^2)	76.4 ± 27.5
HbA1c (%)	9.5 ± 2.4
Diabetic neuropathy (no/yes/unknown)	73/233/3
Diabetic retinopathy (no/yes/unknown)	181/115/13
Diabetic nephropathy (no/yes/unknown)	178/130/1
Cardiovascular disease (no/yes)	270/39
Cerebrovascular disease (no/yes)	279/30
Peripheral artery disease (no/yes)	299/8
Osteoporosis (no/yes)	143/166
Vertebral fracture	
None [n (%)]	191 (61.8%)
Grade 1 [n (%)]	49 15.9%)
Grades 2 and 3 [n (%)]	69 (22.3%)
Oral hypoglycemic agents (no/yes)	114/195
Insulin treatment (no/yes)	224/85
GLP-1 receptor agonists (no/yes)	301/8
ADLs	
Barthel Index	97.6 ± 7.7
SF-36	
Physical functioning	41.4 ± 16.9
Role physical	41.0 ± 14.6
Bodily pain	46.5 ± 13.0
General health	40.7 ± 9.3
Vitality	46.0 ± 11.7
Social functioning	44.8 ± 12.4
Role emotional	43.1 ± 13.8
Mental health	45.9 ± 11.5

GFR glomerular filtration rate, *HbA1c* hemoglobin A1c, *GLP-1* glucagon-like peptide-1

Association of osteoporosis with ADLs and QOL scores

Baseline characteristics between patients with and without osteoporosis were compared (Table 2). The patients with

Table 2 Comparison of background data, ADLs and QOL scores between subjects with and without osteoporosis

Osteoporosis	No	Yes	*p*
Number of subjects	143	166	
Men/women	98/45	98/68	0.085
Age (years)	60.7 ± 11.6	69.2 ± 10.5	< 0.001
Duration of diabetes (years)	10.9 ± 8.8	13.4 ± 9.7	0.018
Body mass index (kg/m²)	25.5 ± 5.1	24.9 ± 5.4	0.345
Estimated GFR (mL/min/1.73 m^2)	78.3 ± 28.3	74.7 ± 26.8	0.257
HbA1c (%)	9.6 ± 2.4	9.4 ± 2.3	0.467
ADLs			
Barthel Index	99.2 ± 4.7	96.3 ± 9.4	0.001
QOL SF-36 components			
Physical functioning	45.5 ± 13.3	37.8 ± 18.7	< 0.001
Role physical	43.8 ± 13.0	38.5 ± 15.4	0.002
Bodily pain	47.7 ± 12.7	45.4 ± 13.2	0.125
General health	41.6 ± 8.9	40.0 ± 9.5	0.133
Vitality	46.4 ± 11.2	45.7 ± 12.0	0.609
Social functioning	46.3 ± 12.0	43.4 ± 12.5	0.040
Role emotional	46.4 ± 12.3	40.4 ± 14.5	< 0.001
Mental health	46.4 ± 11.1	45.5 ± 11.8	0.483

osteoporosis were significantly older ($p < 0.001$) and had a significantly longer duration of T2DM ($p = 0.018$) than those without osteoporosis. The scores of BI, PF, RP, SF, and RE were significantly lower in patients with osteoporosis than in those without it (p values of 0.001, < 0.001, 0.002, 0.040, and < 0.001, respectively). In the logistic regression analysis (Table 3), the presence of osteoporosis was significantly associated with lower BI after adjusting for baseline characteristics [model 1; OR 2.43; 95% CI 1.04, 5.71; $p = 0.041$] although the association became marginal in models 2 and 3 (model 2; OR 2.39; 95% CI 0.94, 6.07; $p = 0.068$; and model 3; OR 2.39; 95% CI 0.94, 6.07; $p = 0.068$). Moreover, the presence of osteoporosis was significantly associated with lower GH, SF, and RE after adjusting for baseline characteristics, other diabetic complications, and treatment for diabetes (model 3; OR 2.56; 95% CI 1.45, 4.51; $p = 0.001$; OR 1.79; 95% CI 1.05, 3.04; $p = 0.032$; and OR 1.92; 95% CI 1.14, 3.25; $p = 0.015$, respectively).

