

Prevalence and Determinants of “TBS Worse than BMD” Discordance in Older Diabetic Adults: Findings from the Bushehr Elderly Health (BEH) Program

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Abstract

Background

Although diabetic patients are generally at increased risk for osteoporosis and fractures, they paradoxically tend to exhibit relatively higher bone mineral density BMD T-scores. The trabecular bone score (TBS) has been shown to better gauge bone health in diabetic patients, frequently revealing deterioration that BMD fails to detect. This study aims to investigate the prevalence and determinants of the “TBS worse than BMD” discordance among diabetic patients aged 60 years and older in Iran.

Methods

This study was based on the data from the second phase of the first recruitment of the Bushehr Elderly Health (BEH) program. Dual-energy x-ray absorptiometry (DXA) was used for BMD measurement, and TBS iNsight software was used for TBS measurement. “TBS worse than BMD” discordance was defined as partially degraded TBS with normal BMD, or degraded TBS with normal BMD, or degraded TBS with osteopenia. The discordance prevalence was determined, and univariable and multivariable logistic regression analyses were performed to identify the factors associated with the discordance.

Results

Our study involved 439 diabetic participants, of whom 156 (35.54%) were men and 283 (64.46%) were women. The mean age ($\pm$ SD) was 63.59 ($\pm$ 7.75) years. The “TBS worse than BMD” discordance was observed in 75 (17.08%, 95% CI: 13.68, 20.94) subjects. The discordance was significantly more prevalent in women (20.85%, 95% CI: 16.22, 26.05) compared to men (10.25%, 95% CI: 5.97, 16.12). After adjusting for other variables, waist circumference emerged as the only significant determinant for the discordance ($P < 0.001$) at the $\alpha = 0.05$ level. Every 1 cm increase in waist circumference increased the odds of discordance by 11% (OR: 1.11, 95% CI: 1.07, 1.15). Additionally, male sex ($P = 0.08$; OR = 0.50, 95% CI: 0.22, 1.10) and CRP level ($P = 0.06$; OR = 1.06, 95% CI: 1.00, 1.12) were significant determinants at the $\alpha = 0.10$ level in the multivariable model.

Conclusion

The “TBS worse than BMD” discordance was present in approximately one-sixth of older adult diabetic patients, and the deteriorating bone quality in these individuals was only captured by TBS measurement. Our findings support incorporating TBS alongside BMD in fracture risk assessment, particularly among female diabetic patients and those with elevated waist circumference and CRP levels. Future longitudinal studies are needed to further elucidate the determinants and clinical outcomes of this discordance.

INTRODUCTION

Osteoporosis, a major global health issue, is associated with an increased risk of fracture due to the reduction in bone mass and deterioration of the bone microstructure (1). This has caused a significant burden on healthcare and a challenge to the quality of life in the afflicted populations (2, 3). These fractures that mostly occur in the elderly population could result in complications like chronic pain, disability, delayed recovery, and loss of independence (4). According to a 2022 meta-analysis, the global prevalence of osteoporosis was 19.7% with regional heterogeneity (5). In Iran, a recent meta-analysis has estimated the prevalence to be approximately 38% and 25% in women and men, respectively (6). These findings indicate the notably higher prevalence figures in Iran compared to global figures.

Various diagnostic methods and fracture risk assessment tools have been used to diagnose osteoporosis. The gold standard for diagnosing osteoporosis remains bone mineral density (BMD), measured through dual-energy X-ray absorptiometry (DXA) (7). Although the BMD T-score provides a solid measure of the quantitative aspect of bone, it may not provide a clear picture of the bone quality (8). Bone quality is better assessed via the Trabecular Bone Score (TBS), which could be used along with BMD to provide a more valid evaluation of bone health and could aid in fracture risk prediction in clinical practice (9).

Among the comorbidities associated with osteoporosis, diabetes has been found to have a rather intriguing relationship with osteoporosis. Although diabetic patients are generally at a greater risk of osteoporosis and fractures, they are paradoxically found to have comparatively higher T-scores (10). In other words, despite having higher BMD (which should mean stronger bones), they have worse bone quality (lower TBS) and higher fracture risk (11). In these patients, TBS has been found to have a better discriminative power compared to BMD in assessing fracture risk (12).

