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A scoring assessment tool for the risk of vertebral fractures in patients with type 2 diabetes mellitus☆

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ABSTRACT

Background: Development of assessment tool for fracture risk is an urgent task, because bone mineral density (BMD) is less useful for evaluating fracture risk in type 2 diabetes mellitus (T2DM).

Subjects and methods: In total, 808 T2DM patients were enrolled in this cross-sectional study. To develop a scoring assessment tool using clinical risks for vertebral fracture (VF), we evaluated which variables were associated with VF by logistic regression analysis, and categorized these variables based on cut-off values obtained by using receiver operating characteristic (ROC) curves. For calculation of the score, the relative weight of the factors was determined, and a tentative score was assigned. Then, cut-off point of the score was examined to predict VF.

Results: Logistic regression analyses showed that age, diabetes duration, body mass index (BMI), serum albumin, and T score at femoral neck (FN-T score) were associated with VF risk. Parameter estimates for each risk factor obtained by logistic analyses were converted to risk scores (maximum score 23). ROC analysis showed that 8.5 was the cut-off value for detecting VF. Multiple logistic regression analysis adjusted for confounding factors showed that score ≥9 was significantly associated with an increased risk of prevalent VF (odds ratio 1.99, 95% confidence interval 1.22–3.24, p = 0.006).

Conclusions: This is the first study to show that a scoring assessment tool using age, duration of diabetes, BMI, serum albumin, and FN-T score is useful to estimate VF risk in patients with T2DM, being more sensitive than BMD alone in detecting bone fragility.

1. Introduction

Accumulating evidence has shown that patients with diabetes mellitus have an increased risk of osteoporotic fractures [1–3]. Previous meta-analyses showed that risks of hip and vertebral fracture (VF) are increased approximately twofold in patients with type 2 diabetes mellitus (T2DM) [4–6]. The increased VF risk in diabetics is shown mainly in Asian population [7], not in other populations [8]. We recently showed that vertebral fracture (VF) affects daily living and quality of life in patients with T2DM, regardless of the presence of other diabetic complications [9], and that it is independently associated with all-cause mortality in this population [10]. Therefore, osteoporosis is recently considered as one of the diabetic complications requiring more attention. Given the rapidly aging population worldwide, the prevalence of both diabetes and osteoporosis is also increasing. Therefore, it is an urgent task to develop a management strategy for diabetes-related bone disease.

Previous studies have shown that the increased risk of fracture is independent of the bone mineral density (BMD) in patients with T2DM [4,7]. Vestergaard reported a meta-analysis showing that patients with T2DM had higher BMD at the lumbar spine (LS) and hip than age- and sex-matched control subjects [4]. Although the estimated fracture risk was 0.77-fold lower according to the BMD values, the risk of hip fracture compared to non-diabetic individuals was 1.4-fold higher.

Abbreviations: BMD, bone mineral density; T2DM, type 2 diabetes mellitus; VF, vertebral fracture; LS, lumbar spine; BMI, body mass index; SD, standard deviation; FN, femoral neck; ROC, receiver operating characteristic; eGFR, estimated glomerular filtration rate; HbA1c, hemoglobin A1c; CV, coefficients of variation; uNTX, urinary N-terminal cross-linked telopeptide of type-I collagen; OR, odds ratio; CI, confidence interval; AUC, area under the curve; FRAX, Fracture Risk Algorithm

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Schwartz et al. showed that the BMD at the femoral neck (FN) compared to the hip fracture risk is 0.59 standard deviation (SD) higher in diabetic women and 0.35 SD higher in diabetic men than in non-diabetic women and men, respectively [11]. We previously demonstrated that the presence of T2DM was an independent risk factor for prevalence of VF in patients with T2DM even after adjusting for BMD, and that the sensitivity and specificity of assessment using BMD for the risk of VF were low in T2DM compared to those in non-diabetic individuals [7]. These findings suggest that BMD measurement alone might be less useful for assessing the risk of fracture in patients with T2DM. Therefore, it is necessary to determine suitable surrogate markers for diabetes-related bone disease that supplement the insensitivity of BMD and assess fracture risk in T2DM.