Association of vertebral fractures with ADLs and QOL scores

Baseline characteristics between patients with and without vertebral fractures were compared by grading (Table 4). The patients with vertebral fractures were significantly older (p trend < 0.001) and had a significantly longer duration of T2DM (p trend = 0.008) compared with those without vertebral fractures. The scores for BI, PF, RP, GH, and RE were significantly lower in patients with vertebral fractures than those without it (p trends of < 0.001, 0.001, 0.007, 0.008, and 0.001, respectively). In the logistic regression analysis (Table 5), the presence of grade-2 or -3 vertebral fractures was significantly associated with lower BI after adjusting for baseline characteristics, other diabetic complications, and treatment for diabetes (model 3; OR 2.58; 95% CI 1.05, 6.38; $p = 0.040$). Moreover, the presence of grade-2 or -3 vertebral fractures was significantly associated with lower BP, GH, VT, SF, and RE (model 3; OR 2.01; 95% CI 1.05, 3.85; $p = 0.034$; OR 3.64; 95% CI 1.81, 7.29; $p < 0.001$; OR 1.99; 95% CI 1.03, 3.81; $p = 0.039$; OR 2.18; 95% CI 1.13, 4.23; $p = 0.021$; and OR 1.97; 95% CI 1.03, 3.78; $p = 0.041$, respectively). The presence of grade-2 or -3 vertebral fracture was marginally but non-significantly associated with lower MH (model 3; OR 1.78; 95% CI 0.94, 3.35; $p = 0.077$).

Discussion

The results of the present study indicated that osteoporosis and vertebral fractures were involved in the deterioration of ADLs and QOL in patients with T2DM. These findings are not surprising because it is well known that osteoporosis deteriorates ADLs and QOL in the general population. However, patients with diabetes have many complications, including micro- and macrovascular diseases, which may affect ADLs and QOL. Most studies examining QOL in T2DM focused on micro- and macrovascular complications. Although coronary arterial disease, renal dysfunction, and visual deficit are involved in the deterioration of QOL in T2DM [11], to the best of our knowledge, no studies to date evaluated the association between diabetes-related osteoporosis and QOL. In this study, the means of all QOL subscales were less than 50. Because a score of 50 represents the mean score for a normal control population, this finding indicates that QOL was deteriorated primarily by the presence of T2DM. In addition, among the patients with decreased QOL, osteoporosis and vertebral fractures significantly affected ADLs and QOL scores even after adjusting for baseline parameters, diabetic complications, and treatments for diabetes. Therefore, the present study is the first to demonstrate that diabetes-related osteoporosis caused a significant decline in ADLs and QOL independently of other diabetic complications.

In general, hip fracture and moderate-to-severe vertebral fractures have a strong impact on QOL [7]. Vertebral fractures cause acute and chronic back pain and lead to decreased physical functioning, immobility, social isolation, and depression [21]. In a large-scale prospective study Multiple Outcomes of Raloxifene Evaluation (MORE) trial, the association between QOL and vertebral fractures at baseline was estimated in 751 postmenopausal women

Table 3 Association between osteoporosis and ADLs as well as QOL

	Barthel Index			Physical functioning			Role physical		
	OR	95% CI	*p*	OR	95% CI	*p*	OR	95% CI	*p*
Without osteoporosis									
Reference	1.00			1.00			1.00		
With osteoporosis									
Crude	3.43	1.63–7.22	0.001	1.79	1.14–2.81	0.012	1.88	1.20–2.96	0.006
Model 1	2.43	1.04–5.71	0.041	1.19	0.72–1.99	0.496	1.42	0.86–2.35	0.170
Model 2	2.39	0.94–6.07	0.068	1.20	0.70–2.05	0.506	1.47	0.87–2.49	0.152
Model 3	2.39	0.94–6.07	0.068	1.18	0.69–2.03	0.549	1.45	0.86–2.47	0.165
	Bodily pain			General health			Vitality		
	OR	95% CI	*p*	OR	95% CI	*p*	OR	95% CI	*p*
Without osteoporosis									
Reference	1.00			1.00			1.00		
With osteoporosis									
Crude	1.43	0.91–2.24	0.121	1.45	0.92–2.27	0.108	1.21	0.77–1.90	0.400
Model 1	1.26	0.77–2.06	0.354	2.39	1.40–4.09	0.002	1.31	0.80–2.16	0.287
Model 2	1.33	0.79–2.23	0.280	2.56	1.46–4.52	0.001	1.23	0.73–2.07	0.447
Model 3	1.31	0.78–2.21	0.308	2.56	1.45–4.51	0.001	1.22	0.72–2.05	0.464
	Social functioning			Role emotional			Mental health		
	OR	95% CI	*p*	OR	95% CI	*p*	OR	95% CI	*p*
Without osteoporosis									
Reference	1.00			1.00			1.00		
With osteoporosis									
Crude	1.70	1.08–2.67	0.021	2.09	1.32–3.30	0.002	1.18	0.75–1.84	0.478
Model 1	1.65	1.00–2.72	0.049	1.85	1.12–3.04	0.016	1.43	0.87–2.36	0.162
Model 2	1.80	1.06–3.04	0.030	1.92	1.14–3.23	0.014	1.42	0.84–2.39	0.192
Model 3	1.79	1.05–3.04	0.032	1.92	1.14–3.25	0.015	1.42	0.84–2.40	0.192

