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Original Article

Evaluation of the severity of lumbar osteoporosis in patients with type 2 diabetes mellitus using q-Dixon magnetic resonance imaging

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Abstract: Objective: To explore the value of q-Dixon magnetic resonance imaging (MRI) in assessing the severity of lumbar osteoporosis in patients with type 2 diabetes mellitus (T2DM). Methods: A retrospective analysis was conducted on 100 T2DM patients admitted to our hospital between 2023 and 2024, who were divided into a control group (n = 43), an osteopenia group (n = 26), and an osteoporosis group (n = 31). General data (including use of hypoglycemic agents and menopausal status) was collected. Bone mineral density (BMD) of L1-L4 was measured using dual-energy X-ray absorptiometry (DXA), and bone marrow fat fraction (FF) was measured using q-Dixon technology. Statistical analysis included ANOVA, correlation tests, receiver operating characteristic (ROC) curve analysis, and DeLong's test. Results: Regarding lumbar BMD and FF, the osteoporosis group had lower L1-L4 and total lumbar BMD than the other groups, and the osteopenia group had lower BMD than the control group (all $P<0.05$); conversely, the osteoporosis group had higher L1-L4 and total lumbar FF than the other groups, and the osteopenia group had higher FF than the control group (all $P<0.05$). In each group, males had higher L1-L4 segmental and total BMD, as well as total FF than females (all $P<0.05$), except for L3 BMD in the control group and L1-L4 segmental FF in the control and osteopenia groups (all $P>0.05$). Significant segmental differences were detected in both BMD and FF across lumbar spine segments. BMD followed a descending order of L3 > L4 > L2 > L1, whereas FF was ordered as L4 > L3 > L2 > L1 (all $P<0.05$). Kendall correlation analysis showed that L1-L4 and total BMD were negatively correlated with osteoporosis (r = -0.587 to -0.790, all $P<0.001$); L1-L4 and total FF were positively correlated with osteoporosis (r = 0.387 to 0.506, all $P<0.001$). Pearson correlation analysis showed that L1-L4 and total FF were negatively correlated with L1-L4 and total BMD (all $P<0.01$), and the correlation was stronger in females than males. ROC curves showed AUC for assessing osteoporosis severity by total FF was 0.856 (sensitivity 77.42%, specificity 81.16%, Youden index 0.586). DeLong's test showed the AUC of total FF was significantly higher than that of L1 FF (0.734, P = 0.034), while there were no statistically significant differences in the AUCs of total FF compared with those of L2-L4 FF (0.821, 0.829, and 0.823, respectively) (all $P>0.05$). Conclusion: The q-Dixon technique can effectively assess the severity of lumbar osteoporosis in patients with T2DM. Total FF is a reasonable and reliable non-invasive indicator because it integrates L1-L4 segmental information, has the highest AUC, and exhibits segmental and gender differences, providing a novel clinical strategy.

Keywords: Type 2 diabetes mellitus, osteoporosis, lumbar vertebrae, q-Dixon magnetic resonance imaging, evaluation value

Introduction

With the changes in modern lifestyles and population aging, the global incidence of type 2 diabetes mellitus (T2DM) continues to rise, with more than 537 million adult patients worldwide. Due to its widespread prevalence and large number of patients with T2DM has evolved into a major public health issue of global concern. Complex skeletal complications have become a key factor affecting patients' quality of life [1]. Patients with T2DM usually have pathophysiological changes such as insulin resistance, hyperglycemia, and metabolic disorders. These changes not only damage multiple organ systems such as the cardiovascular, renal, and nervous systems, but also have a profound adverse effect on bone metabolism.

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Specifically, chronic hyperglycemia can disrupt the normal function of osteoblasts, inhibit bone formation, and at the same time accelerate osteoclast activity and promote bone resorption. This imbalance in bone metabolism will eventually lead to a series of bone-related complications [2]. As a common pathological condition of the skeletal system, the incidence of osteoporosis in patients with T2DM is significantly higher than that in the general population. Epidemiological data show that the incidence of lumbar osteoporosis in patients with T2DM is 30%-50% higher than that in the general population. Furthermore, osteoporosis-induced bone loss often has serious consequences: due to lumbar bone loss, the risk of lumbar fractures in patients with T2DM is increased by 2-3 times [3]. Such fractures not only cause severe pain but also seriously impair patients' motor function and daily living activities, ultimately reducing their overall quality of life. However, there are still significant bottlenecks in the clinical assessment of lumbar osteoporosis in patients with T2DM. Existing assessment methods cannot accurately reflect the true status of lumbar bone mass in these patients, and thus cannot provide accurate evidence for clinical intervention. Therefore, there is an urgent need to develop more precise non-invasive imaging techniques to overcome this dilemma. Achieving accurate assessment of the severity of lumbar osteoporosis in patients with T2DM will enable clinicians to develop targeted intervention strategies as early as possible, which is crucial for delaying the progression of osteoporosis, reducing the risk of fractures, and ultimately improving patient prognosis.

Among the various methods for assessing the severity of lumbar osteoporosis in patients with T2DM, magnetic resonance imaging (MRI) has demonstrated unique advantages due to its non-invasiveness, high resolution, and multi-parameter imaging capabilities [4]. Among them, magnetic resonance q-Dixon (fat quantification) technology is an advanced MRI technology that has been developed in recent years. It can accurately and quantitatively assess the body fat content, providing new possibilities for the assessment of osteoporosis [5]. Through magnetic resonance q-Dixon technique, the fat fraction (FF) of the lumbar vertebral body can be accurately measured, thereby reflecting the severity of osteoporosis [6]. Currently, research on the application of q-Dixon technique in osteoporosis assessment mainly focuses on healthy people or patients with primary osteoporosis. For people with specific metabolic disorders such as T2DM, the pathological mechanism of lumbar osteoporosis is significantly different from that of the general population. However, the key issues related to the effectiveness of q-Dixon technique in assessing lumbar osteoporosis in T2DM patients remain unclear and have not been systematically investigated. These issues include: the correlation between q-Dixon technology parameters and lumbar bone mineral density (BMD), bone marrow FF, and osteoporosis severity in T2DM patients; as well as the diagnostic performance of this technique in predicting lumbar fracture risk in T2DM patients [7]. Based on this, this study, targeting the specific population of T2DM, used q-Dixon technique to quantitatively detect the bone marrow FF in the lumbar spine (L1-L4), and deeply analyzed the intrinsic association between lumbar BMD, bone marrow FF, and the severity of osteoporosis in patients. For the first time, it systematically revealed the segmental specificity of the lumbar spine in T2DM patients (L3 had the highest BMD, and L4 had the highest FF) and its association with metabolic disorders in T2DM. It also demonstrated for the first time that the correlation between BMD and FF was stronger in female T2DM patients than in male patients, providing a basis for gender-specific interventions. Furthermore, it determined that total FF (cutoff value = 50.83%) can be used as a non-invasive indicator for assessing the severity of osteoporosis in T2DM patients, filling a gap in previous studies that did not target the T2DM population.

