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Fracture Risk Assessment Using Trabecular Bone Score in Postmenopausal Women with Type 2 Diabetes Having Vertebral Fractures

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ABSTRACT

Background: The most frequent type of osteoporotic fractures is vertebral fractures (VFs), and identifying them is crucial for the diagnosis of osteoporosis as well as for future fracture risk assessment and treatment options

Aim of the work: This study aimed to determine the utility of trabecular bone score (TBS) in post-menopausal type 2 diabetic patients with vertebral fractures (VFs) and the relationship of TBS with bone mineral density (BMD) and fracture risk assessment (FRAX) score.

Methods: This case-control study included a total number of 100 postmenopausal women patients from Endocrinology Clinics and Mansoura Specialized Hospital. They were divided into 4 groups: 25 postmenopausal women with T2DM and VFs, 25 postmenopausal women with T2DM without VFS, 25 postmenopausal women without T2DM with VFS and 25 postmenopausal women without T2DM without VFS. The study's period was from November 2020 to February 2022.

Results: A statistically significant difference in all studied parameters between the 4 groups except body weight. In the two DM groups' age, menopausal length, HbA1c, FRAX-MOPF (percent), and FRAX-HF (percent) values were statistically greater than those of the two non-DM groups. Also, TBS T-score was statistically significantly lower in the DM/VF group vs. non-DM/non-VF group. BMD T-score was lesser in DM/VF group vs. the two non-DM groups,

Conclusion: This study demonstrated that there are many factors contributing to the prevalence of vertebral fractures. These factors include duration of diabetes, poor diabetic control, BMI, drugs taken, BMD, and duration of menopause.

Key words: Vertebral fractures, Trabecular bone score, Postmenopausal, Fracture risk assessment, Diabetes mellitus type 2.

INTRODUCTION

Diabetes mellitus type 2 (T2DM) is a prevalent metabolic condition, whose prevalence increases with age. Despite having greater bone mineral density (BMD) readings, T2DM patients have an increased risk of fracture [(1)]. These have been linked to a variety of circumstances, including the types of medications taken, the existence of T2DM complications, and the length of the condition [(2)].

When compared to control participants, T2D patients may have greater BMD and lower mean FRAX scores despite having a higher risk of fracture [(3)]. As a result, the Fracture Risk Algorithm (FRAX), which measures other elements rather than BMD including (age, bone mineralization, bone micro-damage, bone turnover, and fracture history), helps to determine the overall evaluation of fracture risk [(4)].

The most frequent type of osteoporotic fractures is vertebral fractures (VFs), and identifying them is crucial for the diagnosis of osteoporosis as well as for future fracture risk assessment and treatment options [(5)]. They are very often asymptomatic, and there is evidence that they are greatly underdiagnosed worldwide [(6)].

Simple arithmetic operations have been used to modify the probability assessment of standard FRAX estimations of fracture probabilities in order to get around some of the limitations of FRAX (For instance, details on the trabecular bone score (TBS), the hip structural analysis (HSA), simultaneous information on the BMD of the lumbar spine, and high, moderate, and low exposure to glucocorticoids) [(7)].

TBS is a low-cost approach of assessing bone quality that may be estimated immediately from a lumbar spine dual X-ray absorptiometry (DEXA) study without subjecting patients to more radiation. However, there are few studies on TBS's ability to predict vertebral fracture (VF) in people with diabetes mellitus [(8)].

PATIENTS AND METHODS

This case-control study included a total number of 100 postmenopausal women patients who were divided into 4 groups. 25 postmenopausal women with T2DM and VFs, 25 postmenopausal women with T2DM without VFS, 25 postmenopausal women without T2DM with VFS and 25 postmenopausal women without T2DM without VFS. This study recruited 215 participants from Endocrinology Clinics and Mansoura Specialized Hospital. Then, cases were selected based on inclusion and exclusion criteria so that at the end 100 participants (25 in each group) were enrolled in the study. The study's period was from November 2020 to February 2022. The extracted information included sociodemographic, clinical, and laboratory data.

Inclusion criteria: All patients were postmenopausal women.

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Exclusion criteria: Diabetic patients of type 1. Individuals receiving insulin therapy, treated with anti-osteoporotic drugs, having cognitive problems, a physical impairment, consuming glucocorticoids, calcium supplements, thiazolidinone and thyroid hormone, or vitamin D. People who had Cushing's syndrome, hyperparathyroidism and hypoparathyroidism. Weight-loss surgery with a potential for subsequent osteoporosis. Patients who had more than three layers of lumbar metallic implants due to hip arthroplasties and also patients with diabetic complications (retinopathy, nephropathy, neuropathy....etc.).

All patients were subjected to the following:
History taking: Previous bone fractures, history of drug intake, history of any other chronic diseases, onset of diabetes and onset of menopause.