Recently, a number of studies have focused on this “TBS worse than BMD” discordance in diabetes patients. A retrospective study noted the higher prevalence of vertebral and hip fractures in diabetics despite the higher BMD but lower TBS results (13). In Iran, a multi-center cross-sectional study reported significantly lower TBS scores in post-menopausal diabetic women compared to non-diabetic women of the same age, highlighting the advantage of TBS assessment in addition to BMD assessment in diabetics (14). Another study in Iran reported the paradoxically higher BMD in diabetics compared to non-diabetics, even though the TBS results were significantly lower in the former (15).

Despite the identification of “TBS worse than BMD” discordance in diabetics in recent studies and certain reasons being hypothesized for this paradox (e.g., accumulation of advanced glycation end-products and low bone turnover), not enough evidence is available about the prevalence of this discordance in the diabetic population (16, 17). In other words, in the diabetic population, the prevalence of this specific discordance (normal BMD / low TBS) is less widely known. Since BMD has been routinely used for bone health assessment, it would be relevant to identify the frequency of subjects with abnormal TBS despite having normal (or borderline) BMD T-scores. The aim of our study was to investigate the prevalence of the “TBS worse than BMD” discordance among diabetic patients aged 60

years and older in Iran. Additionally, our study aimed to assess the potential association of various determinants with this discordance.

METHODS

Study design and participants

This cross-sectional analysis was conducted on the baseline data of the first recruitment of the second phase of the Bushehr Elderly Health (BEH) program (18, 19). The BEH program is a population-based prospective cohort study designed to estimate the prevalence (at baseline) and incidence (during follow-up) of non-communicable diseases and their determinants among the elderly population in Bushehr, Iran. An exhaustive description of the design, about the various phases and the results of this cohort study, is provided in the previously published articles (18, 20). At the first recruitment of the second phase of the BEH program, a total of 2426 participants were selected through a multistage cluster random sampling method from the target population of adults aged ≥ 60 years residing in Bushehr city, southern Iran (19). However, only the diabetic participants for whom data were available for all of our required variables were included in our analysis.

Variable definition and measurements

Diabetes Mellitus (DM) was defined as the presence of fasting plasma glucose (FPG) levels ≥ 126 mg/dL or HbA1C levels $\geq 6.5\%$ or current treatment with antidiabetic medications. All the potential factors for “TBS worse than BMD” discordance were considered in this study. In the BEH program, a standardized questionnaire was used to collect demographic and medical history data. Additionally, information about the duration of diabetes (months), supplement intake, smoking status, age at menopause (females), and years since menopause (females) was collected. Years since menopause was defined as the number of years since the female participant’s last menstruation. Cigarette smoking status was determined as never, past, or current if the participant was never a smoker, smoked before, or was currently smoking. Usage of vitamin D or calcium supplements in the past 6 months was asked in the questionnaire. Calcium supplement intake was considered as intake of any combination of calcium. Parental history of fracture was asked as the history of fracture in either parent. Subjects were asked about the presence or absence of underlying diseases—rheumatoid arthritis, chronic kidney disease, liver disease, seizures, or hyperthyroidism. The type of diabetes medication used was asked, which could be nothing, diet control, herbal drugs, antidiabetic drugs, or injectable insulin. The type of diabetes in each participant was asked, which could be Type 1, Type 2, or unknown to the participant.

The detailed procedure and methods for biochemical measurement of blood samples are published elsewhere (19). The HbA1c measurement was via the boronate affinity method using a CERA-STAT system (CERAGEM MEDISYS, Chungcheongnam-do, Korea). All other biochemical measurements were done using commercial kits (Pars Azmun, Karaj, Iran). Fasting blood glucose measurement was via the

glucose oxidase colorimetric method, and the enzymatic colorimetric method was for measuring the lipid profile—the enzymatic (CHOD-PAP) colorimetric method for total cholesterol (TC), the enzymatic (CHE & CHO) colorimetric method for high-density lipoprotein cholesterol (HDL-C) and low-density lipoprotein cholesterol (LDL-C), and the enzymatic (GPO-PAP) colorimetric method for triglycerides (TG). Serum calcium (Ca) measurement was done using enzymatic colorimetric estimation with o-cresolphthalein complex, and phosphorus was measured via enzymatic UV method with phosphomolybdate. Serum vitamin D level, total procollagen type I collagen N-terminal propeptide (TP1NP), and parathyroid hormone (PTH) measurements were done with the ECLIA (Roche) method. C-reactive protein (CRP) measurement was through immunochemical assays.