Materials and methods

General information

This retrospective study selected 100 T2DM patients admitted to our hospital from January 2023 to January 2024 (**Figure 1**). According to the correlation coefficient ($r = 0.63$) between lumbar FF and BMD in patients with T2DM reported in previous studies, the sample size was calculated using G*Power 3.1 software. The significance level was set at $\alpha = 0.05$, the power at $\beta = 0.2$, and the effect size at $f = 0.35$, resulting in a minimum total sample size of 8-9

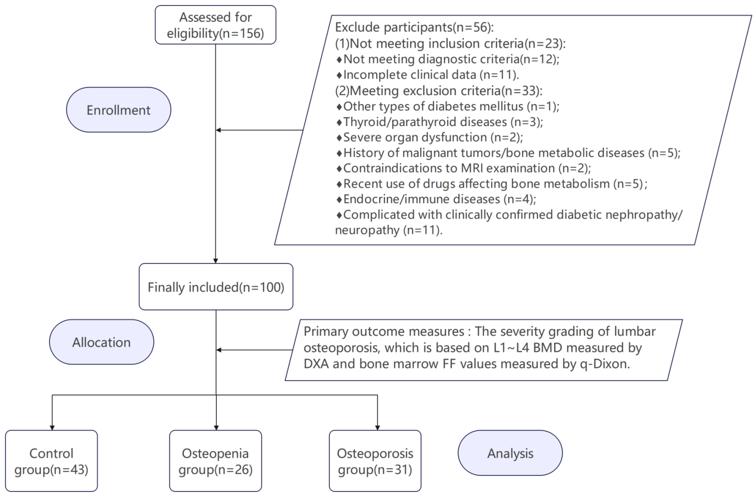


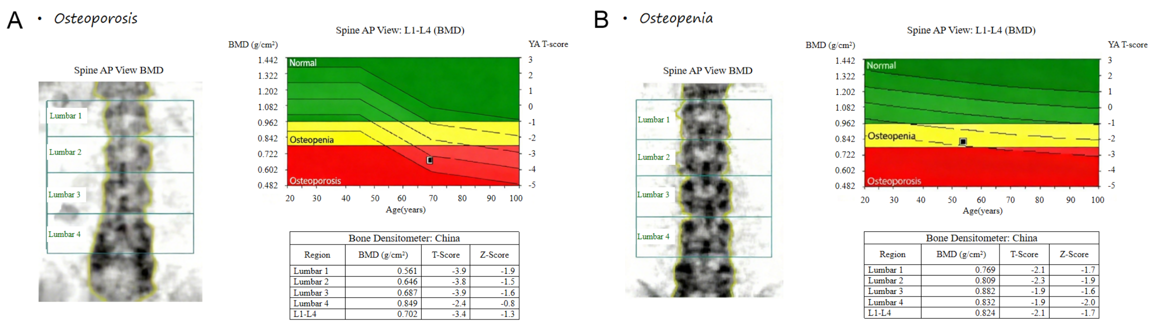
Figure 1. Patient screening flowchart.

cases [8, 9]. Considering the 20% dropout/ exclusion rate, a total of 100 patients were included in this study, which met the statistical requirements. In accordance with the latest World Health Organization (WHO) criteria [10] and the Chinese Guidelines for the Diagnosis and Treatment of Primary Osteoporosis (2022) [11], the patients were divided into three groups: control group (43 cases), osteopenia group (26 cases), and osteoporosis group (31 cases). During patient enrollment, a non-matched stratified sampling method was used to stratify patients by age (<50 years/≥ 50 years) and T2DM duration (<5 years/≥ 5 years) to ensure a balanced sample proportion in each stratified subgroup of the three groups and to avoid selection bias due to excessive concentration of core risk factors.

Diagnostic criteria: The diagnosis of T2DM was in accordance with the *Guidelines for the Prevention and Treatment of Type 2 Diabetes in China (2020 Edition)* [12]. The guidelines stipulate the following criteria: ① Fasting plasma glucose (FPG) ≥ 7.0 mmol/L; ② 2-hour postprandial glucose (2HPG) ≥ 11.1 mmol/L in oral glucose tolerance test (OGTT); ③ Random blood glucose ≥ 11.1 mmol/L; ④ Glycated hemoglobin (HbA1c) ≥ 6.5%. If any of the above criteria are met, T2DM can be diagnosed. Inclusion criteria: ① Meet the above diagnostic criteria; ② Age ≥ 18 years; ③ Complete clinical data. Exclusion criteria: ① Other types of diabetes mellitus; ② Patients with severe organ dysfunction; ③ Patients with thyroid disease or parathyroid disease; ④ Patients with a history of malignant tumors or bone metabolic diseases; ⑤ Patients with contraindications to MRI examination; ⑥ Patients who had taken drugs affecting bone metabolism recently; ⑦ Patients with endocrine diseases or immune diseases. ⑧ Patients with complications such as diabetic nephropathy (Urinary Microalbumin/Creatinine Ratio ≥ 30 mg/g for more than 3 consecutive months) or diabetic neuropathy (Common Peroneal Nerve Conduction Velocity <45 m/s accompanied by clinical symptoms such as limb numbness and hypoesthesia, or confirmed by neuroelectrophysiological examination). This study was approved by the Ethics Committee of Lanzhou No. 2 People's Hospital (approval number: lzsdermyyyxllwyh202306), and all operations were in line with the ethical requirements of the Helsinki Declaration.