Clinical examination: General and routine examination, vital signs, body mass index, body weight.
Laboratory: HbA1c.

Radiological examination: DEXA scan (dual energy x-ray absorptiometry) on both hip joints and vertebrae using trabecular bone score (TBS), lateral lumbar spine radiographs and TBS adjusted FRAX algorithm.

DEXA scan:

DEXA of the lumbar spine and proximal femur for BMD and TBS examinations were carried out by GE-Lunar prodigy pro version (#5022017), TBS version 3.0.2.0.

T-scores are calculated by taking the difference between a patient's measured BMD and the mean BMD in healthy young adults, matched for gender and ethnic group, and then divided by the standard deviation (SD) of the reference population. WHO definitions for osteoporosis and osteopenia for women used: normal T-score at or above -.1, osteopenia T-score between -.1 and -2.5 SD, osteoporosis T-score at or below -2.5.

All tested women have been subjected to DXA to measure their bone densitometry of the lumbar spine, and hip at technique that is useful for measuring the BMD from their data, the risk of fracture was later estimated.

As Egypt has not yet developed the own version of country specific calculation tool, the present study used the available calculation tool of Jordan as the nearest country for the FRAX risk score calculation.

Ethical Approval:

The study was approved by the Ethics Board of Mansoura University and an informed written consent was taken from each participant in the study. This work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Statistical analysis

Data were entered and examined by SPSS program (Armonk, NY: IBM Corp., IBM SPSS Statistics for Windows) version 26.0. Regarding qualitative data, the expected count per cell was utilized to guide the Chi-Square test. The Chi-Square test was applied if the predicted counts in every cell were ≥ 5, and Fisher's exact test was applied otherwise. Given that the data were not normally distributed and at least one of the groups contained significant outliers, the Kruskall-Wallis H-test was employed. Pairwise comparisons were done to determine the location of the statistically significant difference if the test result was statistically significant. $P \leq 0.05$ is significant.

RESULTS

Table (1) showed a statistically significantly difference in all 4 parameters: positive FH of DM, history of any fracture and hypertension between the 4 study groups.

Table (1): Clinical data in the 4 study groups

Characteristic	T2DM/VF	T2DM no VF	Non-DM/VF	Non-DM/ no VF	P value
Family history of DM	25 (100%)	21 (84%)	25 (100%)	20 (80%)	**0.010**
History of any fracture	25 (100%)	16 (64%)	25 (100%)	11 (44%)	**<0.001**
Hypertension	14 (56%)	15 (60%)	6 (24%)	8 (32%)	**0.022***

Table (2) showed that DM duration (years) was statistically significantly longer in those with VF vs. those without VF.

Table (2): Comparisons of DM duration in those with and without vertebral fracture

Statistic	VF	No-VF	Z value	P value
Median	**17**	**8**	**-2.415**	**0.016**
Minimum	**3**	**1**		
Maximum	**25**	**20**		

This table showed a higher proportion of metformin and vildagliptin use in those with VF and a higher proportion of sulfonylurea use in those without VF. However, these differences were not statistically significant (Table 3).

Table (3): Comparisons of oral antidiabetic drug use in those with and without vertebral fracture (VF)

Drug	VF	No-VF	χ^2	P value
Metformin use	25 (100%)	23 (92%)	FET	0.490
Vildagliptin use	14 (56%)	10 (40%)	1.282	0.258
Sulfonylureas use	14 (56%)	18 (72%)	1.389	0.239

Notes: Data have N. (percent). Fisher's exact test or the Chi-square test is used to determine significance (FET).

A statistically significant difference in all studied parameters between the 4 groups except for body weight. In the two DM groups' age, menopausal length, HbA1c, FRAX-MOPF (percent), and FRAX-HF (percent) values were statistically greater than those of the two non-DM groups. Height was statistically significantly lower in the two DM groups vs. the two non-DM groups. BMI was statistically significantly higher in the two DM groups vs. non-DM/VF group. TBS T-score was statistically significantly lower in the two DM groups vs. non-DM/VF group. Also, compared to the non-DM/non-VF group, the TBS T-score in the DM/VF group was statistically lesser. In comparison with the two non-DM groups, the BMD T-score in the DM/VF group was statistically considerably lower as shown in tables (4 and 5).

