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Evaluation of bone mineral density and trabecular bone score for diagnosis of osteoporosis in Iranian diabetic patients

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Abstract

Introduction: Type 2 diabetes mellitus (T2DM) increases the risk of bone fractures.
Objectives: This study aimed to examine the use of trabecular bone score (TBS) and BMD to select the best diagnostic tool for osteoporosis caused by type 2 diabetes.
Patients and Methods: One hundred and four patients (52 individuals with type 2 diabetes and 52 ones without diabetes) aged at most 50 years were enrolled in a cross-sectional study that was conducted with dual-energy X-ray absorptiometry (DXA) images of patients referred to Khorshid and Al-Zahra hospitals, Isfahan, Iran.
Results: Lumbosacral bone mineral density (BMD) was significantly lower in the diabetic group than in the control group (0.76 versus 0.82, $P=0.041$). The mean lumbosacral TBS was significantly lower in the diabetic group than in the controls (1.24 versus 1.36, $P=0.001$). Therefore, the lumbosacral TBS provided a more reliable indicator than lumbosacral BMD to discriminate between controls and women with T2DM.
Conclusion: The TBS is recommended for early diagnosis of osteoporosis in diabetic patients because of its independence from BMD-related parameters. The TBS can capture a larger portion of the bone deterioration in women with T2DM that cannot be detected using methods based solely on BMD.

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Introduction

Osteoporosis means systemic skeletal disorder that influences all populations and may bring about both direct and indirect expenses and consequences for the patients. The most common characteristic of osteoporosis is low bone mass and poor bone microarchitecture, which leads to a decrease in bone strength and increase in the risk of fracture (1). Osteoporosis is classified into primary and secondary types. The primary type is correlated with the aging process, and the secondary type is related to various underlying diseases, such as Cushing's disease, primary hyperparathyroidism, inflammatory arthritis and type 2 diabetes mellitus (T2DM). Most osteoporotic patients suffer from the secondary type of the disease (2,3).

Similarly, T2DM is a common chronic disease and a prominent health issue related to aging. Several studies have shown that T2DM significantly intensifies the risk of fractures at all skeletal sites even though the patients have a higher-than-normal or normal bone mineral density (BMD) (4). Alterations of the skeletal elements or microstructure due to T2DM may attenuate strength and bone turnover, resulting in an increased likelihood of fractures in patients with T2DM (5,6). Although BMD, which is determined by the dual-energy X-ray absorptiometry (DXA), is used mainly to predict fracture risk, 50% of people with a fragility fracture are reported as having normal or osteopenic BMD (7). Therefore, other parameters, including bone geometry, bone microarchitecture, and bone mineral turnover, are effective on bone strength and fracture risk as well (8,9).

Trabecular bone score (TBS) is used as an indirect indicator of trabecular microarchitecture determined using the DXA images of the lumbar spine. As a non-invasive and suitable method for patients with T2DM, TBS can provide information

Key point

Type 2 diabetes mellitus (T2DM) increases the risk of developing osteoporosis. Our study indicated that the trabecular bone score could represent a greater proportion of bone deterioration left undetected by BMD in women suffering from T2DM. Therefore, the trabecular bone score can be considered a reliable tool for early diagnosis of osteoporosis in these women.

that is independent of BMD. TBS includes data regarding bone quality on the basis of the DXA image pixel gray-level variations (10,11). Ample evidence shows that the lumbosacral TBS decreases in patients with T2DM compared to healthy individuals (12,13). TBS is calculated by the slope of the log-log transform of variograms calculated by the estimation of the 3D structure onto a 2D plane. TBS is correlated with bone microstructure, so that low TBS represents porosity in the microstructure (14). This score can comparably show a higher proportion of the diabetes-related risk of fracture compared to the BMD (13).

Objectives

Given the above-cited arguments and findings, the purpose of the study was to study the use of BMD and TBS in patients with T2DM and controls to predict skeletal deterioration for the early diagnosis of osteoporosis caused by T2DM. The secondary aim of the current study was to study thyroid-stimulating hormone (TSH), 25(OH) vitamin D, and parathyroid hormone (PTH) as biochemical indicators of osteoporosis status in the studied groups.