Methods

DXA examination: Z-An X-ray bone mineral density analyzer was used to measure the average BMD of the lumbar vertebrae (L1-L4) under conditions of tube voltage 76 kV and tube current 3 mA, with the results expressed in g/cm^2. The diagnostic criteria for osteopenia were a T-score between -2.5 and -1.0 (postmenopausal women/men ≥ 50 years old) or a Z-score ≤ -2.0 (other populations); the diagnostic criteria for osteoporosis were a T-score ≤ -2.5 (postmenopausal women/men ≥ 50 years old) or a Z-score ≤ -2.0 with evidence of abnormal bone metabolism (other populations), strictly following the Guidelines for the Diagnosis and Treatment of Primary Osteoporosis in China (2017) and the World Health Organization diagnostic criteria. For postmenopausal women and men ≥ 50 years old, BMD was evaluated using the T-score (compared to peak bone mass in younger adults): ≥ -1 was normal; -2.5 to -1 indicated osteopenia; ≤ -2.5 indicated osteoporosis. For children, premenopausal women, and men <50 years of age, BMD was assessed using the Z-score (compared to the age-matched mean): a Z-score ≤ -2.0 indicated low bone mass or fail-



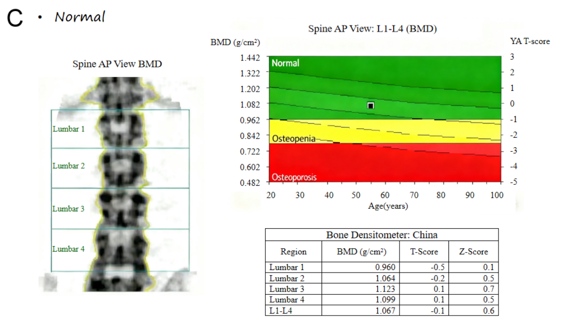


Figure 2. DXA Images of Control Group, Osteopenia Group, and Osteoporosis Group (A: DXA diagnosis of osteoporosis; B: DXA diagnosis of low bone mass; C: DXA diagnosis of control bone mass).

ure to meet the expected range for the age group (**Figure 2**).

q-Dixon MRI Technique: Lumbar spine MRI was performed using a MAGNETOM Prisma 3.0T MRI scanner from Siemens, Germany, employing a sagittal multi-echo q-Dixon fat quantification sequence. Scanning parameters were as follows: repetition time (TR) = 9 ms; 6 echo times (TEs): TE1 = 1.18 ms, TE2 = 2.46 ms, TE3 = 3.69 ms, TE4 = 4.92 ms, TE5 = 6.15 ms, TE6 = 7.38 ms; flip angle = 4.0 degrees; slice thickness = 3.0 mm; bandwidth = 260 Hz/Px; number of excitations (NEX) = 1; scan time = 3 minutes 15 seconds. After scanning, the system automatically generated 6 images: aqueous phase, fat phase, Goodness-calibrated phase, T2* phase, R2* phase, and FF phase.

Image processing: Two experienced associate chief radiologists analyzed the MRI images and measured bone marrow fat. For each vertebra, FF images from three planes (the midsagittal plane and its two adjacent anterior and posterior planes) were selected. Regions of interest (ROIs) of approximately 10-15 mm^2 were manually delineated in the cancellous bone, avoiding cortical bone, vertebral vein inlets, intervertebral discs, and other structures. FF values were measured in the L1-L4 vertebrae, with the average of three measurements taken for each subject (**Figure 3**). After the two associate chief radiologists independently delineated the ROIs, the intraclass correlation coefficient (ICC) was used to assess consistency. The results showed that the inter-observer ICC was 0.88 (95% CI: 0.82-0.93), and the within-observer ICC was 0.91 (95% CI: 0.86-0.95), both >0.85, indicating good reliability of the measurement results.

Statistical analysis

Data analysis was performed using SPSS 27.0 and MedCalc 19.2 software. Categorical data were expressed as (n, %), and comparisons between groups were performed using the x^2 test or Fisher's exact test. Normally distributed continuous data were expressed as (mean ± standard deviation), with one-way ANOVA used for comparisons among multiple groups, LSD-t post-hoc test for pairwise multiple comparisons, and non-parametric tests used for non-normally distributed data. Correlation analysis: Pearson's correlation analysis was used for bivariate normally distributed data; otherwise Kendall's correlation analysis was used. Multiple linear regression was used to adjust for confounding factors such as menopausal status and age to analyze the independent association between FF and BMD. DeLong's test was used for ROC curve analysis to compare differences in AUC. $P<0.05$ was considered statistically significant.

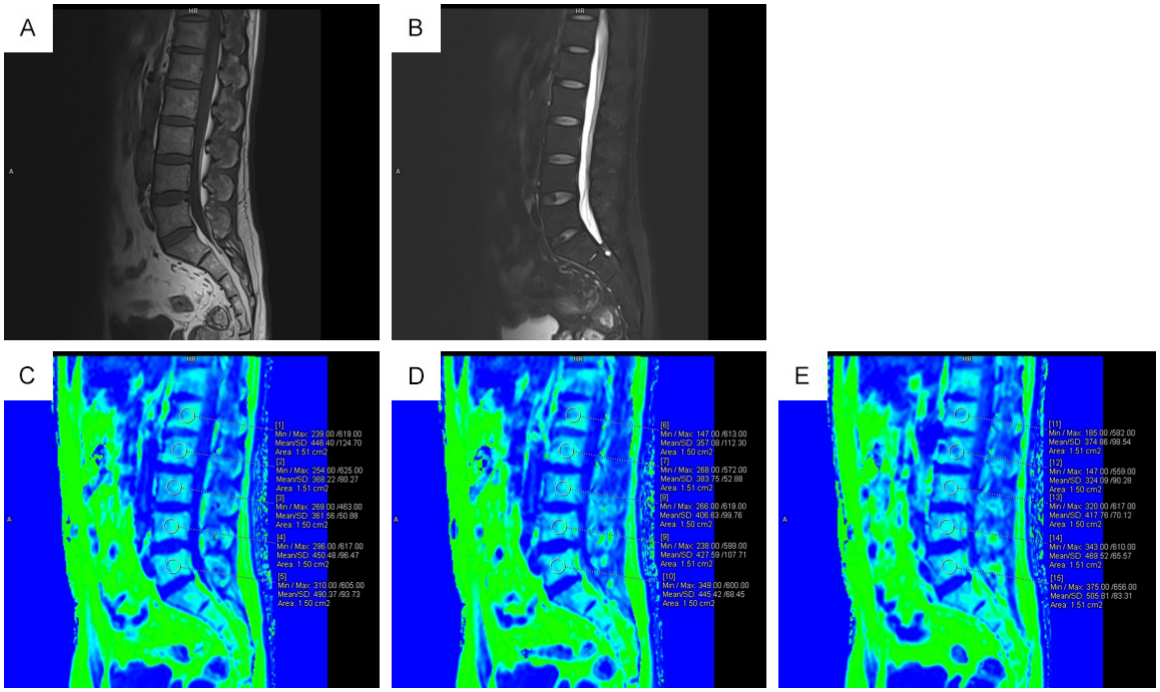


Figure 3. A: T1-weighted imaging (T1W1) phase image of the lumbar vertebra; B: T2-weighted imaging (T2W1) phase image of the lumbar vertebra; C-E: FF phase images of the most median sagittal plane of the lumbar vertebra and its two adjacent planes.