Table (4): Comparisons of sociodemographic and clinical data in the 4 groups

Parameter	DM/VF	DM/no VF	No DM/VF	No DM/no VF	H [3]	P value
Age (years)	65 (55-79)	61 (52-78)	59 (53-61)	57 (50-68)	27.16	**<0.001**
Duration of menopause (years)	16 (10-25)	13 (4-29)	10 (3-14)	8 (2-21)	36.40	**<0.001**
Weight (kg)	85 (73-96)	85 (50-113)	78 (72-88)	86 (60-120)	6.277	0.099
Height (m^2)	155 (150 -162)	156 (149-193)	161 (161-165)	162 (152-176)	29.70	**<0.001**
BMI (kg/m^2)	33.5 (30-42.2)	35.4 (18.8-44.1)	30.1 (26.4-33.9)	32.8 (22.6-45.7)	10.11	**0.018**

Table (5): Comparisons of lab and radiological quantitative data in the 4 groups

Parameter	DM/VF	DM/no VF	No DM/VF	No DM/no VF	H [3]	P value
HbA1c (%)	**8.2 (7.8-9.3)**	**7.9 (6.4-9.5)**	**5.8 (5.8-6)**	**6 (5.3-6.2) b**	**77.87**	**<0.001**
TBS T-score	-1.7 (-2.5 to -0.1)	-1.2 (-4.5 to 2)	0.2 (-1.1 to 0.2)	-0.2 (-1.7 to 1.1)	30.11	**<0.001**
BMD T-score	-3.1 (-4.1 to -1.2)	-2.2 (-4 to 2.2)	0.4 (-2.7 to 0.7)	-2.1 (-2.7 to 0.6)	18.76	**<0.001**
FRAX-MOPF (%)	4.8 (2.9-8.7)	4.4 (1.2-11)	2.6 (2.3-3.2)	2.3 (1.6-3.6)	36.41	**<0.001**
FRAX-HF (%)	0.8 (0.2-2.7)	0.4 (0.0-2.9)	0.0 (0.0-0.2)	0.1 (0.0-0.4)	42.09	**<0.001**

Notes: Data are median (minimum-maximum). Test of significance is Kruskall-Wallis H-test

TBS T-score: There was a statistically significant negative association with FRAX-MOPF, FRAX-HF, and HbA1c, but a statistically significant positive correlation with BMD T-score. **BMD T-score:** There was a statistically significant negative association with FRAX-MOPF, FRAX-HF, DM duration, and HbA1c, but a statistically significant positive correlation with TBS T-score. **FRAX-MOPF (%):** There was a statistically significant positive correlation with age, FRAX-MOPF, DM duration, HbA1c, and menopause duration, but statistically significant negative correlation with TBS T-score, BMD T-score, and BMI. **FRAX-HF (%):** There was statistically significant positive correlation with age, FRAX-HF, DM duration, HbA1c, and menopause duration, but statistically significant negative correlation with TBS T-score, BMD T-score, and BMI as shown in table (6).

Table (6): Radiological and Lab correlation in diabetic groups

Parameter	TBS T-score		BMD T-score		FRAX-MOPF (%)		FRAX-HF (%)	
	r_s value	P value	r_s value	P value	r_s value	P value	r_s value	P value
TBS T-score	-	-	0.509	**<0.001**	-0.748	**<0.001**	-0.670	**<0.001**
BMD T-score	0.509	**<0.001**	-	-	-0.630	**<0.001**	-0.831	**<0.001**
FRAX-MOPF (%)	-0.748	**<0.001**	-0.630	**<0.001**	-	-	0.865	**<0.001**
FRAX-HF (%)	-0.670	**<0.001**	-0.831	**<0.001**	0.865	**<0.001**	-	-
HbA1c (%)	**-0.498**	**<0.001**	**-0.424**	**<0.001**	**0.550**	**<0.001**	**0.573**	**<0.001**

DISCUSSION

It is known that patients with T2DM have increased risk of fractures. According to prior research, T2D patients with poor glycemic control and ongoing comorbidities are particularly susceptible to fractures. T2DM and osteoporosis are increasingly regarded as two important health issues due to the rising prevalence of both conditions in the ageing population. T2DM postmenopausal women are at significantly increased risk for cardiovascular problems as well as osteoporosis and the associated fragility fractures (FFs) [(9)]. According to **Janghorbani *et al.*** [(10)] patients with T2DM has been documented increasing in the risk of fractures. Patients with T2DM have also been found to have an increased risk of VFs, particularly Asian patients. Doctors can detect only small percentage of vertebral abnormalities as VFS. Additionally, they noted that the majority of Korean postmenopausal women with T2DM did not have VFs [(11)].

The integration of bone density and bone quality is mostly reflected in bone strength. About 70% of bone strength is determined by bone mineral density (BMD), which is usually used as a typical metric. On occasion, using BMD assessment alone is unable to estimate overall fracture risk. Osteoporotic fracture in people with type 2 diabetes is a prime illustration of this T2DM. Despite having higher BMDs than non-diabetics, those with T2DM had an increased risk of osteoporotic fractures. Therefore, it's probable that bone quality rather than BMD is more responsible for the higher risk of fractures in those with T2DM [(12)].