Model 1: adjusted for age, gender, duration of diabetes, body mass index, HbA1c, estimated GFR

Model 2: adjusted for model 1 plus neuropathy, retinopathy, nephropathy, cardiovascular disease, cerebrovascular disease, peripheral artery disease

Model 3: adjusted for model 2 plus treatments with oral hypoglycemic agents, insulin, and GLP-1 receptor agonists

OR odds ratio, *CI* confidence interval

with low BMD (T score ≥ -2.5) using the QOL questionnaires Qualeffo-41, Nottingham Health Profile, and EQ-5D [22]. Our results indicated that the prevalence of vertebral fractures was associated with decreased QOL, especially for domains PF, BP, SF, and GH, and that QOL was progressively decreased as the number of vertebral fractures was increased. Moreover, in a prospective analysis using a subset of 361 postmenopausal women, incident vertebral fractures were associated with an increase of back pain, and deterioration of PF and GH [23]. In contrast, mental function was not significantly different between the patients with and without vertebral fractures [22, 23]. Rostom et al. conducted a cross-sectional study involving 201 women in Saudi Arabia and observed that vertebral fractures were associated with decreased PF, BP, GH, VT, and SF, but not with RE or MH, assessed using SF-36 [24]. In this study, the non-adjusted model indicated that grade 2 or 3 vertebral fracture was significantly or marginally associated with a decrease in all subscales of QOL, and these results are consistent with previous studies.

Many patients with diabetes have depression [25, 26], and the prevalence of depression in this population was shown to be 1.5-to-3.0-fold higher than that in the general population [25, 26]. Because depression usually affects the clinical course of diabetes progression [27], the mechanism underlying the association between diabetes and depression should be clarified. Although many factors, including diabetes status and diabetes complications, should affect mental health in patients with diabetes, our results revealed that moderate-to-severe vertebral fractures were associated with

Table 4 Comparison of background data, ADLs and QOL scores between subjects with and without vertebral fracture

Vertebral fracture	None	Grade 1	Grades 2 and 3	*p* trend
Number of subjects	191	49	69	
Men/women	113/78	35/14	48/21	0.061
Age (years)	62.5 ± 12.0	68.6 ± 9.3	70.7 ± 10.4	< 0.001
Duration of diabetes (years)	11.3 ± 9.3	12.8 ± 8.2	14.5 ± 10.2	0.008
Body mass index (kg/m²)	25.0 ± 5.2	25.8 ± 5.0	25.3 ± 5.6	0.681
Estimated GFR (mL/min/1.73 m^2)	78.5 ± 28.8	75.1 ± 22.3	71.2 ± 26.7	0.095
HbA1c (%)	9.7 ± 2.4	9.2 ± 2.3	9.2 ± 2.2	0.158
ADLs				
Barthel Index	98.9 ± 5.0	95.9 ± 12.1	95.4 ± 9.3	< 0.001
QOL SF-36 components				
Physical functioning	43.8 ± 14.7	41.5 ± 17.6	34.6 ± 20.0	0.001
Role physical	42.5 ± 13.8	42.9 ± 12.3	35.3 ± 16.7	0.007
Bodily pain	47.2 ± 12.9	48.0 ± 13.9	43.3 ± 12.4	0.106
General health	41.6 ± 9.5	40.8 ± 10.3	38.2 ± 7.3	0.008
Vitality	46.9 ± 11.1	46.6 ± 13.1	43.9 ± 11.9	0.250
Social functioning	45.6 ± 12.4	44.5 ± 11.2	42.5 ± 13.1	0.058
Role emotional	45.1 ± 12.7	43.1 ± 12.9	37.9 ± 16.1	0.001
Mental health	46.5 ± 10.9	47.4 ± 11.7	43.3 ± 12.6	0.221