Results

Comparison of general data among the three groups

There were no statistically significant differences in baseline characteristics among the three groups in terms of sex, age, BMI, duration of T2DM, glycated hemoglobin level, history of lumbar vertebral fracture, alcohol consumption, smoking status, and use of hypoglycemic drugs (all P>0.05). However, there was a significant difference in menopausal status among female participants (P = 0.002), with the highest proportion of postmenopausal women in the osteoporosis group (85.71%), followed by the osteopenia group (60.00%) and the control group (40.00%). This confounding variable was adjusted for in subsequent multivariate analysis (**Table 1**).

Comparison of BMD and FF values among the three groups

There were significant differences in both BMD and FF values among the three groups (all $P<0.05$). Specifically, compared with the osteopenia group and the control group, the osteoporosis group exhibited significantly lower BMD in each lumbar vertebra (L1-L4) and total lumbar vertebrae. Furthermore, bone mineral density values at all measurement sites in the osteopenia group were significantly lower than those in the control group (all $P<0.05$). FF of each lumbar vertebra and the total FF of the lumbar vertebrae in the osteoporosis group were significantly higher than those in the other groups. Similarly, the FF at all measurement sites in the osteopenia group were significantly higher than those in the control group (all $P<0.05$) (**Table 2**).

Comparison of BMD and FF values between genders

In each group, male patients had higher L1-L4 segment, total BMD and FF values than female patients with statistically significant differences (all $P<0.05$) except for L3 BMD in the control group ($P = 0.240$). In the control group, males had 7.8%, 7.6%, 8.5%, and 8.7% higher L1, L2, L4, and total BMD, respectively, and 12.9% higher total FF than females. In the osteopenia group, males had 7.3%, 5.6%, 7.5%, and 7.2% higher L1-L4 segmental BMD, and 20.4% higher total BMD, than females (all $P<0.05$); for FF

Table 1. Comparison of general data [$\bar{x}$±s/n (%)]

Item	Control Group (n = 43)	Osteopenia Group (n = 26)	Osteoporosis Group (n = 31)	F/χ^2	*P*
Gender				3.336	0.192
Male	23 (53.49%)	11 (42.31%)	10 (32.26%)		
Female	20 (46.51%)	15 (57.69%)	21 (67.74%)		
Age (years)	48.67±6.48	49.45±6.24	50.12±5.26	0.507	0.604
Age stratification (years)				4.128	0.127
<50	28 (65.12)	14 (53.85)	12 (38.71)		
≥ 50	15 (34.88)	12 (46.15)	19 (61.29)		
Menopausal status (female)				12.864	0.002
Premenopausal	12 (60.00)	6 (40.00)	3 (14.29)		
Postmenopausal	8 (40.00)	9 (60.00)	18 (85.71)		
BMI	22.32±2.02	21.76±2.42	21.65±2.78	0.820	0.444
T2DM duration (years)	5.83±2.12	6.24±2.54	5.43±3.24	0.657	0.521
T2DM duration stratification (years)				1.205	0.548
<5	23 (53.49)	12 (46.15)	16 (51.61)		
≥ 5	20 (46.51)	14 (53.85)	15 (48.39)		
HbA1c (%)	6.56±0.54	6.87±0.72	6.73±0.81	1.692	0.189
History of previous lumbar fractures				4.015	0.134
Yes (within 1 year)	3 (6.98)	4 (15.38)	7 (22.58)		
Yes (more than 1 year)	5 (11.63)	4 (15.38)	5 (16.13)		
No	35 (81.40)	18 (69.23)	19 (61.29)		
Drinking history				0.810	0.691
Yes	21 (48.84%)	15 (57.69%)	18 (58.06%)		
No	22 (51.16%)	11 (42.31%)	13 (41.94%)		
Smoking history				0.689	0.683
Yes	18 (41.86%)	12 (46.15%)	11 (35.48%)		
No	25 (58.14%)	14 (53.85%)	20 (64.52%)		
Hypoglycemic drug use history				2.357	0.800
None	10 (23.26)	7 (26.92)	8 (25.81)		
Metformin	20 (46.51)	12 (46.15)	14 (45.16)		
SGLT2 inhibitor	5 (11.63)	3 (11.54)	3 (9.68)		
GLP-1 receptor agonist	3 (6.98)	1 (3.85)	2 (6.45)		
Insulin	5 (11.63)	3 (11.54)	4 (12.90)		

Note: BMI: Body Mass Index; T2DM: Type 2 Diabetes Mellitus; HbA1c: Glycated Hemoglobin; SGLT2: Sodium-Glucose Cotransporter 2; GLP-1: Glucagon-Like Peptide-1.

values, the total FF of males was 20.1% higher than that of females ($P = 0.033$), with no statistically significant differences in L1-L4 segmental FF between genders (all $P>0.05$). In the osteoporosis group, males had 22.4%-43.3% higher L1-L4 and total BMD, and 15.1%-21.7% higher FF than females (all $P<0.05$) (**Table 3**).

Comparison of BMD and FF values among different lumbar segments

The BMD of the lumbar vertebrae was ranked as L3 > L4 > L2 > L1 ($P<0.05$), with the highest BMD at L3 (1.11±0.18 g/cm^2), significantly higher than other segments. The FF was ranked as L4 > L3 > L2 > L1 ($P<0.05$), with the highest FF at L4 (52.72±11.01%), significantly higher than other segments (**Table 4**).

Correlation between osteoporosis and BMD/FF values

Kendall's correlation analysis showed that L1-L4 segment and total BMD were significantly negatively correlated with the occurrence of osteoporosis (r = -0.587 to -0.790, all $P<0.001$),

Table 2. Comparison of BMD and FF values among the three groups [$\bar{x}\pm s$]

Indicator	Category	Control Group (n = 43)	Osteopenia Group (n = 26)	Osteoporosis Group (n = 31)	*F*	*P*
BMD (g/cm^2)	L1	0.97±0.12	0.86±0.07^a	0.76±0.09^{a,b}	40.708	<0.001
	L2	1.06±0.12	0.92±0.06^a	0.81±0.06^{a,b}	73.881	<0.001
	L3	1.26±0.11	1.11±0.08^a	0.89±0.05^{a,b}	156.635	<0.001
	L4	1.17±0.09	1.00±0.07^a	0.83±0.04^{a,b}	201.866	<0.001
	Total	1.12±0.09	0.97±0.06^a	0.82±0.05^{a,b}	162.340	<0.001
FF value (%)	L1	35.80±9.32	40.66±13.05^a	48.47±8.20^{a,b}	14.155	<0.001
	L2	38.82±8.42	45.14±11.60^a	53.12±8.03^{a,b}	21.598	<0.001
	L3	42.27±8.11	49.05±9.25^a	56.83±8.68^{a,b}	25.927	<0.001
	L4	45.73±8.01	53.79±9.61^a	61.53±9.07^{a,b}	29.456	<0.001
	Total	40.66±7.48	47.16±9.55^a	54.99±7.18^{a,b}	29.099	<0.001

Note: BMD: Bone Mineral Density; FF: Fat Fraction. ^{a}*P*<0.05 vs. Control Group; ^{b}*P*<0.05 vs. Osteopenia Group.