In this study, we aimed to determine the assessment tool for VF risk of T2DM patients in clinical settings, and we hypothesized that a scoring assessment tool using multiple risk factors might be useful. We also aimed to investigate the independent association of the clinical factors with the presence of VF in patients with T2DM.

2. Materials and methods

2.1. Subjects

Data of patients who were admitted at Shimane University Hospital for education and treatment in relation to T2DM from 2002 to 2017 were screened. We excluded the patients with diseases, including malignant disorders, hyperthyroidism, hyperparathyroidism, growth hormone deficiency, acromegaly, liver cirrhosis, and renal dysfunction [estimated glomerular filtration rate (eGFR) < 30 mL/min/1.73 m^2], as well as those who were administered glucocorticoids, hormonal therapy, and anti-osteoporosis drugs, such as bisphosphonates, denosumab, and selective estrogen receptor modulators, because these diseases and medications influence bone metabolism. We also excluded men younger than 50 years and premenopausal women. Although a total of 1331 patients met the inclusion criteria, the bone parameters of 808 patients (505 men older than 50 years and 303 postmenopausal women) were available for this analysis. This study was approved by the institutional review board of Shimane University Faculty of Medicine (IRB approval number 3280), and the requirement for informed patient consent was waived because no intervention and further examinations were performed.

The patients' demographic data, biochemical parameters, and BMD are shown in Table 1. The number of patients taking insulin, thiazolidine, metformin, and sulfonylurea which might affect the fracture risk [12–15], was 206, 64, 158, and 307 respectively. The number of patients with VF was 313.

2.2. Biochemical measurements

After overnight fasting, serum and first void urine samples were collected. Biochemical markers were measured by standard methods as previously described [16–18]. Hemoglobin A1c (HbA1c) was determined by high-performance liquid chromatography (HLC-723G8, Tosoh Bioscience, Tokyo, Japan). HbA1c values were estimated as National Glycohemoglobin Standardization Program equivalent values. Serum total osteocalcin was measured by a radioimmunoassay (LSI Medience Corporation, Tokyo, Japan) with the coefficients of variation (CV) of 5.5%. Urinary N-terminal cross-linked telopeptide of type-I collagen (uNTX) was measured by an enzyme-linked immunosorbent assay (Alere Medical Co., Ltd., Tokyo, Japan) with CV of 6.6%.

2.3. Radiography

Lateral X-ray films of the thoracic and LS were taken in the same week of the serum and urine collection. The anterior, central, and posterior heights of each of the 13 vertebral bodies from Th4 to L4 were measured. A patient was diagnosed as having VF when at least one of the three vertebral height measurements decreased by > 20% when compared to the height of the nearest uncompressed vertebral body [19]. A VF was diagnosed by two investigators who were blinded to each other's reading. If the investigators' judgment of VFs was not in agreement, the film was independently reassessed. If the re-evaluated findings were again different, we regarded that case as a nonfracture.

BMD of LS 2–4 and FN was measured by the dual-energy X-ray absorptiometry (QDR-4500; Hologic, Waltham, MA). The CVs of LS- and FN-BMD measurements using our methods were 0.9% and 1.7%, respectively. T score indicates a deviation from the average BMD in young sex-matched Japanese subjects normal reference mean, whereas Z-scores indicate a deviation from the average BMD in normal age- and sex-matched Japanese subjects in the standardized normal distribution.

Table 1
Baseline characteristics of subjects.

Number of subjects (male/female)	808 (505/303)
Age (years)	66.7 ± 9.1
Duration of diabetes (years)	12.3 ± 9.7
BMI (kg/m^2)	23.8 ± 4.1
HbA1c (%)	8.8 ± 2.2
eGFR (mL/min/1.73 m^2)	76.9 ± 21.2
ALT (U/L)	26 ± 19
Serum albumin (g/dL)	4.1 ± 0.5
Urine albumin (mg/day)	82.9 ± 237.4
Osteocalcin (ng/mL)	5.7 ± 2.8
Urinary NTX (nMBCE/mM-Cr)	41.6 ± 29.9
LS BMD (g/cm^2)	0.978 ± 0.221
T score	−0.48 ± 1.83
Z score	0.60 ± 1.26
FN BMD (g/cm^2)	0.700 ± 0.139
T score	−1.14 ± 1.09
Z score	0.26 ± 1.12
Insulin	206
Thiazolidine	64
Metformin	158
Sulfonylurea	307
Vertebral fracture n (%)	313 (38.7%)