a decrease in the mental components of QOL such as RE and MH in patients with T2DM. These findings suggest that diabetes-related osteoporosis may cause the deterioration of physical activity, social functioning, and mental health in this population.

In this study, the prevalence of osteoporosis was significantly associated with a decrease in GH, SF, and RE, and marginally associated with lower ADLs scores. Because osteoporosis was diagnosed if the patients had fragility fracture including vertebral fractures, the association between osteoporosis and decreased QOL scores might be at least partly caused by vertebral fractures. Unfortunately, the number of subjects was not large enough to investigate the effects of osteoporosis without fracture on QOL. However, previous studies reported that osteoporotic patients had deteriorated QOL even in cases in the absence of fractures [28]. Bianchi et al. conducted a case control study and observed that postmenopausal women with and without fractures had chronic pain, impaired physical ability, reduced social activity, poor well-being, and depressed mood compared with the non-osteoporotic control group [29]. Similarly, de Oliveira et al. demonstrated that QOL was impaired in osteoporotic postmenopausal women without vertebral fracture compared with those without osteoporosis, and that QOL was not significantly different between those with and without vertebral fractures [30]. Although the mechanism by which ADLs and QOL are impaired in osteoporotic patients without fractures is still unclear, osteoporosis might be an important factor for patients with T2DM regardless of the presence of fragility fractures. In this study, multiple logistic regression analyses adjusted for various diabetic complications and treatment for T2DM; however, sarcopenia, which is characterized by muscle mass reduction and impaired physical performance, was not included as an adjusted variable. Accumulating evidence has shown that sarcopenia is a complication of diabetes [31, 32]. In addition, osteoporosis and sarcopenia are reported to be associated with each other [33]. Since the limitation of physical performance might induce osteoporosis [34], impaired ADLs by diabetes-related sarcopenia might be a cause of osteoporosis because of the decreased mechanical stress on the bone.

The present study had several limitations. First, the sample size was not large enough to make definite conclusions. Moreover, male and female subjects were mixed in this study. Although gender was adjusted, there is a possibility that the effects of osteoporosis and vertebral fracture on ADLs and QOL might be different between men and women. Second, we analysed the subjects who visited Shimane University Hospital, a tertiary center, for evaluation or treatment of T2DM. Therefore, some patients enrolled in the study might have relatively severe disease. Third, the patients with blindness and end-stage renal disease were excluded. Fourth, the history of vascular diseases was based on self-reports. Fifth, non-diabetic control subjects were not examined in this study. Sixth, detailed data on treatment of osteoporosis and diabetes were not analysed in this study. Finally, the study had a cross-sectional design; therefore, prospective studies are necessary to evaluate whether osteoporosis and vertebral fractures worsen ADLs and QOL in patients with T2DM.

In conclusion, we found for the first time that osteoporosis and moderate-to-severe vertebral fractures were associated

Table 5 Association between the presence of vertebral fracture and ADLs as well as QOL