Table 3. Comparison of BMD and FF values between genders [$\bar{x}\pm s$]

Subgroup	Indicator	Female	Male	*t*	*P*
Control Group (n = 43)	L1 BMD	0.90±0.11	0.97±0.07	-2.446	0.019
	L2 BMD	1.05±0.11	1.13±0.14	-2.097	0.042
	L3 BMD	1.18±0.10	1.14±0.12	1.192	0.240
	L4 BMD	1.06±0.09	1.15±0.09	-3.271	0.002
	Total BMD	1.04±0.10	1.13±0.11	-2.810	0.008
	L1 FF	32.53±10.35	37.46±9.15	-1.643	0.108
	L2 FF	37.56±9.65	39.37±10.22	-0.597	0.554
	L3 FF	41.23±8.63	42.89±9.03	-0.616	0.541
	L4 FF	44.86±8.66	46.63±8.43	-0.677	0.502
	Total FF	39.43±7.32	44.53±7.72	-2.222	0.032
Osteopenia Group (n = 26)	L1 BMD	0.82±0.06	0.88±0.08	-2.089	0.047
	L2 BMD	0.90±0.07	0.95±0.05	-2.129	0.044
	L3 BMD	1.06±0.09	1.14±0.10	-2.100	0.046
	L4 BMD	0.97±0.07	1.04±0.09	-2.144	0.042
	Total BMD	0.93±0.06	1.12±0.12	-4.811	<0.001
	L1 FF	38.67±10.56	41.65±10.25	-0.723	0.477
	L2 FF	45.54±9.67	45.02±10.04	0.132	0.896
	L3 FF	48.76±10.37	49.67±9.96	-0.226	0.823
	L4 FF	53.97±9.78	53.32±9.35	0.172	0.865
	Total FF	42.25±9.65	50.74±9.27	-2.268	0.033
Osteoporosis Group (n = 31)	L1 BMD	0.67±0.07	0.82±0.05	-6.854	<0.001
	L2 BMD	0.74±0.09	0.88±0.06	-5.155	<0.001
	L3 BMD	0.83±0.08	0.92±0.05	-4.273	<0.001
	L4 BMD	0.79±0.07	0.85±0.06	-2.468	0.020
	Total BMD	0.79±0.06	0.86±0.07	-2.717	0.011
	L1 FF	46.34±8.54	53.35±8.82	-2.098	0.046
	L2 FF	49.26±9.78	57.51±10.36	-2.109	0.044
	L3 FF	52.21±10.43	60.61±10.25	-2.121	0.043
	L4 FF	57.65±9.62	65.42±9.34	-2.145	0.040
	Total FF	50.27±8.76	58.23±9.34	-2.261	0.031

Note: BMD: Bone Mineral Density; FF: Fat Fraction.

Table 4. Comparison of BMD and FF values among different lumbar segments [$\bar{x}\pm s$]

Segment	BMD (g/cm^2)	FF value
L1	0.88±0.14	40.99±11.38
L2	0.95±0.14^c	44.90±10.99^c
L3	1.11±0.18^{c,d}	48.55±10.54^{c,d}
L4	1.02±0.16^{c,d,e}	52.72±11.01^{c,d,e}
F	39.020	20.856
P	<0.001	<0.001

Note: BMD: Bone Mineral Density; FF: Fat Fraction. ^{c}*P*<0.05 vs. L1 segment; ^{d}*P*<0.05 vs. L2 segment; ^{e}*P*<0.05 vs. L3 segment.

with total BMD showing the strongest correlation (r = -0.790); L1-L4 segment and total FF values were significantly positively correlated with the occurrence of osteoporosis (r = 0.387 to 0.506, all *P*<0.001), with total FF showing the strongest correlation (r = 0.506) (**Table 5**).

Correlation between BMD and FF values

Pearson correlation analysis revealed that except for the weak and statistically insignificant correlation between L1 FF and L1 BMD (r = -0.180, *P* = 0.072), a strong negative correlation between the FF of each lumbar vertebra (L1-L4) and the overall lumbar spine and its corresponding BMD measurement (all *P*<0.05) (**Table 6**).

Gender-specific correlation between BMD and FF values

Pearson correlation analysis showed that in both male and female patients, lumbar spine segment and total FF values were significantly negatively correlated with their corresponding BMD measurements (all *P*<0.001). Stratified analysis by gender showed that in female patients, the strongest negative correlation between total BMD and L2 BMD was observed (r = -0.525, *P*<0.001), while in male patients, the strongest negative correlation was observed between total BMD and lumbar BMD (r = -0.499, *P*<0.001). Notably, the correlation strength was generally higher in female patients than in male patients (**Tables 7** and **8**).

Gender-specific correlation between osteoporosis and FF values

Pearson correlation analysis showed that in both male and female patients, osteoporosis was positively correlated with L1, L2, L3, L4, and total FF values, with the correlation strength being greater in females than in males (*P*<0.001) (**Table 9**).

Value of FF in evaluating the severity of osteoporosis

ROC curve analysis showed that the AUCs of L1, L2, L3, L4, and total FF values for evaluating osteoporosis were 0.734, 0.821, 0.829, 0.823 and 0.856, respectively; the sensitivities were 74.19%, 90.32%, 90.32%, 87.10% and 77.42%, respectively; the specificities were 69.57%, 69.57%, 65.22%, 72.46% and 81.16%, respectively. Overall, the total FF value had the best performance in evaluating osteoporosis (**Table 10** and **Figure 4**).

Discussion

T2DM is a chronic metabolic disease characterized by impaired insulin action and insufficient insulin secretion, which may lead to persistent hyperglycemia. Typical clinical manifestations include polyuria, polydipsia, polyphagia, weight loss, fatigue, and visual impairment. Epidemiological data consistently show that patients with T2DM have a significantly increased risk of osteoporosis, with a reported prevalence of 20% to 60% [13]. Osteoporosis may cause serious consequences such as fractures, which seriously affects the quality of life of patients. For these patients, early detection and intervention of osteoporosis can effectively prevent the occurrence of adverse events such as fractures, thereby improving the quality of life of patients. Magnetic resonance q-Dixon (fat quantification) technology is a fat quantification technology based on MRI, which can accurately measure the content and distribution of fat in the body through specific sequences and algorithms [5]. This technique has certain application prospects in assessing the severity of lumbar osteoporosis in patients with T2DM. The q-Dixon technique provides a non-invasive and accurate way to measure fat content in the lumbar spine region, indirectly assessing the degree of osteoporosis. This is significant for disease monitoring, treatment planning, and efficacy evaluation.