BMI, body mass index; HbA$_{1c}$, hemoglobin A$_{1c}$; eGFR, estimate glomerular filtration rate; NTX, N-terminal cross-linked telopeptide of type-I collagen; LS, lumbar spine; FN, femoral neck; BMD, bone mineral density.

2.4. Statistical analysis

First, we examined which variables are associated with the presence of VF by logistic regression analysis. Then, to categorize the continuous variables, we examined the cut-off point by receiver operating characteristic (ROC) curves analysis. Previous studies have shown that obesity increases the risk of VF [20–22], and we previously showed that the association between BMI and VF risk showed a J-curve, specifically both overweight (BMI > 23.5 kg/m^2) and underweight (BMI < 21.2 kg/m^2) were associated with VF risk in Japanese patients with T2DM [23]. Therefore, we used BMI as a risk factor for VF to develop a scoring assessment tool although BMI was not associated with the presence of VF in the first step. We used −1.0 SD and −2.5 SD as cut-off values for T score because these are normally used to diagnose osteoporosis in clinical settings. We examined which T scores at LS or FN is a good predictor for assessing the presence of VF by using odds ratio (OR), area under the curve (AUC), and p values of ROC curve analysis. Then, the variables were categorized with appropriate references and OR was calculated for each reference. For calculation of the risk score, the relative weight of a factor for predicting fracture was determined, and a tentative sore was assigned by conversion of parameter estimates as previously described [24]. In brief, to convert parameter estimates into integral number, tentative scores were calculated 10 times for each parameter estimate, decimals were rounded, and the score was rounded to the next integer. To reduce the total score, the final score was

Table 2
Association of various parameters with the presence of vertebral fracture.

	Crude			Adjusted		
	OR	95% CI	p	OR	95% CI	p
Age (per 10 years increase)	1.73	1.47–2.05	< 0.001			
Sex (men, 1)	1.08	0.81–1.46	0.595			
Duration of diabetes (per 10 years increase)	1.19	1.03–1.37	0.023			
BMI (per SD increase)	1.02	0.89–1.18	0.778			
HbA1c (per 1% increase)	0.94	0.87–1.00	0.057	0.96	0.90–1.04	0.304
eGFR (per SD increase)	0.90	0.78–1.04	0.162	1.09	0.93–1.28	0.297
ALT (per SD increase)	0.92	0.78–1.10	0.360	0.99	0.84–1.18	0.926
Serum albumin (per SD increase)	0.76	0.66–0.87	< 0.001	0.81	0.70–0.93	0.004
Urine albumin (per SD increase)	1.06	0.89–1.26	0.524	1.10	0.91–1.32	0.342
LS-T score (per SD increase)	0.77	0.67–0.90	< 0.001	0.70	0.59–0.84	< 0.001
LS-T score (per SD increase)[a]	0.80	0.68–0.94	0.007	0.73	0.60–0.88	0.001
FN-T score (per SD increase)	0.64	0.55–0.75	< 0.001	0.65	0.54–0.78	< 0.001
Osteocalcin (per SD increase)	0.92	0.79–1.07	0.284	0.89	0.76–1.05	0.154
Urine NTX (per SD increase)	1.06	0.92–1.22	0.434	1.08	0.92–1.26	0.332
Insulin use (yes, 1)	1.13	0.82–1.57	0.451	0.99	0.69–1.42	0.939
Thiazolidine use (yes, 1)	1.43	0.85–2.39	0.178	1.36	0.80–2.33	0.260
Metformin use (yes, 1)	0.78	0.54–1.13	0.192	0.78	0.53–1.14	0.198
Sulfonylurea (yes, 1)	0.89	0.66–1.20	0.438	0.80	0.59–1.09	0.157