Patients and Methods

Study design

Fifty-two patients with a definite diagnosis of T2DM were included in this case-control study. The cases were selected from among the diabetic patients referred to the Khorshid and Al-Zahra hospitals in Isfahan, Iran for measurement of BMD. A total of 52 controls were selected from the non-diabetic patients who were referred to the hospitals with no history of non-specific musculoskeletal pains and diabetes in their families. Finally, a total of 104 patients including both male and female genders (52 patients with T2DM and 52 controls without diabetes) aged ≥50 years were included in the investigation.

Inclusion criteria were being at least 50 years old and having sufficient mental and physical ability to participate in the study. Informed written consent to participate in the study was obtained from all potential participants. The exclusion criterion was having a history of fractures or underlying diseases, including spondyloarthropathy, rheumatoid arthritis, systemic lupus erythematosus, vasculitis, hyperthyroidism, hypothyroidism, hyperparathyroidism, and renal failure.

A real BMD (g/cm^2) of the skeletal sites (femoral neck, lumbar spine, and total hip) was measured by means of the Hologic Discovery W DXA system (Hologic Inc., USA), and the results were interpreted as per the manufacturer's instructions. The lumbar spine anterior-posterior DXA images of participants were also applied to estimate TBS. The BMD precision error (percent coefficient of variation) for lumbar spine scans was 0.97%, and it was calculated at 1.8% and 1.7% for the femoral neck and total hip, respectively. L_{2-4} was included in data analysis if the L_{1-4} was not considered to be appropriate because of the severe sclerotic change or compression fracture.

To determine vitamin D status, serum vitamin D level was measured using the Elecsys vitamin D immunoassay (Roche Diagnostics, Mannheim, Germany) with a reference range of 2.0 (target range: 1.0-3.0) and 37.0 ng/mL (target range: 33.0-41.0). Intra-assay and inter-assay coefficients of variation CVs were calculated at 5.5% and 7%, respectively.

Serum PTH level was measured using the Elecsys PTH immunoassay (Roche Diagnostics, Mannheim, Germany) with a reference range of 1.6-6.9 pmol/L. Intra-assay and inter-assay CVs were calculated at 1.6% and 5.7%, respectively. Moreover, the mean age and gender frequency (percentage) were specified in the two groups. Mean menopause age was determined for the women in both groups. Body mass index (BMI) was calculated by dividing weight (kg) by height squared (m^2).

Statistical analysis

The Shapiro-Wilks normality test was applied to all variables. For non-normally distributed data (S-W<0.95), non-parametric statistics (independent *t* test/Mann-Whitney U test) were used. In this study, P value < 0.05 was considered to be statistically significant.

Results

Table 1 shows the descriptive data of our participants. The mean ± standard deviation (SD) age of the T2DM and control groups was 62.71 ± 5.34 and 60.53 ± 6.71 years, respectively. The percentage of women was 82.7% and 92.3% in the T2DM and control groups, respectively. BMI was 28.57 ± 4.01 and 28.16 ± 4.26 kg/m^2 in the T2DM and control groups, respectively.

The mean age of menopausal women in the T2DM and control groups was 47.55 ± 11.15 and 44.54 ± 17.25 years, respectively. Thus, the two groups were not significantly different with respect to age (P = 0.071), gender (P = 0.138), menopause age (P = 0.320), and BMI (P = 0.613). The oral intake of calcium and vitamin D in the two groups were not statistically significant as well (P > 0.05).

The mean level of HbA1c was 6.90 ± 0.83 in the T2DM group. 40.4% of diabetic patients used insulin, and 59.6% of them used an oral agent (metformin or glibenclamide) alone or either of the oral agents with insulin (Table 2).

No significant differences were found in the laboratory tests between the two studied groups. Serum calcium level, TSH level and serum vitamin D3 level between two groups were similar (P = 0.800, P = 0.294, P = 0.205, respectively). Furthermore, serum PTH level did not show any statistical differences between the two groups (P = 0.767). The mean values of hip BMD and lumbosacral BMD were significantly lower in patients with T2DM than in the controls (P = 0.027 for hip BMD and P = 0.041 for lumbosacral BMD).