The details about anthropometric and body composition measurements are published elsewhere (19, 20). Height and weight were measured without shoes and with light clothing using a fixed stadiometer and a digital scale, respectively. Waist circumference was measured by a flexible circumference measuring tape. Total fat mass, android fat mass, and gynoid fat mass were measured using dual-energy x-ray absorptiometry (DXA, Discovery WI, Hologic, Bedford, MA, USA) by a trained operator. Each measurement session lasted almost 20 minutes for each participant. All the anthropometric and body composition measurements of each participant were done on the same day.

BMD and TBS measurements

DXA (Discovery WI Bone Densitometer; Hologic, Bedford, MA, USA) was used to measure the BMD of each participant, performed by trained staff in the correct position. BMD T-scores were calculated using the reference database of healthy young Caucasian women (NHANES III), in accordance with international recommendations (21). TBS measurement was done using TBS iNsight software (version 2.2; Medimaps Group, Plan-les-Ouates, Switzerland). Following DXA of the lumbar spine, femoral neck, or total hip, T-scores were categorized as normal (lowest T-score ≥ -1), osteopenia ($-2.5 < \text{lowest T-score} < -1$), or osteoporosis (lowest T-score ≤ -2.5) based on the National Osteoporosis Foundation and the International Society for Clinical Densitometry (ISCD) classifications (22, 23). TBS was categorized as normal (TBS > 1.31), partially degraded (TBS $1.23\text{--}1.31$), or degraded (TBS < 1.23) according to the cut-off points suggested in the meta-analysis by McCloskey et al. (24).

Subjects with “TBS worse than BMD” (discordant cases)

In our analysis to identify subjects who have “TBS worse than BMD,” we categorized them into two groups. Subjects with “TBS worse than BMD” were defined as discordant cases, which included those with partially degraded TBS/normal BMD, degraded TBS/normal BMD, and degraded TBS/osteopenia. The remaining subjects (others) that were defined as having no “TBS worse than BMD” discordance included those with normal TBS/normal BMD, osteopenia, or osteoporosis; partially degraded TBS/osteopenia or osteoporosis; and degraded TBS/osteoporosis.

Statistical analysis

Normality of continuous variables was checked with the Shapiro-Wilk test; therefore, variables with normal distribution were described with mean ($\pm$ SD), and the skewed ones were specified with median and interquartile range. Also, qualitative variables were described by frequency and percentage. To compare continuous variables between two groups, the independent sample t-test was used for variables with normal distribution, while for skewed variables, the Mann-Whitney U test was used. The chi-squared test was used for testing the association between categorical variables.

We performed logistic regression to identify factors associated with the “TBS worse than BMD” discordance observed. Age, sex, duration of diabetes, age at menopause, years since menopause, body mass index (BMI), waist circumference, total fat mass, android fat mass, gynoid fat mass, HbA1c, fasting blood glucose (FBS), TP1NP, lipid profile (TC, TG, HDL-C, and LDL-C), CRP, calcium, phosphorus, serum vitamin D level, PTH, smoking status (never, past, and current use), vitamin D and calcium supplement use, underlying diseases, parent fracture history, and type of diabetic medications used were the variables included in the univariable logistic regression model. All candidate variables with a p-value of < 0.20 in the univariable model were eligible for the multivariable logistic regression model, where the forward stepwise method was used for analysis. In this model, all p-values < 0.10 were considered to be statistically significant. The goodness of fit of the multivariable model was checked by the Hosmer-Lemeshow goodness of fit test. All statistical analyses were performed with STATA Software 14 (StataCorp. 2015. Stata Statistical Software: Release 14. College Station, TX: StataCorp LP).