Multiple logistic regression analyses were performed. Adjusted model; age, sex, duration of diabetes, and BMI. OR, odds ratio; CI, confidence interval.
[a] Patients with vertebral fracture at lumbar 2–4 was excluded.

calculated as the tentative score divided by 2 with rounding of decimals. And then, we examined the cut-off value of the scoring assessment tool by ROC curves. Finally, to examine the internal validation, multiple logistic regression analyses were used for multivariate analysis to adjust for confounding factors. Statistical analyses were performed using statistical computer programs StatView (Abacus Concepts, Berkeley, CA) and IBM SPSS version 19 (SPSS Japan Inc., Tokyo, Japan). A p value of < 0.05 was considered statistically significant. Data are expressed as means ± SD.

3. Results

3.1. Association between various parameters and VF risk

To determine the risk factors for VF, several clinical characteristics including BMD and bone turnover markers were investigated by logistic regression analysis. As shown in Table 2, age [OR 1.73, 95% confidence interval (CI) 1.47–2.05 per 10-year increase, p < 0.001], duration of diabetes (OR 1.19, 95% CI 1.03–1.37 per 10-year increase, p = 0.023), serum albumin (OR 0.76, 95% CI 0.66–0.87 per SD increase, p < 0.001), LS-T score (OR 0.77, 95% CI 0.67–0.90 per SD increase, p < 0.001), and FN-T score (OR 0.64, 95% CI 0.55–0.75 per SD increase, p < 0.001) were significantly associated with VF risk. Bone turnover markers, such as osteocalcin and urinary NTX, were not associated with VF risk. Furthermore, medications, such as insulin, thiazolidine, metformin, and sulfonylurea were not associated with VF risk. After adjusting for age, sex, duration of diabetes, and BMI, serum albumin (OR 0.81, 95% CI 0.70–0.93 per SD increase, p = 0.004), LS-T score (OR 0.70, 95% CI 0.59–0.84 per SD increase, p < 0.001), and FN-T score (OR 0.65, 95% CI 0.54–0.78 per SD increase, p < 0.001) were significantly associated with VF risk.

The distribution of VF was shown in Fig. 1. A total of fractured vertebrae was 533. Although more than half of VFs occurred at Th11 (14.8%), Th12 (25.3%), and L1 (22.5%), VFs also occurred at L2 (9.6%), L3 (5.1%), and L4 (4.3%). Because VF at L2–4 might affect LS-BMD, we excluded patients with VF at L2–4 and examined the association between LS-T score and VF risk. However, LS-T score was still significantly associated with VF risk in crude (OR 0.80, 95% CI 0.68–0.94, p = 0.007) and adjusted models (OR 0.73, 95% CI 0.60–0.88, p = 0.001) in patients without VF at L2–4.

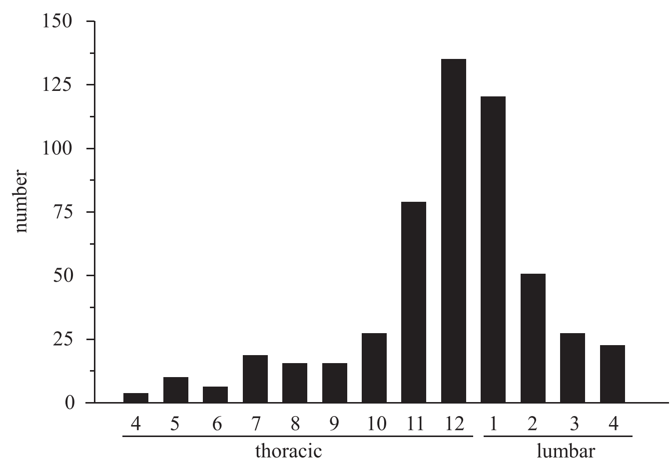

Fig. 1. The distribution of the position of vertebral fracture.