The score of hip fracture risk calculated by the Fracture

Table 1. Comparison of clinical characteristics of diabetic patients and control group

Variable	Groups			*P* value
	Diabetes (n=52)	No diabetes (n=52)	Total (n=104)	
Gender (female)	43(82.7%)	48(92.3%)	91(87.5%)	0.138[a]
Calcium and vitamin D intake (yes)	45(86.5%)	37(71.2%)	82(78.8%)	0.055[a]
Age (year)	62.71±5.34	60.53±6.71	61.62±6.13	0.071[b]
Body mass index (kg/m^2)	28.57±4.01	28.16±4.26	28.37±4.12	0.613[b]
Menopause age (year)	47.55±11.15	44.54±17.24	45.96±14.68	0.320[b]
Calcium (mg/dl)	9.15±0.46	9.18±0.46	9.17±0.46	0.800[b]
Vitamin D (nmol/l)	36.45±14.43	33.48±8.50	34.97±11.88	0.205[b]
Thyroid-stimulating hormone (mU/L)	2.58±0.79	2.73±0.56	2.65±0.68	0.294[b]
Parathyroid hormone (pg/ml)	46.43±15.16	45.66±11.13	46.05±13.24	0.767[b]
Hip bone mineral density (g/cm^2)	0.64±0.09	0.68±0.11	0.66±0.10	0.027[b]
L_1-L_4 bone mineral density (g/cm^2)	0.76±0.11	0.82±0.14	0.79±0.13	0.041[b]
Hip FRAX	2.58±2.67	1.30±2.61	1.94±2.71	0.015[b]
FRAX for major osteoporotic fracture	7.37±5.03	4.20±4.29	5.79±4.29	0.001[b]
Hip T-score	-1.99±0.85	-1.54±0.96	-1.77±0.93	0.014[b]
Hip Z-score	-0.51±0.76	-0.22±1.08	-0.37±0.94	0.108[b]
L_1-L_4 trabecular bone score	1.24±0.05	1.36±0.07	1.30±0.08	<0.001[b]
Trabecular bone score-Z-score	-0.20±0.76	0.64±0.96	0.22±0.96	<0.001[b]
Trabecular bone score-T-score	-2.25±0.87	-0.91±0.74	-1.58±1.05	<0.001[b]
Trabecular bone score-bone mineral density	0.78±0.11	0.87±0.19	0.83±0.16	0.004[b]
Hip FRAX-trabecular bone score (%)	2.97±2.86	1.34±2.72	2.15±2.90	0.004[b]
FRAX for major osteoporotic fracture-trabecular bone score (%)	8.53±5.40	4.73±4.26	6.63±5.20	<0.001[b]
Lumbosacral T-score	-2.39±1.03	-1.70±1.27	-2.04±1.20	0.003[b]
Lumbosacral Z-score	-0.90±1.32	-0.41±1.27	-0.66±1.31	0.056[b]

Data are expressed as mean ± SD or frequency (%). FRAX, Fracture Risk Assessment Tool.
[a] Chi-square test, [b] Independent *t* test.

Risk Assessment Tool (FRAX) was significantly higher in the T2DM group than in the control group ($P \leq 0.015$). The FRAX score for major osteoporotic fracture (major FRAX) was significantly higher in the T2DM group than in the control group ($P \leq 0.001$). There were significant differences ($P = 0.014$) in the hip T-score between the T2DM patients and the control group. The lumbosacral T-score was significantly lower in the T2DM group. Moreover, L_1-L_4 TBS was significantly lower in the T2DM group ($P = 0.001$), revealing statistically significant differences in the TBS T-score and TBS Z-score compared to the control group.