	Barthel Index			Physical functioning			Role physical		
	OR	95% CI	*p*	OR	95% CI	*p*	OR	95% CI	*p*
None									
Reference	1.00			1.00			1.00		
Grade 1									
Crude	1.88	0.76–4.61	0.171	1.06	0.56–1.98	0.867	1.06	0.56–1.98	0.867
Model 1	1.73	0.65–4.63	0.272	0.78	0.39–1.54	0.467	0.84	0.43–1.65	0.612
Model 2	1.41	0.46–4.29	0.549	0.87	0.42–1.77	0.692	0.97	0.48–1.95	0.925
Model 3	1.39	0.45–4.30	0.568	0.86	0.42–1.77	0.690	0.95	0.47–1.93	0.889
Grades 2 or 3									
Crude	3.39	1.64–7.00	< 0.001	2.06	1.16–3.65	0.013	2.06	1.16–3.65	0.013
Model 1	2.70	1.18–6.17	0.019	1.42	0.75–2.68	0.277	1.61	0.86–3.02	0.134
Model 2	2.50	1.02–6.11	0.045	1.35	0.70–2.61	0.376	1.59	0.83–3.06	0.164
Model 3	2.58	1.05–6.38	0.040	1.32	0.68–2.58	0.410	1.55	0.80–3.00	0.194
	Bodily pain			General health			Vitality		
	OR	95% CI	*p*	OR	95% CI	*p*	OR	95% CI	*p*
None									
Reference	1.00			1.00			1.00		
Grade 1									
Crude	0.95	0.51–1.79	0.883	0.81	0.43–1.52	0.507	0.87	0.47–1.64	0.673
Model 1	0.91	0.47–1.75	0.769	1.02	0.51–2.04	0.953	1.04	0.53–2.02	0.911
Model 2	0.90	0.45–1.80	0.770	1.16	0.56–2.40	0.699	1.03	0.51–2.08	0.925
Model 3	0.89	0.44–1.80	0.751	1.13	0.54–2.39	0.743	1.02	0.51–2.07	0.947
Grades 2 or 3									
Crude	1.94	1.10–3.40	0.022	2.30	1.29–4.11	0.005	1.82	1.02–3.24	0.041
Model 1	1.82	1.00–3.33	0.052	3.42	1.77–6.59	< 0.001	2.33	1.25–4.35	0.008
Model 2	2.07	1.09–3.94	0.026	3.66	1.83–7.31	< 0.001	2.02	1.06–3.87	0.034
Model 3	2.01	1.05–3.85	0.034	3.64	1.81–7.29	< 0.001	1.99	1.03–3.81	0.039
	Social functioning			Role emotional			Mental health		
	OR	95% CI	*p*	OR	95% CI	*p*	OR	95% CI	*p*
None									
Reference	1.00			1.00			1.00		
Grade 1									
Crude	1.53	0.81–2.88	0.189	1.13	0.60–2.12	0.710	0.82	0.44–1.56	0.552
Model 1	1.84	0.93–3.62	0.079	1.08	0.56–2.10	0.819	0.99	0.50–1.94	0.967
Model 2	2.02	0.99–4.12	0.054	1.19	0.60–2.37	0.623	1.04	0.52–2.11	0.909
Model 3	2.02	0.98–4.18	0.058	1.19	0.59–2.38	0.628	1.03	0.51–2.08	0.945
Grades 2 or 3									
Crude	1.68	0.96–2.93	0.069	1.98	1.13–3.48	0.017	1.47	0.84–2.55	0.176
Model 1	2.04	1.11–3.78	0.023	1.83	1.00–3.37	0.052	1.96	1.07–3.60	0.030
Model 2	2.26	1.18–4.33	0.015	2.04	1.07–3.88	0.030	1.78	0.95–3.35	0.074
Model 3	2.18	1.13–4.23	0.021	1.97	1.03–3.78	0.041	1.78	0.94–3.35	0.077

Model 1: adjusted for age, gender, duration of diabetes, BMI, HbA1c, eGFR

Model 2: adjusted for model 1 plus neuropathy, retinopathy, nephropathy, cardiovascular disease, cerebrovascular disease, peripheral artery disease

Model 3: adjusted for model 2 plus treatments with oral hypoglycemic agents, insulin, and GLP-1 receptor agonists

OR odds ratio, *CI* confidence interval

with impaired ADLs and decreased QOL in patients with T2DM even after adjusting for age, duration of diabetes, BMI, HbA_{1c}, renal function, other diabetic complications, and treatment of diabetes. Therefore, we should pay careful attention to diabetes-related osteoporosis to avoid the deterioration of ADLs and QOL in patients with T2DM.

Acknowledgements The authors are grateful to the patients and hospital staff who participated in this study. This study was funded by the Japan Osteoporosis Foundation and partly supported by research Grant from Eli Lilly Japan. I.K. is fully responsible for the content of the manuscript.