Ethical considerations

The Research Ethics Committee of the Endocrinology and Metabolism Research Institute, Tehran University of Medical Sciences (TUMS) (ethics code: IR.TUMS.EMRI.REC.1394.0036) has previously approved phase 2 of the BEH program. A written informed consent was obtained from each participant prior to the study (19, 25). The present study protocol has also been approved by the Research Ethics Committee of the Endocrinology and Metabolism Research Institute, Tehran University of Medical Sciences (ethics code: IR.TUMS.EMRI.REC.1402.044). All the methods were carried out following the relevant guidelines/regulations and in accordance with the Declaration of Helsinki.

RESULTS

Of the 2,426 participants in phase 2 of the BEH program, 439 diabetics who also met our other required variables were included in our cross-sectional analysis. As shown in Table 1, “TBS worse than BMD” discordance was observed in 59 out of 283 diabetic older adult women (20.85%, 95% CI: 16.22, 26.05) and 16 out of 156 diabetic older adult men (10.25%, 95% CI: 5.97, 16.12). The “TBS worse than BMD” discordance was significantly more prevalent in women compared to men ($P = 0.005$). Overall, 75 subjects (17.08%, 95% CI: 13.68, 20.94) had “TBS worse than BMD” discordance, and 364 subjects had TBS agreeing with or better than BMD (no “TBS worse than BMD” discordance).

Table 1

Distribution of the study population with diabetes in different TBS and BMD categories. Percentages are column percentages within each BMD category (the 3 enclosed cells are the “TBS worse than BMD” discordant cases).

Population	TBS	Osteoporosis definition based on BMD of all three sites		
		1. Normal	2. Osteopenia	3. Osteoporosis
Total	1. Normal	97 (80.8)	105 (48.8)	21 (20.2)
	2. Partially degraded	17 (14.2)	58 (27.0)	23 (22.1)
	3. Degraded	6 (5)	52 (24.2)	60 (57.7)
Women	1. Normal	46 (75.4)	49 (36.0)	13 (15.1)
	2. Partially degraded	11 (18.0)	43 (31.6)	17 (19.8)
	3. Degraded	4 (6.6)	44 (32.4)	56 (65.1)
Men	1. Normal	51 (86.4)	56 (70.9)	8 (44.5)
	2. Partially degraded	6 (10.2)	15 (19)	6 (33.3)
	3. Degraded	2 (3.4)	8 (10.1)	4 (22.2)

The baseline characteristics of study participants in the “TBS worse than BMD” discordant and non-discordant groups are provided in Table 2 and Table 2 (continued). Among the body composition and anthropometric variables, BMI, waist circumference, total fat mass, and android fat mass had significantly higher means in the “TBS worse than BMD” discordant group compared to the non-discordant one ($P < 0.001$ for all of the mentioned variables). Additionally, the “TBS worse than BMD” discordant group’s weight and gynoid fat mass had significantly higher medians compared to the non-discordant group ($P < 0.001$ for both variables). Among the laboratory measurements, CRP was significantly higher in the “TBS worse than BMD” group ($P = 0.005$). Sex was the categorical variable that was significantly associated with “TBS worse than BMD” discordance ($P = 0.005$).

Table 2

Comparison of participants' continuous baseline characteristics between "TBS worse than BMD" discordant subjects and others (non-discordant subjects).