3.2. Categorization of fracture risks

Next, to categorize the continuous variables which were associated with VF in the logistic regression analysis, we performed the ROC analyses to evaluate the cut-off values of these parameters to predict the presence of VF (Table 3). The cut-off value, AUC, and p value were 66.5 years, 0.638, and < 0.001 for age; 9.5 years, 0.551, and 0.016 for duration of diabetes; 4.1, 0.584, and < 0.001 for serum albumin; −0.99, 0.562, and 0.003 for LS-T score; −0.46, 0.554, and 0.021 for

Table 3
ROC analysis.

Variables	AUC	Sensitivity	Specificity	95% CI	p	Cut-off
Age	0.638	0.668	0.569	0.599–0.678	< 0.001	66.5
Duration of diabetes	0.551	0.651	0.468	0.510–0.592	0.016	9.5
Serum albumin	0.584	0.470	0.660	0.543–0.625	< 0.001	4.1
LS-T score	0.562	0.619	0.470	0.521–0.604	0.003	−0.99
LS-T score[a]	0.554	0.580	0.506	0.508–0.599	0.021	−0.46
FN-T score	0.611	0.579	0.591	0.572–0.651	< 0.001	−1.24

[a] Patients with vertebral fracture at lumbar 2–4 was excluded.

Table 4
Categorization of the predictors of vertebral fracture.

Variables	OR	95% CI	p
Age (years)			
< 65	1.00		
65–75	2.17	1.55–3.04	< 0.001
≥75	3.50	2.38–5.14	< 0.001
Duration of diabetes (years)			
< 10	1.00		
10–20	1.63	1.17–2.29	0.004
≥20	1.65	1.15–2.37	0.007
BMI (kg/m^2)			
< 21	1.78	1.15–2.74	0.010
21–24	1.00		
≥24	1.42	0.98–2.06	0.062
Serum albumin (g/dL)			
≥4.0	1.00		
< 4.0	1.71	1.26–2.31	< 0.001
FN-T score			
≥ −1.0	1.00		
−1.0 to −2.5	1.63	1.20–2.23	0.002
≤ −2.5	3.58	2.20–5.80	< 0.001

Table 5
Scores for the categories of each fracture predictor.

Predictor	Parameter estimates by logistic regression	Tentative score[a]	Final score[b]
Age (years)			
< 65			0
65–75	0.773	8	4
≥75	1.252	13	7
Duration of diabetes (years)			
< 10			0
≥10	0.495	5	3
BMI (kg/m^2)			
< 21	0.575	6	3
21–24			0
≥24	0.352	4	2
Serum albumin (g/dL)			
≥4.0			0
< 4.0	0.534	6	3
FN-T score			
≥ −1.0			0
−1.0 to −2.5	0.491	5	3
≤ −2.5	1.274	13	7

[a] Calculated 10 times for each parameter estimate, decimals rounded off, and rounded up to the next integer.
[b] Tentative score divided by 2, decimals rounded off, and rounded to an integer < 10.

LS-T score after excluding patients with VF at L2–4; −1.24, 0.611, and < 0.001 for FN-T score, respectively. To detect the prevalence of VF, OR, AUC, and p values of the FN-T score were better than those of the LS-T score; therefore, we decided to use the FN-T score for the next step.

We categorized these risk factors and performed logistic regression analysis using categorized fracture risks (Table 4). When the OR for age was calculated versus < 65 years, the VF risk was 2.17 times higher at age 65–75 years ($p < 0.001$) and was 3.50 times higher at age ≥75 years ($p < 0.001$). For duration of diabetes, the OR was calculated versus short duration (< 10 years); the VF risk was 1.63 times higher at moderate duration (10 to 20 years) ($p = 0.004$) and was 1.65 times higher at long duration (≥20 years) ($p = 0.007$). The OR of moderate duration was almost similar to that of long duration. For BMI, the OR was calculated versus middle BMI (21–24 kg/m^2); the VF risk was 1.78 times higher at low BMI (< 21 kg/m^2) ($p = 0.010$) and was 1.42 times higher at high BMI (≥24 kg/m^2) ($p = 0.062$). For serum albumin, the OR was calculated versus normal serum albumin (≥4.0 g/dL); the VF risk was 1.71 times higher at low serum albumin (< 4.0 g/dL) ($p < 0.001$). For the FN-T score, the OR was calculated versus normal BMD (T score ≥ −1.0); the VF risk was 1.63 times higher at osteopenia (T score −1.0 to −2.5) ($p = 0.002$) and was 3.58 times higher at osteoporosis (T score ≤ −2.5) ($p < 0.001$).