Author contributions IK collected and analysed the data and prepared the manuscript. AT, KT, and YY collected the data. TS contributed to the discussion and reviewed the manuscript. All authors participated in the preparation of the manuscript and approved its final version for publication.

Funding This study was funded by the Japan Osteoporosis Foundation.

Compliance with ethical standards

Conflict of interest Ippei Kanazawa, Ayumu Takeno, Ken-ichiro Tanaka, Yuko Yamane and Toshitsugu Sugimoto declare that they have no conflicts of interest.

References

1. Barret-Connor E, Holbrook TL (1992) Sex differences in osteoporosis in older adults with non-insulin-dependent diabetes mellitus. JAMA 268:3333–3337
2. Vestergaard P (2007) Discrepancies in bone mineral density and fracture risk in patients with type 1 and type 2 diabetes—a meta-analysis. Osteoporos Int 18:427–444
3. Yamamoto M, Yamaguchi T, Yamauchi M, Kaji H, Sugimoto T (2009) Diabetic patients have an increased risk of vertebral fractures independent of bone mineral density or diabetic complications. J Bone Miner Res 24:702–709
4. Haentjens P, Magaziner J, Colon-Emeric CS, Vanderschueren D, Milisen K, Velkeniers B, Boonen S (2010) Meta-analysis: excess mortality after hip fracture among older women and men. Ann Intern Med 152:380–390
5. Ensrund KE, Thompson DE, Cauley JA, Nevitt MC, Kado DM, Hochberg MC, Santora AC 2nd, Black DM (2009) Prevalent vertebral deformities predict mortality and hospitalization in older women with low bone mass. J Am Geriatr Soc 48:241–249
6. Miyake H, Kanazawa I, Sugimoto T (2018) Association of bone mineral density, bone turnover markers, and vertebral fractures with all-cause mortality in type 2 diabetes mellitus. Calcif Tissue Int 102:1–13
7. Lips P, van Schoor NM (2005) Quality of life in patients with osteoporosis. Osteoporos Int 16:447–455
8. Cauley JA, Lui LY, Paudel ML, Taylor BC, Cawthon PM, Hillier TA, Schousboe JT, McCulloch CE, Ensrud KE (2016) Impact of radiographic vertebral fractures on inpatient healthcare utilization in older women. Bone 88:165–169
9. Yamaguchi T, Sugimoto T, Yamada H, Kanzawa M, YanoS Yamauchi M, Chihara K (2002) The presence and severity of vertebral fractures is associated with the presence of esophageal hiatal hernia in postmenopausal women. Osteoporos Int 13:331–336
10. Yamaguchi T, Sugimoto T, Yamauchi M, Matsumori Y, Tsutsumi M, Chihara K (2005) Multiple vertebral fractures are associated with refractory reflux esophagitis in postmenopausal women. J Bone Miner Metab 23:36–40
11. Trikkalinou A, Papazafiropoulou AK, Melidonis A (2017) Type 2 diabetes and quality of life. World J Diabetes 8:120–129
12. Adriaanse MC, Drewes HW, van der Heide I, Struijs JN, Baan CA (2016) The impact of comorbid chronic conditions on quality of life in type 2 diabetes patients. Qual Life Res 25:175–182
13. Solli O, Stavem K, Kristiansen IS (2010) Health-related quality of life in diabetes: the associations of complications with EQ-5D scores. Health Qual Life Outcomes 8:18
14. Yasuda H, Sanada M, Kitada K, Terashima T, Kim H, Sakaue Y, Fujitani M, Kawai H, Maeda K, Kashiwagi A (2007) Rationale and usefulness of newly devised abbreviated diagnostic criteria and staging for diabetic polyneuropathy. Diabetes Res Clin Pract 77(Suppl 1):S178–S183
15. Inomat S, Haneda M, Morita T, Katayama S, Iwamoto Y, Sakai H, Tomino Y, Matsuo S, Asano Y, Makino H, Committee Diabetic Nephropha (2005) Revised criteria for the early diagnosis of diabetic nephropathy. Nihon Jinzo Gakkai Shi 47:767–769
16. Soen S, Fukunaga M, Sugimoto T, Sone T, Fujiwara S, Endo N, Gorai I, Shiraki M, Hagino H, Hosoi T, Ohta H, Yoneda T, Tomomitsu T, Japanese Society for Bone and Mineral Research and Japan Osteoporosis Society Joint Review Committee for the Revision of the Diagnostic Criteria for Primary Osteoporosis (2013) Diagnostic criteria for primary osteoporosis: year 2012 revision. J Bone Miner Metab 31:247–257
17. Genant HK, Wu CY, van Kuijk C, Nevitt MC (1993) Vertebral fracture assessment using a semiquantitative technique. J Bone Miner Res 8:1137–1148
18. Mahoney FI, Barthel DW (1965) Functional evaluation: the Barthel index. Md State Med J 14:61–65
19. Ware JE Jr, Sherbourne CD (1992) The MOS 36-item short form health survey (SF-36). Conceptual framework and item selection. Med Care 30:473–483
20. Ware JE Jr (2000) SF-36 health survey update. Spine 25:3130–3139
21. Kanis JA, Minne HW, Meunier PJ, Ziegler R, Allender E (1992) Quality of life and vertebral osteoporosis. Osteoporos Int 2:161–163
22. Oleksik A, Lips P, Dawson A, Minshall ME, Shen W, Cooper C, Kanis JA (2000) Health related quality of life (HRQOL) in postmenopausal women with low BMD with or without prevalent vertebral fractures. J Bone Miner Res 15:1384–1392
23. Oleksik AM, Ewing S, Shen W, van Schoor NM, Lips P (2005) Impact of incident vertebral fractures on health related quality of life (HRQOL) in postmenopausal women with prevalent vertebral fractures. Osteoporos Int 16:861–870
24. Rostom S, Allali F, Bahiri R, Abouqal R, Hajjaj-Hassouni N (2012) Phychometric properties evaluation of the quality of life questionnaire of the European Foundation for osteoporosis in Arabic population. Rheumatol Int 32:2037–2049
25. Goldney RD, Phillips PJ, Fisher LJ, Wilson DH (2004) Diabetes, depression, and quality of life: a population study. Diabetes Care 27:1066–1070
26. Gavard JA, Lustman PJ, Clouse RE (1993) Prevalence of depression in adults with diabetes. An epidemiological evaluation. Diabetes Care 16:1167–1178
27. Rose M, Fliege H, Hildebrandt M, Schirop T, Klapp BF (2002) The network of psychological variables in patients with diabetes and their importance for quality of life and metabolic control. Diabetes Care 25:35–42