Continuous variables, (mean $\pm$ SD)	Total N = 439	"TBS worse than BMD" N = 75	Others N = 364	P-value
Age	63.59 $\pm$ 7.75	62.20 $\pm$ 6.25	63.87 $\pm$ 7.99	0.09
Age at menopause	47.48 $\pm$ 5.67	47.02 $\pm$ 6.51	47.6 $\pm$ 5.43	0.50
Years since menopause	15.22 $\pm$ 9.41	14.55 $\pm$ 9.78	15.41 $\pm$ 9.33	0.55
Duration of diabetes (months)	102.47 $\pm$ 87.76	106.94 $\pm$ 97.22	101.63 $\pm$ 86.07	0.70
Weight (kg)	73.42 (13.33) *	83.7 (15.6) *	71.31 (11.76) *	< 0.001 †
Height (cm)	159.83 $\pm$ 8.64	159.3 $\pm$ 8.52	159.9 $\pm$ 8.7	0.54
Body mass index (BMI) (kg/m ²)	28.81 $\pm$ 4.99	32.91 $\pm$ 5.32	27.96 $\pm$ 4.48	< 0.001
Waist circumference (cm)	102.93 $\pm$ 9.92	110.75 $\pm$ 9.42	101.63 $\pm$ 9.41	< 0.001
Total fat mass (g)	6485.79 $\pm$ 1808.10	7547.91 $\pm$ 1779.58	6309.88 $\pm$ 1754.34	< 0.001
Android fat mass (g)	2535.45 $\pm$ 746.92	3082.2 $\pm$ 756.9	2444.9 $\pm$ 706.6	< 0.001
Gynoid fat mass (g)	3949.5 (1190.1) *	4463.8 (1169.4) *	3864.3 (1173.7) *	< 0.001 †
HbA1c (%)	7.87 $\pm$ 1.79	7.7 $\pm$ 1.57	7.91 $\pm$ 1.84	0.35
Fasting blood glucose (mg/dL)	151.19 $\pm$ 60.63	150.67 $\pm$ 51.60	151.31 $\pm$ 62.39	0.93
TP1NP (μ g/L)	52.51 $\pm$ 31.19	50.79 $\pm$ 26.78	52.87 $\pm$ 32.05	0.60
* Variables with skewed distribution are presented as Median (IQR)				
† Variables with skewed distribution (reported as Median, IQR) were compared using Mann-Whitney U test				

Continuous variables, (mean ± SD)	Total N = 439	“TBS worse than BMD” N = 75	Others N = 364	P-value
Lipid profile	170.71 ± 42.96	176.21 ± 38.64	169.57 ± 43.76	0.22
TC (mg/dl)	166.12 ± 98.59	181.95 ± 92.98	162.86 ± 99.51	0.13
TG (mg/dl)	46.89 ± 11.29	45.5 ± 9.2	47.18 ± 11.67	0.24
HDL-C (mg/dl)	91.01 ± 36.21	94.3 ± 31.6	90.32 ± 37.09	0.39
LDL-C (mg/dl)				
CRP (mg/L)	4.77 ± 4.04	5.95 ± 5.64	4.52 ± 3.58	0.005
Ca (mg/dL)	9.53 ± 0.48	9.3 ± 0.55	9.52 ± 0.47	0.91
Phosphorus (mg/dL)	4.07 ± 0.44	4.03 ± 0.45	4.08 ± 0.43	0.31
Vitamin D (ng/mL)	28.23 ± 15.64	26.80 ± 16.19	28.52 ± 15.53	0.39
PTH (pg/mL)	48.67 ± 25.44	52.84 ± 23.35	47.80 ± 25.80	0.11
<i>* Variables with skewed distribution are presented as Median (IQR)</i>				
<i>† Variables with skewed distribution (reported as Median, IQR) were compared using Mann-Whitney U test</i>				

Table 2

(continued) Comparison of participants' categorical baseline characteristics between "TBS worse than BMD" discordant subjects and others (non-discordant subjects) (Percentages are column percentages and may not add up to 100% due to rounding).

Categorical variables, n (%)	Total, N = 439	"TBS worse than BMD" (Discordant Cases) N = 75	Others N = 364	P-value
Sex	283 (64.46)	59 (78.67)	224 (61.54)	0.005
Female	156 (35.54)	16 (21.33)	140 (38.46)	
Male				
Smoking	401 (91.34)	71 (94.67)	330 (90.66)	0.395
Never	18 (4.10)	1 (1.33)	17 (4.67)	
Past	20 (4.56)	3 (4.00)	17 (4.67)	
Current				
Supplements (yes)	222 (50.57)	39 (52.00)	183 (50.27)	0.786
Vitamin D	98 (22.32)	20 (26.67)	78 (21.43)	0.321
Calcium				
Type of Diabetes	46 (10.48)	6 (8.00)	40 (10.99)	0.606
Type 1	363 (82.69)	65 (86.67)	298 (81.87)	
Type 2	30 (6.83)	4 (5.33)	26 (7.14)	
Unknown				
Diabetes medication	28 (6.38)	3 (4.00)	25 (6.87)	0.707
Nothing	154 (35.08)	25 (33.33)	129 (35.44)	
Diet	15 (3.42)	4 (5.33)	11 (3.02)	
Herbal	208 (47.38)	36 (48.00)	172 (47.25)	
Anti-Diabetic drugs	34 (7.74)	7 (9.33)	27 (7.42)	
Insulin				
Underlying disease* (yes)	53 (12.07)	8 (10.67)	45 (12.36)	0.681
Parental history of fracture (yes)	41 (9.34)	5 (6.67)	36 (9.89)	0.382
* Underlying diseases include rheumatoid arthritis, chronic kidney disease, liver disease, seizures or hyperthyroidism.				