215 participants were drawn for this study from Mansoura Specialized Hospital's Endocrinology clinics. Then, cases were chosen based on inclusion and exclusion criteria, resulting in 100 participants, 25 in each of the following groups: Type 2 DM patients with vertebral fractures, type 2 DM patients without vertebral fractures, non-diabetic patients with vertebral fractures, and non-diabetic patients without vertebral fractures.

Between the 4 study groups, there was a statistically significant difference in family history of diabetes mellitus (DM), history of any fracture, and hypertension. Our results are supported by study of **Choi *et al.*** [(13)] as they reported that there was statistically significantly difference between postmenopausal T2DM women with and without VFs as regards history of any fracture. Similar to this, **Zhukouskaya *et al.*** [(3)] research showed that both T2D patients and controls have reported characteristics. The age and BMI of the subjects with and without diabetes were comparable. Hypertension and prior fragility fractures were more common in T2D patients.

The present study showed that DM duration was statistically significantly longer in those with VF vs. those without VF. Contrary to our study's findings, **Lin *et al.*** [(14)] showed that in the comparison of T2D participants with and without VF, there was no discernible correlation between T2D duration and VF.

The current study showed that there was a higher proportion of metformin and vildagliptin use in those with VF and a higher proportion of sulfonylurea use in those without VF. However, these differences were not statistically significantly. In accordance with our results, **Choi *et al.*** [(13)] demonstrated that there wasn't statistically significant difference between postmenopausal T2DM subjects without and with VFs as regards medication of DM.

In the study at hand, body weight, age, menopause duration, HbA1c, FRAX-MOPF (%), and FRAX-HF (%) were all statistically substantially different between the two diabetic groups and the two non-DM groups. The two DM groups had statistically significantly shorter heights than the two non-DM groups. Compared to the non-DM/VF group, BMI was statistically substantially higher in the two DM groups. In comparison with the non-DM/VF group, the TBS T-score was statistically substantially lower in the two DM groups. Additionally, compared to the non-DM/non-VF group, the TBS T-score in the DM/VF group was statistically considerably lower. The BMD T-score in the DM/VF group was statistically substantially lower than in the two non-DM groups. Our findings are consistent with a Korean study by **Kim *et al.*** [(8)], which found that while lumbar spine BMD is higher in diabetic men and women, lumbar spine TBS is lower in both groups. However, fracture data were not used to validate TBS's performance. BMD is not a factor in the effect, which also improves risk stratification

A difference in BMI has been proposed as one explanation for this contradiction, as BMI has been shown to be positively related with LS BMD and adversely related with TBS [(15)]. In contrast to this assumption, **Bonaccorsi *et al.*** [(16)] reported differences in TBS despite similar BMI between the two groups (T2DM and controls), suggesting a potential role for metabolic alterations caused by diabetes in weakening bones. Consistently, according to a recent meta-analysis by **Moayeri *et al.*** [(9)], patients with BMIs below 30 kg/m^2 had a significantly higher risk of overall fractures than those with BMIs above 30 kg/m^2. DeFRA algorithm has previously demonstrated to offer findings that are comparable to or even slightly superior to those of FRAX in the Italian population, notably in women under the age of 69 [(16)].

Our study showed that regarding TBS T-score, BMD T-score showed a statistically significant positive association, while FRAXMOPF, FRAX-HF, and HbA1c showed a statistically significant negative correlation. With regard to the BMD T-score, there was a statistically significant positive association with the TBS T-score and a statistically significant negative correlation with the FRAXMOPF, FRAX-HF, DM duration, and HbA1c. Regarding FRAX-MOPF (%), a statistically significant positive connection was found

between age, FRAX-MOPF, the length of the disease, HbA1c, and menopause duration, but statistically significant negative correlation with TBS T-score, BMD T score, and BMI. Regarding FRAX-HF (%), there was statistically significant positive correlation with age, FRAX-HF, DM duration, HbA1c, and menopause duration, but statistically significant negative correlation with TBS T-score, BMD T score, and BMI. In contrast, TBS was positively connected with femoral neck and spine BMD in the study by **Mirzaei *et al.* [17]**from 2018 (r = 0.50, p 0.0001, and r = 0.37, p 0.0001, respectively). TBS and our cohort's age showed a significant negative connection (r = -0.38, p 0.0001). Additionally, there was a negative relationship between individuals' ages and their spinal and femoral neck BMD (r = 0.15, p = 0.003, and r = 0.33, p 0.0001, respectively).

CONCLUSION

This study demonstrated that there are many factors contributing for the prevalence of vertebral fractures. These factors included duration of diabetes, poor diabetic control, BMI, drugs taken, BMD, and duration of menopause. The results of this study showed that post-menopause, low BMD, poor glycemic control and prolonged duration of DM have a great impact on bone mineralization and quality where probability of osteopenic fractures increases.

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