3.3. Constructing the scoring assessment tool for predicting the prevalence VF

Parameter estimates for each risk factor obtained by logistic regression analysis were converted to tentative scores using the formula described in the "Materials and methods" section (Table 5). Final scores were obtained by modifying the tentative scores. We then performed a ROC analysis using the final scores to define the optimal cut-off score. As shown in Fig. 2A and Table 6, the cut-off value, AUC, and p value were 8.5, 0.671, and < 0.001, respectively.

To examine the internal validation, we performed logistic regression analyses using the cut-off value of the scoring assessment tool. As shown in Table 7, total score ≥9 was significantly associated with VF risk (Crude; OR 3.25, 95% CI 2.38–4.44, $p < 0.001$). Moreover, the association between total score ≥9 and VF risk remained significant even after adjusting for individual components of the scoring assessment tool, such as age, duration of diabetes, BMI, serum albumin, and FN-T score (Model 1; OR 2.09, 95% CI 1.32–3.31, $p = 0.002$). Finally, when the association was adjusted for sex, HbA1c, eGFR, osteocalcin, urinary NTX, insulin, thiazolidine, metformin, and sulfonylurea use, it still remained significant (Model 4; OR 1.98, 95% CI 1.21–3.23, $p = 0.006$).

Then, we assessed the scoring assessment tool without the FN-T score. When the scores were calculated without the FN-T score, ROC analysis showed that the cut-off value, AUC, and p value were 6.5, 0.655, and < 0.001, respectively (Fig. 2B and Table 6). Moreover, multiple logistic regression analysis showed that total score ≥7 was significantly associated with VF risk even after adjusting for various parameters (Model 4; OR 1.96, 95% CI 1.18–3.27, $p = 0.010$) (Table 7).

4. Discussion

In this study, we established a scoring assessment tool using individual risk factors weighted by logistic regression analysis. ROC analysis showed that the AUC and sensitivity of the scoring assessment tool were better than those of the individual risk factors. Moreover, the scoring assessment tool was significantly associated with prevalent VF even after adjusting for the risk factors. These findings suggest that the scoring assessment tool is useful for assessing VF risk in patients with T2DM.

Previous studies have shown that the increased risk of fractures is independent of BMD in patients with T2DM [4,7]; therefore, in case of T2DM, BMD is not always a good marker for assessing fracture risk. In fact, in this study, the cut-off values of T scores were higher than −2.5 SD and their sensitivities were lower than 0.7, although LS- and FN-T scores were significantly associated with the prevalence of VF. Thus, if all of the focus is given only to BMD values, we might underestimate the fracture risks in T2DM. It is therefore an important task to determine the suitable surrogate markers for diabetes-related bone disease that supplement the insensitivity of BMD and assess fracture risk in T2DM.

We assessed the scoring assessment tool without the FN-T score, because BMD measurement by DXA is often not available in clinics, which may be disadvantageous for patients. However, assessment tools without BMD measurement can be beneficial for many patients. WHO Fracture Risk Algorithm (FRAX), which is an assessment tool for fracture risk that can be calculated even if BMD is unavailable, was designed to provide an estimate of absolute fracture risk in older adults [25]. However, the FRAX algorithm does not include T2DM as a risk factor for fracture, and previous studies have shown that not only BMD but also FRAX was less useful for predicting osteoporotic fractures in