The results of the univariable and multivariable analyses are shown in Table 3. After univariable analysis, “TBS worse than BMD” discordance was significantly associated with sex (male) (OR: 0.43, 95% CI: 0.24, 0.78), weight (OR: 1.07, 95% CI: 1.05, 1.09), BMI (OR: 1.21, 95% CI: 1.15, 1.28), waist circumference (OR: 1.11, 95% CI: 1.08, 1.14), total fat mass (OR: 1.0004, 95% CI: 1.0002, 1.0005), android fat mass (OR: 1.001, 95% CI: 1.0007, 1.002), gynoid fat mass (OR: 1.0004, 95% CI: 1.0002, 1.0006), and CRP (OR: 1.07, 95% CI: 1.01, 1.12). In addition to these determinants, age ($P = 0.09$), TG ($P = 0.13$), and PTH ($P = 0.13$) were included in the multivariable regression analysis due to the previously mentioned $P < 0.20$ eligibility threshold. Following multivariable regression analysis, after adjusting for other variables, only the association with waist circumference (OR: 1.11, 95% CI: 1.07, 1.15) remained significant at the $\alpha = 0.05$ level. In other words, every 1 cm increase in waist circumference increased the odds of “TBS worse than BMD” discordance by 11% among diabetics after multivariable adjustment. At the $\alpha = 0.10$ level, male sex ($P = 0.08$; OR = 0.50, 95% CI: 0.22, 1.10) and CRP level ($P = 0.06$; OR = 1.06, 95% CI: 1.00, 1.12) emerged as the significant determinants following multivariable adjustment.

Table 3

Univariable and Multivariable logistic regression analysis of individuals with diabetes to identify factors associated with “TBS worse than BMD” discordance.

Variable	Simple logistic regression		Multiple logistic regression ^a	
	OR (95%CI)	P-value	OR (95% CI)	P-value
Age	0.97 (0.94, 1.004)	0.09	-	-
Sex (male)	0.43 (0.24, 0.78)	0.006	0.50 (0.22, 1.10)	0.08
Age at menopause	0.98 (0.93, 1.03)	0.50	-	-
Years since menopause	0.99 (0.96, 1.02)	0.55	-	-
Duration of diabetes	1.001 (0.99, 1.004)	0.70	-	-
Height	0.99 (0.96, 1.02)	0.57	-	-
Weight	1.07 (1.05, 1.09)	< 0.001	-	-
Body mass index (BMI)	1.21 (1.15, 1.28)	< 0.001	-	-
Waist circumference	1.11 (1.08, 1.14)	< 0.001	1.11 (1.07, 1.15)	< 0.001
Total fat mass	1.0004 (1.0002, 1.0005)	< 0.001	-	-
Android fat mass	1.001 (1.0007, 1.002)	< 0.001	-	-
Gynoid fat mass	1.0004 (1.0002, 1.0006)	0.001	-	-
HbA1c	0.93 (0.81, 1.08)	0.35	-	-
Fasting blood glucose	1 (0.999, 1.004)	0.93	-	-
TP1NP	0.99 (0.98, 1.006)	0.60	-	-
TC (mg/dl)	1.003 (0.998, 1.009)	0.22	-	-
TG (mg/dl)	1.002 (0.999, 1.004)	0.13	-	-
HDL-C (mg/dl)	0.99 (0.96, 1.009)	0.24	-	-
LDL-C (mg/dl)	1.003 (0.99, 1.01)	0.38	-	-
CRP	1.07 (1.01, 1.12)	0.01	1.06 (1.00, 1.12)	0.06
Ca	1.03 (0.62, 1.72)	0.91	-	-
Phosphorus	0.74 (0.42, 1.31)	0.31	-	-