L1-L4 is an internationally recognized "standard area" for BMD measurement. This area has a clear anatomical structure and well-

Table 5. Correlation between osteoporosis and BMD/FF values

Kendall Correlation		L1 BMD	L2 BMD	L3 BMD	L4 BMD	Total BMD	L1 FF	L2 FF	L3 FF	L4 FF	Total FF
Osteoporosis	*R*	-0.587	-0.701	-0.742	-0.774	-0.790	0.387	0.448	0.474	0.494	0.506
	P	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001

Note: BMD: Bone Mineral Density; FF: Fat Fraction.

Table 6. Correlation between BMD and FF values

Pearson Correlation		L1 BMD	L2 BMD	L3 BMD	L4 BMD	Total BMD
L1 FF	*R*	-0.180	-0.291	-0.246	-0.212	-0.308
	P	0.072	0.003	0.014	0.034	0.002
L2 FF	*R*	-0.367	-0.455	-0.449	-0.519	-0.476
	P	<0.001	<0.001	<0.001	<0.001	<0.001
L3 FF	*R*	-0.334	-0.519	-0.490	-0.523	-0.520
	P	<0.001	<0.001	<0.001	<0.001	<0.001
L4 FF	*R*	-0.365	-0.505	-0.562	-0.559	-0.531
	P	<0.001	<0.001	<0.001	<0.001	<0.001
Total FF	*R*	-0.332	-0.515	-0.492	-0.562	-0.533
	P	<0.001	<0.001	<0.001	<0.001	<0.001

Note: BMD: Bone Mineral Density; FF: Fat Fraction.

Table 7. Correlation between BMD and FF values in males

Pearson Correlation		L1 BMD	L2 BMD	L3 BMD	L4 BMD	Total BMD
L1 FF	*R*	-0.288	-0.313	-0.379	-0.353	-0.454
	P	0.058	0.039	0.011	0.019	0.002
L2 FF	*R*	-0.220	-0.346	-0.349	-0.263	-0.346
	P	0.152	0.021	0.020	0.085	0.021
L3 FF	*R*	-0.281	-0.516	-0.397	-0.468	-0.371
	P	0.065	<0.001	0.008	0.001	0.013
L4 FF	*R*	-0.384	-0.575	-0.411	-0.489	-0.328
	P	0.010	<0.001	0.006	<0.001	0.030
Total FF	*R*	-0.290	-0.272	-0.442	-0.459	-0.499
	P	0.056	0.074	0.003	0.002	<0.001

Note: BMD: Bone Mineral Density; FF: Fat Fraction.

defined boundaries, and is highly reproducible in imaging examinations such as dual-energy DXA and MRI, thus becoming the main observation target for most bone metabolism studies. Accordingly, this study selected the L1-L4 segment of the lumbar spine as the core observation area. The primary finding of this study demonstrated that as bone loss progresses, the BMD of each segment (L1-L4) and the overall lumbar spine shows a significant decreasing trend, while the corresponding FF shows a significant increasing trend. Specifically, compared with the osteopenia group and the control group, the BMD values of all measurement sites in the osteoporosis group were significantly lower, and the BMD of the osteopenia group was also lower than that of the control group. Conversely, the FF of the osteoporosis group was significantly higher than that of the other groups, and the FF of the osteopenia group was also higher than that of the control group. These results further verify that there is an inverse relationship between BMD and bone marrow fat content during the development of osteoporosis. Previous studies have also found similar findings. Li et al. confirmed that FF was negatively correlated with lumbar spine BMD and pointed out that the bone marrow fat content of

Table 8. Correlation between BMD and FF values in females

Pearson Correlation		L1 BMD	L2 BMD	L3 BMD	L4 BMD	Total BMD
L1 FF	*R*	-0.463	-0.417	-0.453	-0.511	-0.465
	P	<0.001	<0.001	<0.001	<0.001	<0.001
L2 FF	*R*	-0.459	-0.388	-0.256	-0.408	-0.388
	P	<0.001	0.003	0.057	0.002	0.003
L3 FF	*R*	-0.325	-0.335	-0.373	-0.418	-0.436
	P	0.014	0.012	0.005	0.001	<0.001
L4 FF	*R*	-0.243	-0.449	-0.410	-0.612	-0.421
	P	0.071	<0.001	0.002	<0.001	0.001
Total FF	*R*	-0.422	-0.525	-0.300	-0.475	-0.389
	P	0.001	<0.001	0.025	<0.001	0.003

Note: BMD: Bone Mineral Density; FF: Fat Fraction.

Table 9. Gender-specific correlation between osteoporosis and FF values

Gender		L1 FF		L2 FF		L3 FF		L4 FF		Total FF	
		Male	Female	Male	Female	Male	Female	Male	Female	Male	Female
Osteoporosis	*R*	0.497	0.587	0.271	0.560	0.455	0.497	0.466	0.637	0.479	0.562
	P	<0.001	<0.001	0.076	<0.001	0.002	<0.001	0.001	<0.001	<0.001	<0.001

Note: FF: Fat Fraction.

Table 10. Value of FF values in evaluating the severity of osteoporosis

Variable	B	SE	AUC	Sensitivity	Specificity	95% *CI*	Youden Index	Cut-off Value	*P**
L1 FF	8.3355	1.4971	0.734	74.19%	69.57%	0.634-0.835	0.438	44.61	0.0340
L2 FF	8.1627	1.4661	0.821	90.32%	69.57%	0.735-0.907	0.599	43.75	0.5244
L3 FF	8.8235	1.5847	0.829	90.32%	65.22%	0.747-0.911	0.555	47.52	0.6354
L4 FF	9.2199	1.6559	0.823	87.10%	72.46%	0.738-0.907	0.596	54.31	0.5849
Total FF	7.2987	1.3109	0.856	77.42%	81.16%	0.779-0.934	0.586	50.83	-

Note: *P** is the comparison with the AUC of total FF.