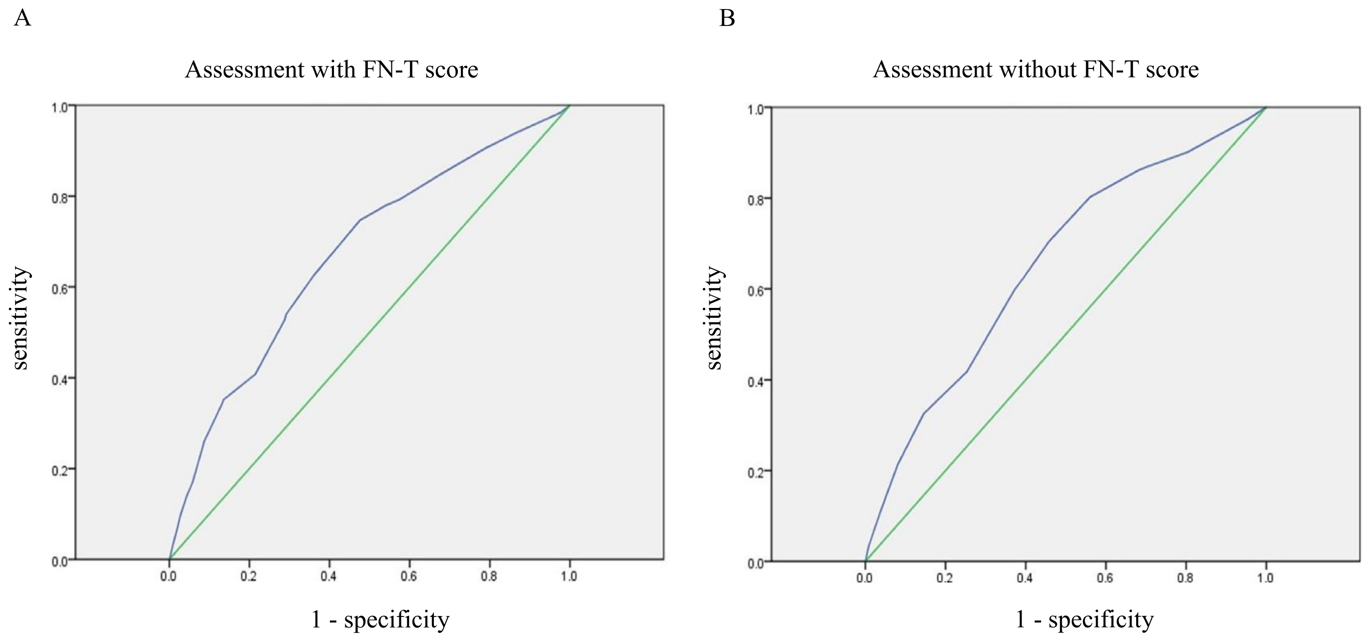

Fig. 2. Receiver operating characteristic curves to evaluate the cut-off values of the scoring assessment tool with and without FN-T score to predict the prevalence of VF. (A) Assessment with FN-T score. (B) Assessment without FN-T score. FN-T: bone mineral density T score at the femoral neck.

patients with T2DM [11]. Thus, another assessment tool should be developed for patients with T2DM. In this study, we evaluated whether the scoring assessment tool without the FN-T score is useful for detecting the prevalence of VF. The AUC and sensitivity by ROC analysis were slightly decreased when the scoring did not include the FN-T score compared to when the scoring included the FN-T score; however, the AUC and sensitivity of the scoring assessment tool without the FN-T score were better than those of the individual risk factors. Moreover, the scoring assessment tool without the FN-T score was significantly associated with prevalent VF even after adjusting for the risk factors. Therefore, this scoring assessment tool may be useful in clinics where DXA is not available.

This study has some limitations. First, we analyzed only subjects who visited the Shimane University Hospital, a tertiary center, for treatment of diabetes mellitus. Therefore, the participants enrolled in this study might have relatively severe states of the disorder and might not be representative of the Japanese patients with the disorder. Second, more than half of subjects were administered hypoglycemic drugs. Therefore, we cannot exclude the possibility that the treatment of diabetes affected the occurrence of VF, although the association was adjusted for usage of insulin, thiazolidine, metformin, and sulfonylurea. Third, the subjects in this study were only Japanese. To confirm the present findings, a reliable external validation study with a sufficiently large sample size is required [26]. Capacity of insulin secretion and degree of obesity in Asian are known to be different from Western people [27]; therefore, the cut-off value of BMI should be different among races. Thus, the universality of our findings should be clarified, and some modification may be necessary. Fourth, given that the underlying mechanisms of primary osteoporosis are different between men and women [28], it may be better to develop a separate assessment tool for men and women. However, in this study, we aimed to develop an assessment tool that could be widely applied; therefore, we developed a tool for both men and women. Moreover, the present study showed that sex was not associated with the prevalence of VF in patients with T2DM, and the association between the scoring and VF risk remained significant even after adjusting for sex. Fifth, Bone and Diabetes Working Group of International Osteoporosis Foundation suggested that FRAX adjusted for diabetes might be useful for diagnosis and management of bone fragility in diabetes [3]. However, other clinical important risk factors for fractures, such as family history,