Table 2. Quantity of hemoglobin A1C (HbA1c) and medications in diabetic patients

HbA1c (mean ± SD)		6.90±0.83
Medication, No. (%)	Insulin	21 (40.4%)
	Metformin	13 (25%)
	Glibenclamide	4 (7.7%)
	Glibenclamide + metformin	4 (7.7%)
	Insulin + metformin	6 (11.5%)
	Insulin + glibenclamide	4 (7.7%)

In addition, the FRAX score of hip TBS was significantly higher in the diabetic group than in the control group. Therefore, the major FRAX score of TBS was significantly higher in the T2DM group compared to the control group. The comparison of mean values of L_1-L_4 BMD and L_1-L_4 TBS in the T2DM and control groups showed that L_1-L_4 BMD and L_1-L_4 TBS were not significantly different between men, while the corresponding values were significantly lower in diabetic women than in female controls (Figure 1a and b).

In women, the mean values of L_1-L_4 TBS were higher than the mean values of L_1-L_4 BMD in both diabetic and non-diabetic individuals. In diabetic and non-diabetic groups, the standardized mean difference of L_1-L_4 TBS (1.45) was higher than the standardized mean difference of L_1-L_4 BMD (0.44) (Table 3).

Discussion

In this study, the use of TBS and BMD for the diagnosis of osteoporosis in diabetic patients was investigated. Available evidence shows that the fracture risk in two groups of diabetic men and women is higher than that in healthy

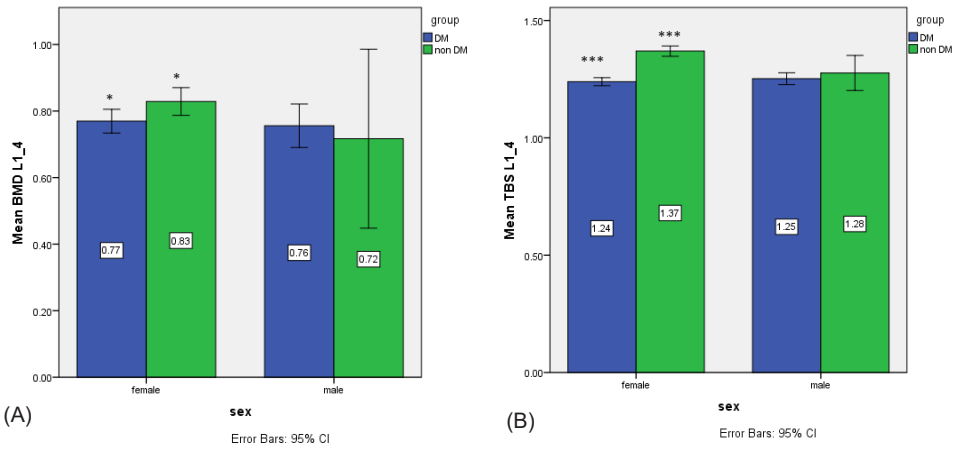

Figure1. The mean values of L_1-L_4 body mass index (BMD) and L_1-L_4 trabecular bone score (TBS) in diabetic and non-diabetic people; a) Mean values of L_1-L_4 BMD in people with type 2 diabetes mellitus (T2DM) and control group (non DM), (b) Mean values of L_1-L_4 TBS in people with T2DM and control group (non DM). * Significant differences at $P < 0.05$. *** Significant differences at $P < 0.01$.

individuals (15,16). However, the BMD measurement using DXA is paradoxically in the normal range or higher in patients with diabetes.

Our results showed significant differences in lumbosacral TBS and BMD between the two studied groups. The lower BMD in diabetic patients in our study can be attributed to nutritional status, inactivity, lifestyle, genetic features, and insufficient intake of dairy products. In women, the mean difference in L_1-L_4 TBS between case and control groups was higher than the corresponding mean difference in L_1-L_4 BMD. Therefore, TBS can serve as a better tool for measuring bone density in women with T2DM. In addition, our results revealed that the relationship between the BMD and TBS is similar to that of other previous studies suggesting that the relationship may depend on ethnicity (17,18).

In the current study, T2DM was associated with decreased BMD and lower lumbosacral TBS in the two studied groups. The lumbosacral TBS declined with increasing age so that it showed a significant, positive correlation with the lumbosacral BMD. Irrespective of diabetes status, more men and women have normal lumbosacral BMD rather than normal lumbosacral TBS. In women, the comparison of distribution percentages of lumbosacral TBS and lumbosacral BMD indicated that the lumbosacral TBS could discriminate between individuals with and without T2DM.