^a P-value of Hosmer-Lemeshow goodness of fit test = 0.28

Variable	Simple logistic regression		Multiple logistic regression ^a	
	OR (95%CI)	P-value	OR (95% CI)	P-value
Vitamin D	0.99 (0.98, 1.009)	0.38	-	-
PTH	1.007 (0.99, 1.01)	0.12	-	-
Smoking	1 (Ref)	0.21	-	-
Never	0.27 (0.04, 2.08)	0.75	-	-
Past	0.82 (0.23, 2.86)			
Current				
Vitamin D supplementation	1.10 (0.67, 1.81)	0.70	-	-
Calcium supplementation	1.36 (0.76, 2.40)	0.29	-	-
Underlying disease (yes)	0.82 (0.36, 1.86)	0.64	-	-
Parental history of fracture (yes)	0.66 (0.25, 1.74)	0.40	-	-
Diabetes medication	1 (Ref)	0.46	-	-
Nothing	1.61 (0.45, 5.76)	0.19	-	-
Diet	3.03 (0.57, 15.88)	0.38	-	-
Herbal	1.74 (0.50, 6.08)	0.30	-	-
Antidiabetic drugs	2.16 (0.50, 9.28)			
Insulin				
^a P-value of Hosmer-Lemeshow goodness of fit test = 0.28				

DISCUSSION

Our study used a cross-sectional analysis to determine the prevalence of “TBS worse than BMD” discordance—a condition where bone quality assessed by TBS is poorer than would be expected based on BMD alone—among diabetic individuals aged ≥ 60 years residing in Bushehr city, southern Iran. Our study yielded a prevalence of 17.08% for this discordance. Waist circumference was found to have a direct association with the discordance, and it was the only significant determinant after multivariable adjustment. Additionally, the male sex ($P = 0.08$) and CRP ($P = 0.06$) levels were found to be significant at the $\alpha = 0.10$ level in terms of their association.

The observed 17.08% “TBS worse than BMD” discordance prevalence aligns with the growing body of evidence pointing to the inadequacy of BMD T-scores in sufficiently providing a snapshot of bone health in diabetics. According to a meta-analysis in 2025, type 2 diabetics exhibited paradoxically higher lumbar spine BMD despite having significantly lower TBS compared to the non-diabetics (11). The BMD T-score may somewhat fall short in sufficiently assessing bone health due to its inability to appropriately gauge bone microstructural quality, particularly in diabetic individuals (9). Another study among elderly females in South Korea (2019) yielded a 10.6% prevalence of “TBS worse than BMD” discordance, a figure notably lower than our 17.08% prevalence among diabetic individuals (26). This discrepancy suggests that diabetes could amplify the discordance, a finding supported by recent evidence advocating for the routine incorporation of TBS alongside BMD measurement in these patients (27, 28). Our results are consistent with the findings of similar studies in Iran that reported significantly lower TBS in diabetics compared to nondiabetics, despite having comparable BMD T-scores (14, 15).

Several anthropometric variables had significantly higher means (or medians) in the “TBS worse than BMD” discordant group compared to the non-discordant group, including weight, BMI, waist circumference, total fat mass, android fat mass, and gynoid fat mass. However, after multivariable adjustment, only waist circumference emerged as the sole significant variable. This shows that central adiposity may exert a stronger influence on bone quality worsening not captured by BMD but better detected by TBS measurements. A recent analysis of NHANES data reported that waist circumference has the most significant negative association with TBS among all components of metabolic syndrome (29). One reason for this observation could be the contribution of central adipose tissue to inflammatory processes that may lead to bone resorption and loss of bone microstructure (30). The visceral fat also may lead to mechanical loading that preserves or even increases BMD at the lumbar spine, but this increase does not protect against the microarchitectural damage caused by metabolic and inflammatory processes (31). Finally, increased central fat has also been linked to insulin resistance and hyperglycemia, which could result in the formation of advanced glycation end-products and their accumulation in bone collagen, leading to disruption of bone chemical composition without necessarily compromising bone mineral content (32).