28. Wilson S, Sharp CA, Davie MWJ (2012) Health-related quality of life in patients with osteoporosis in the absence of vertebral fracture: a systematic review. Osteoporos Int 23:2749–2768
29. Bianchi ML, Orsini MR, Saraifoger S, Ortolani S, Radaelli G, Betti S (2005) Quality of life in post-menopausal osteoporosis. Health Qual Life Outcomes 3:78
30. de Oliveria Ferreira N, Arthuso M, da Silva R, Pedro AO, Pinto Neto AM, Costa-Paiva L (2009) Quality of life in women with postmenopausal osteoporosis: correlation between QUALEFFO 41 and SF-36. Maturitas 62:85–90
31. Andersen H, Nielsen S, Mogensen CE, Jakobsen J (2004) Muscle strength in type 2 diabetes. Diabetes 53:1543–1547
32. Park SW, Goodpaster BH, Lee JS, Kuller LH, Boudreau R, de Rekeneire N, Harris TB, Kritchevsky S, Tylavsky FA, Nevitt M, Cho YW, Newman AB, Health, Aging, and Body composition Study (2009) Excessive loss of skeletal muscle mass in older adults with type 2 diabetes. Diabetes Care 32:1993–1997
33. Hirshfeld HP, Kinsella R, Duque G (2017) Osteosarcopenia: where bone, muscle, and fat collide. Osteoporos Int 28:2781–2790
34. Huang CY, Liao LC, Tong KM, Lai HL, Chen WK, Chen CI, Lu CY, Chen FJ (2015) Mediating effects on health-related quality of life in adults with osteoporosis: a structural equation modeling. Osteoporos Int 26:875–883