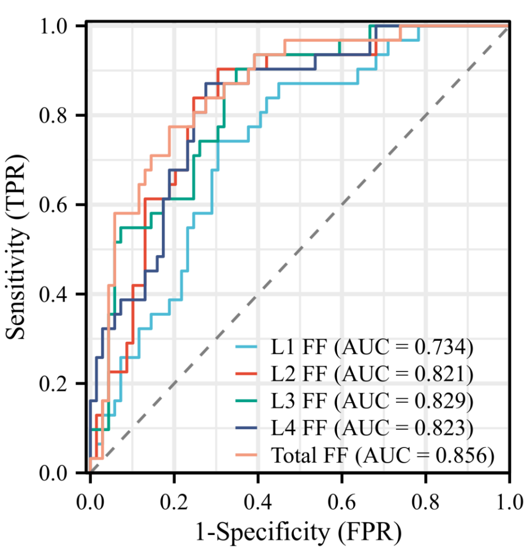


Figure 4. ROC curves of FF values for evaluating the severity of osteoporosis

patients with osteopenia and osteoporosis was significantly higher than that of people with normal bone mass [14]. A retrospective study by Chang et al. reported that the FFs in the control group, osteopenia group, and osteoporosis group were 30.1±6.2%, 52.6±7.6%, and 77.5± 7.9%, respectively, with significant differences between and within groups [15], which is consistent with our findings. From a pathophysiological perspective, osteoporosis is characterized by bone metabolism disorder, with osteoclasts absorbing more bone than osteoblasts forming bone, resulting in a decrease in bone mineral content per unit volume, which in turn leads to a decrease in BMD [16]. Increased bone marrow adipose infiltration signifies a change in the differentiation fate of bone marrow mesenchymal stem cells (BMSCs). In particular, insulin resistance promotes the differentiation of bone marrow mesenchymal stem cells into adipocytes by downregulating the Wnt/β-catenin signaling pathway, while inhibiting their differentiation into osteoblasts [17]. On the other hand, the increase in T2DM-related inflammatory factors (TNF-α, IL-6) activates the nuclear factor-κB receptor activator ligand (RANKL) pathway, accelerates osteoclast proliferation, and promotes adipocyte secretion of leptin and adiponectin, further exacerbating bone metabolism imbalance [18]. The above mechanisms together lead to increased lumbar spine fat fraction and decreased bone mineral density in T2DM patients, forming a vicious cycle of "bone loss-fat increase" [19, 20]. The differences in various indicators among T2DM patients with different bone mass grades in this study precisely reflect the manifestation of this pathological process at different stages, providing clinical data support for the "fat-bone axis" regulation mechanism of T2DM complicated with osteoporosis.

This study is the first to systematically analyze the moderating role of gender in the correlation between BMD and vertebral FF value in T2DM patients. The results showed that in the control group, osteopenia group and osteoporosis group, the BMD at each lumbar segment (except for L3 vertebral BMD in the control group, P = 0.240), total lumbar BMD and FF were significantly higher in men than in women. It is worth noting that the negative correlation between BMD and FF values is significantly stronger in women than in men. Specifically, Pearson's correlation analysis showed that the correlation coefficient between vertebral FF and BMD in women was between -0.300 and -0.612, which was significantly higher than that in men between -0.263 and -0.575. Similarly, the positive correlation between osteoporosis and FF value was more pronounced in women (r = 0.497 to 0.637), compared with men (r = 0.271 to 0.497), which is consistent with previous studies [21]. This phenomenon is closely related to sex-specific physiological hormonal regulation. After menopause, women experience a sharp decline in estrogen levels, which not only directly accelerates bone resorption and reduces BMD but also promotes abdominal and bone marrow fat accumulation by affecting fat metabolism, leading to an increased FF. Therefore, in the osteoporosis stage, where bone loss is more significant, women exhibit more pronounced abnormalities in BMD and FF, and the differences from men are more comprehensive [22, 23]. Studies using estrogen to inhibit bone marrow fat accumulation in the treatment of osteoporosis have also confirmed this view [24]. In contrast, men are protected by androgens in adulthood, resulting in relatively stable bone metabolism. Only when bone mass is normal or mildly abnormal does the sex difference in BMD and FF manifest as segmental differences (such as L1 and L4) [25]. This also explains why, in clinical practice, the incidence and severity of osteoporosis in female T2DM patients are generally higher than in male patients. From the perspective of lumbar segment specificity, this study found that the L3 segment had the highest BMD (1.11±0.18 g/cm^2), significantly higher than the L4 (1.02±0.16 g/cm^2), L2 (0.95±0.14 g/cm^2), and L1 (0.88±0.14 g/cm^2) segments; while the FF values showed a gradient distribution of L4 (52.72±11.01%) > L3 (48.55±10.54%) > L2 (44.90±10.99%) > L1 (40.99±11.38%). This regularity is closely related to the biomechanical characteristics and anatomical structure of the lumbar spine: L3 is located at the apex of the lumbar lordosis and is the main weight-bearing segment for vertical trunk load. Mechanical stress stimulation of T2DM patients partially counteracts the inhibitory effect of insulin resistance on osteoblasts through the integrin αvβ3 pathway, promotes osteoblast activity, and increases bone mineral deposition, thus resulting in the highest BMD [26]. In contrast, the L4 segment, which is adjacent to the sacrum, has a larger vertebral endplate area and is affected by lumbosacral movement, resulting in slower local microcirculation blood flow. Under the metabolic disorder caused by insulin resistance in T2DM patients, local hypoxia is further aggravated, promoting the infiltration and accumulation of adipocytes in this area (hypoxia-inducible factor 1α upregulates the expression of peroxisome proliferator-activated receptor γ), leading to the highest FF [27]. The effect coefficient of insulin resistance on fat infiltration in the L4 segment was significantly higher than that in the L3 segment, confirming this segment-specific effect. This finding has important implications for clinical assessment. When using q-Dixon technique to evaluate lumbar osteoporosis in T2DM patients, combined analysis of the L3 (best representative of BMD) and L4 (highest sensitivity of FF value) segments can improve the accuracy and reliability of the assessment and avoid bias caused by single-segment measurements.