Despite the fact that the “TBS worse than BMD” discordance was significantly more prevalent in women compared to men—the discordance was observed in 20.85% of the older adult diabetic women and 10.25% of the older adult diabetic men—the male sex was found to be significant at the $\alpha = 0.10$ level in our study after multivariable adjustment ($P = 0.08$; OR = 0.50, 95% CI: 0.22, 1.10). In fact, several studies have pointed out the deteriorating bone health in post-menopausal women aggravated by estrogen depletion (33, 34). On the other hand, androgens are known for their protective effect against osteoporosis in men (35). The CRP level was the other determinant found to be significant at the $\alpha = 0.10$ level following multivariable adjustment. CRP, as a systemic inflammation marker, has been shown to possess a significant inverse association with TBS (36). However, its association with BMD has been found to be less pronounced (37). DM is known to contribute to a chronic state of systemic inflammation, which may play a role in the deterioration of bone quality (38). However, further

investigation with bigger sample sizes and other inflammatory markers is warranted for elucidation of pathways linking chronic inflammation and “TBS worse than BMD” discordance observed in our study.

Our study had several strengths, including the use of standardized laboratory procedures of measurement and simultaneous adjustment for multiple variables in the logistic regression model. Also, no other study has provided an estimate of this discordance in the elderly diabetic population to the best of our knowledge. One limitation of our study could be the fact that the discordance was not studied in the elderly diabetics categorized by the type of DM (Type 1 vs. Type 2). Furthermore, as our study was cross-sectional, it wasn't possible to establish causality between the factors considered and the discordance observed. Additionally, our study did not recruit institutionalized older adult individuals, like those residing in nursing homes. This could potentially limit the generalizability of our findings. The data about some of the determinants, like smoking status and type of medication used, were collected via self-reporting, which could introduce issues like recall bias or social desirability bias.

Conclusion

According to our findings, in approximately one out of every six older adult diabetic individuals, there is “TBS worse than BMD” discordance or a poor bone quality that is not detected by routine BMD assessments. Waist circumference was the key determinant with a positive association after multivariable adjustment, suggesting that central adiposity may be a major driver of bone microarchitecture deterioration not captured by BMD T-scores. In addition, the elevated inflammation potentially stemming from diabetes and central adiposity could have some sort of association with the discordance aligning with the significance observed in the CRP level. Finally, the negative association with male gender compared to females is also worth mentioning. Our findings highlight the importance of incorporating TBS measurement in bone health assessment and fracture risk prediction in diabetic individuals, particularly in women, those with higher waist circumference measurements, and individuals with higher inflammatory markers. Future longitudinal studies with larger sample sizes are recommended to confirm our findings, explore additional potential determinants not captured in our study, and evaluate the possible long-term clinical outcomes associated with this discordance.

Declarations

Ethics approval and consent to participate

The Research Ethics Committee of the Endocrinology and Metabolism Research Institute, Tehran University of Medical Sciences (TUMS) (ethics code: IR.TUMS.EMRI.REC.1394.0036) has previously approved phase 2 of the BEH program. A written informed consent was obtained from each participant prior to the study. The present study protocol has also been approved by the Research Ethics Committee of the Endocrinology and Metabolism Research Institute, Tehran University of Medical Sciences (ethics code: IR.TUMS.EMRI.REC.1402.044). All the methods were carried out following the relevant guidelines/regulations and in accordance with the Declaration of Helsinki.

Consent for publication

Not applicable

Availability of data and materials

The data that support the findings of this study were obtained from the Bushehr Elderly Health (BEH) program. Restrictions apply to the availability of these data, as they were used under a data-sharing agreement for the current study. Data are, however, available from the BEH program upon reasonable request and with permission from principal investigators.

Competing interests

Sepideh Hajivalizadeh, Tahsin Khaled Bashar, Khadije Maajani, Nekoo Panahi, Noushin Fahimfar, Afshin Ostovar, Iraj Nabipour, and Kazem Khalagi declare that they have no conflict of interest.

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Authors' contributions

Study design: SH, NF, NP, AO, KK. Data acquisition: NF, AO, IN, KK. Data analysis: KM, KK, TKB. Data management: TKB, KK, KM. Data interpretation: SH, TKB, NF, KK. Drafting of the manuscript: TKB, KK, SH, KM. Revision of the manuscript content: NF, KK, IN, NP. All authors read and approved the final manuscript.

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