According to some studies, diabetic patients with all ranges of BMD are at a greater fracture risk (19,20). The mechanism of diabetes impact on the risk of fracture is potentially multifactorial. Extra-skeletal parameters, such as peripheral neuropathy and visual disturbance, may contribute substantially to increasing the fall risk (16). However, even after controlling for fall frequency, the fracture risk remains higher in diabetic patients than in the controls (21). According to our findings, the lumbosacral TBS was significantly lower in diabetic people, implying that diabetes may have an adverse impact on bone integrity. Low TBS can imply a weak bone strength that is not traceable using the DXA and may explain the high risk of fracture in diabetic people (22). In a cohort study performed in Canada, Leslie et al reported the lumbosacral TBS as a BMD-independent predictor of risk of fracture in older women with diabetes (13). Despite the fact that our data showed no increase in BMD scores in the diabetic group, we found that the TBS is an acceptable measure to assess fracture risk. The results of a study on Korean men and women showed high levels of blood glucose and HbA1c are associated with lower TBS (12).

This study was carried out on a relatively large number

Table 3. Comparison of standardized and non-standardized values (mean±SD) of L_1-L_4 bone mineral density and L_1-L_4 trabecular bone score between diabetic patients and control group

	Gender	Non-standardized values			Standardized values			
		Groups		Mean difference	Groups		Standardized mean difference	*P* value[a]
		Diabetic (n=52)	Non-diabetic (n=52)		Diabetic (n=52)	Non-diabetic (n=52)		
L_1-L_4 bone mineral density	Female	0.76±0.11	0.82±0.14	0.059	-0.18±0.87	0.26±1.08	0.44	0.035
	Male	0.75±0.08	0.71±0.16	0.039	-0.28±0.62	0.58±1.29	-0.29	0.580
L_1-L_4 trabecular bone score	Female	1.23±0.05	1.36±0.07	0.130	-0.69±0.62	0.75±0.84	1.45	<0.001
	Male	1.25±0.03	1.27±0.04	0.024	-0.54±0.37	0.27±0.51	0.26	0.300

[a] Independent *t* test.

of patients with T2DM despite some limitations such as lack of determination of the duration of diabetes in these patients, which may be important factors for increased risk of fracture. However, other diabetes-related complications and nutritional and pharmaceutical parameters should be taken into account in additional studies.

Conclusion

In this article, BMD and TBS were investigated in diabetic patients and a control group. In addition, the TSH, and PTH levels vitamin D, were studied in the two groups. Because of osteoporosis is very common in diabetic patients, early diagnosis of osteoporosis plays a prominent part in preventing the complications of the disease. Lumbosacral TBS, as a BMD-independent variable, can be used to detect the microstructural skeletal deterioration in diabetic patients. Here, BMD and TBS were lower in diabetic women than in non-diabetic ones. Based on the results of this study, the TBS is a better indicator than BMD to diagnose osteoporosis in diabetic women. The use of TBS to detect the changes in bone microarchitecture may greatly assist in the clinical management and treatment of osteoporosis.

Limitations of the study

Small sample size and the lack of a more detailed investigation of all factors related to diabetes and osteoporosis are among the limitations of the present investigation.

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Authors' contribution

Conceptualization: MM.
Methodology: BP.
Validation: SAS.
Formal analysis: HK.
Investigation: HK.
Resources: MS.
Data curation: SAS.
Writing—original draft preparation; MM.
Writing—review and editing: MS.
Visualization: BP.
Supervision: MS.
Project administration: MS.
Funding acquisition: MM.

Conflicts of interest

The authors declare that they have no competing interests.

Ethical issues

The research followed the tenets of the Declaration of Helsinki. The Ethics Committee of Isfahan University of Medical Sciences approved this study (Ethical thesis#IR.MUI.MED.REC.1398.617). Accordingly, written informed consent was taken from all participants before any intervention. This study was extracted from rheumatology subspecialty thesis of Shahin Asgari Savadjani at this university (Thesis#398830). Besides, ethical issues (including plagiarism, data fabrication and double publication) have been completely observed by the authors.

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