Table 7
Association between the assessment tool and vertebral fracture.

Total score	OR	95% CI	p
Assessment with FN-T score			
Reference (total score < 9)	1.00		
Total score ≥9			
Crude	3.25	2.38–9.44	< 0.001
Model 1	2.09	1.32–3.31	0.002
Model 2	2.11	1.33–3.35	0.002
Model 3	2.03	1.25–3.29	0.004
Model 4	1.98	1.21–3.23	0.006
Assessment without FN-T score			
Reference (total score < 7)	1.00		
Total score ≥7			
Crude	2.82	2.08–3.82	< 0.001
Model 1	1.88	1.16–3.05	0.010
Model 2	1.89	1.16–3.07	0.010
Model 3	1.98	1.19–3.29	0.009
Model 4	1.96	1.18–3.27	0.010

Multiple logistic regression analyses were performed. Model 1; adjusted for age, duration of diabetes, BMI, serum albumin, and FN-T score. Model 2; adjusted for model 1 plus sex, HbA1c, and eGFR. Model 3; adjusted for model 2 plus osteocalcin and urinary NTX. Model 4; adjusted for model 3 plus insulin, thiazolidine, metformin and sulfonylurea use.

Table 6
ROC analysis.

Variables	AUC	Sensitivity	Specificity	95% CI	p	Cut-off
Assessment with FN-T score	0.671	0.747	0.524	0.632–0.710	< 0.001	8.5
Assessment without FN-T score	0.655	0.704	0.543	0.616–0.694	< 0.001	6.5

smoking and alcohol, were not included in this analysis because of the unavailability of these data. Thus, we can't compare this scoring assessment tool and FRAX in this study. Moreover, previous studies reported that several biomarkers are associated with fracture risk in patients with T2DM. Circulating levels of insulin-like growth factor-I [29–31], sclerostin [31], pentosidine [32,33], and homocysteine [34] were significantly associated with fracture risk in patients with T2DM. Furthermore, parameters of bone microstructure estimated by trabecular bone score [35,36] and high-resolution peripheral quantitative computed tomography [37,38] were involved in fracture risk in patients with T2DM. If other important risk factors were included in this assessment tool, the sensitivity might be further improved. However, these parameters are not easily and widely available in clinical settings. Sixth, we could not examine other important fragility fractures, such as hip fracture, in this study. Finally, the conclusions of this study are weakened by its cross-sectional design. Hence, it is necessary to conduct longitudinal studies to confirm the present findings in the future. Despite these limitations, this study has a strength because age, duration of diabetes, BMI, and serum albumin can be easily assessed. Thus, this scoring assessment tool may be widely useful for assessing fracture risk in patients with T2DM.

In conclusion, this is the first study to show that the scoring assessment tool using age, duration of diabetes, BMI, serum albumin, and FN-T score is useful in estimating the prevalence of VF in patients with T2DM. Although BMD alone is not enough to assess fracture risk in diabetic patients, the scoring assessment tool can improve the sensitivity to detect bone fragility.

Disclosure statement

The authors have nothing to disclose.

Author contributions

I.K. researched data and wrote manuscript. K.T., A.T., M.N., H.M. contributed to collect the data and discuss the results. T.S. contributed to discussion and reviewed/edited manuscript.

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Disclosure summary

Ippei Kanazawa, Ken-ichiro Tanaka, Ayumu Takeno, Masakazu Notsu, Hitomi Miyake, and Toshitsugu Sugimoto declare that they have no conflicts of interest.

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