Correlation analysis further revealed the intrinsic association between BMD, FF and osteoporosis: Kendall correlation analysis showed that the total bone mineral density of each vertebra and the total BMD of the L1-L4 lumbar vertebrae were significantly negatively correlated with the risk of osteoporosis (r = -0.587 to -0.790), while the values of each segment and the total FF were significantly positively correlated with the risk of osteoporosis (r = 0.387 to 0.506); Pearson correlation analysis showed that FF values of each segment were significantly negatively correlated with BMD at corresponding site (r = -0.180 to -0.612), and the correlation strength of female patients was generally higher than that of male patients. Wang et al. used IDEAL-IQ technology to analyze the relationship between FF and BMD, reporting a negative correlation (r = -0.66) [28]. In another study, Naik et al. used Dixon technique to investigate the correlation between vertebral bone marrow FF and DXA-measured BMD in 31 patients suspected of osteoporosis, and also found that fat fraction was negatively correlated with BMD [29]. Mechanistically, as the core diagnostic indicator of osteoporosis, the decrease in BMD directly reflects the decline in bone strength, and is therefore negatively correlated with the risk of osteoporosis [8]. An increase in FF value is essentially a sign of the deterioration of the bone marrow microenvironment: inflammatory factors secreted by adipocytes activate the nuclear factor κB receptor activator ligand signaling pathway, promote the differentiation and maturation of osteoclasts, and inhibit the function of osteoblasts, leading to a further decrease in BMD [30, 31]. In terms of gender differences, estrogen deficiency in postmenopausal women not only enhances osteoclast activity, but also promotes the differentiation of bone marrow mesenchymal stem cells into adipocytes by upregulating the expression of peroxisome proliferator-activated receptor γ, making the correlation between FF value and BMD more intense and stronger [32]. In contrast, androgens in men can buffer the negative impact of FF value on BMD to a certain extent by inhibiting adipogenic differentiation and promoting osteogenic differentiation, thus the correlation is relatively weak [33]. This result suggests that gender differences should be fully considered when formulating intervention strategies for T2DM complicated with osteoporosis: female patients should pay attention to bone marrow fat infiltration earlier, while male patients need to balance BMD monitoring and metabolic index control.

Through ROC curve analysis, this study was the first to confirm that vertebral FF value has good value in assessing the severity of osteoporosis in T2DM patients. Among them, the total FF value had the best evaluation efficiency (AUC = 0.856, 95% *CI*: 0.779-0.934), with a cut-off value of 50.83, a sensitivity of 77.42%, a specificity of 81.16%, and a Youden index of 0.586. In contrast, the AUC values of the L1-L4 segments were 0.734, 0.821, 0.829, and 0.823, respectively, all lower than the total FF value. The clinical application value of this study is mainly reflected in three aspects: ① Screening stage: In routine physical examinations of patients with T2DM, a total FF in the lumbar spine greater than 50.83% indicates a high risk of osteoporosis, requiring further diagnosis via dual-energy DXA. ② Auxiliary diagnosis: When DXA results are uncertain (e.g., a T-value close to -2.5), the total FF value can serve as a supplementary diagnostic indicator to help clarify the diagnosis; ③ Risk stratification: Patients with a total FF >50.83% and who are postmenopausal/aged ≥ 60 years should be classified as high-risk for fractures and require enhanced intervention measures. The Kappa value of this threshold, consistent with the diagnostic criteria of DXA, is 0.72, indicating that it can be used as a non-invasive supplementary examination method to DXA. Meanwhile, the results of this study indicate that a comprehensive assessment of the fat content of each lumbar segment can more fully reflect the degree of bone marrow fat infiltration, thereby more accurately assessing the risk of osteoporosis. A study by Zhang et al. used q-Dixon technology to predict the lumbar FF values in 45 elderly patients with osteoporosis. The results showed that the average lumbar FF value had an AUC of 0.822, sensitivity of 73.3%, specificity of 86.7%, and a cut-off value of 57.27%, which is similar to the diagnostic efficacy of this study [7]. Compared with the traditional DXA for BMD measurement, q-Dixon technique can not only provide an indicator reflecting the bone marrow metabolic status-fat score, but also assess indirect information related to bone mineral density at the same time, and there is no risk of radiation exposure, making it more suitable for long-term follow-up monitoring of T2DM patients [29, 34]. From a clinical application perspective, the total FF value integrates information from the L1-L4 segments and can more comprehensively reflect the degree of bone marrow fat infiltration in the lumbar spine, thus achieving the highest diagnostic accuracy. The L2 and L3 FF values with high sensitivity (90.32%) are suitable as screening indicators for osteoporosis and can effectively identify high-risk patients. The L4 FF value with high specificity (72.46%) can be used in the diagnostic stage to reduce false positive diagnoses. In addition, the AUC of the total FF value (0.856) is similar to the results of Cheng et al. using the IDEAL-IQ technique (AUC = 0.691-0.797), which further verifies the reliability of the magnetic resonance fat quantification technique in osteoporosis assessment [35]. Moreover, q-Dixon technique has the advantages of short scanning time and simple post-processing, making it easier to promote and apply in clinical practice.

Limitations

This study has the following limitations. First, the sample size was only 100 cases, and it was a single-center retrospective study, which may have selection bias. Future multi-center, large-sample prospective studies are needed to further validate the conclusions. Second, patients with T2DM combined with other complications (such as diabetic retinopathy) were not included, which may limit the extrapolation of the conclusions; Third, long-term follow-up was not conducted to assess the longitudinal association between FF values and fracture occurrence. Future prospective studies are required to validate the predictive value of FF values. Last, the association between FF value and bone metabolism markers (such as alkaline phosphatase and β-CTX) was not explored. Further analysis can be conducted to improve the mechanism.

Conclusion

q-Dixon MRI technology can effectively measure lumbar spine FF values in T2DM patients with different bone mineral density levels. FF value is closely related to BMD and the occurrence of osteoporosis, and can effectively assess the severity of lumbar spine osteoporosis. Among the various parameters, the total FF value (cut-off = 50.83%) showed the best assessment efficacy, while the L3 segment BMD and L4 segment FF values were more representative. Gender differences affected these indicators and their correlations, with stronger correlations observed in women. This technology can provide a reliable basis for the early screening, diagnosis, and risk stratification of T2DM-related lumbar osteoporosis, and has significant clinical application value. The core innovations of this study are reflected in three aspects. First, it reveals for the first time the segmental heterogeneity of lumbar BMD/FF values in T2DM patients: the L3 vertebral body has the highest BMD due to bearing the greatest weight, while the L4 vertebral body has the most significant fatty infiltration and the highest FF value due to its microcirculatory characteristics, providing a basis for clinical selection of key observation segments. Second, it elucidates the impact of gender differences on bone metabolism in T2DM patients: the women have a stronger correlation between BMD and FF value, which is closely related to the imbalance of bone and fat metabolism mediated by estrogen deficiency after menopause, providing theoretical support for gender-specific interventions. Third, it establishes the total FF value (cut-off = 50.83%) as a non-invasive indicator for assessing the severity of osteoporosis in patients with type 2 diabetes, with an AUC of 0.856, which is superior to segmental FF value, filling the gap in previous studies that did not establish a cutoff standard for FF value in the T2DM patients.

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Disclosure of conflict of interest

None.

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