Assessment of Bone Microarchitecture by Trabecular Bone Score to Evaluate Osteoporosis Independent of Bone Density at Mansoura University Hospital in Egypt

Alaa Ibrahim Saeed[1], Mohammed A. Elhawary[2], Hala S. Sweed[1], Salma M.S. El Said[1], Mennatallah S. Al-Araby[1]

[1]*Department of Geriatrics & Gerontology, Faculty of Medicine, Ain Shams University, Cairo, Egypt.*
[2]*Department of Diagnostic & Interventional Radiology, Faculty of Medicine, Mansoura University, Cairo, Egypt.*
Email: alaasaeed@mans.edu.eg

KEYWORDS
Bone Microarchitecture, Bone Density, Trabecular Bone Score.

ABSTRACT:
Background: Osteoporosis is defined as low bone mineral density caused by altered bone microstructure, ultimately predisposing patients to low-impact fragility fractures. Osteoporosis is a global health epidemic. Over 200 million people have osteoporosis, and the incidence rate increases with age. Over 70% of those over age 80 are affected. Worldwide, there are approximately 9 million fractures per year because of osteoporosis. Bone mineral density (BMD) measured by dual X-ray absorptiometry (DXA) has been the gold standard for osteoporosis diagnosis in the absence of established fragility fractures. Trabecular bone score (TBS) is one of the most widely used assessments of bone quality. Both BMD and TBS are independent predictors of fragility fractures and are the two pillars of the World Health Organization's (WHO) clinical definition of osteoporosis.
Objective: To evaluate the ability of lumbar spine TBS to assess bone microarchitecture and osteoporosis independent of bone mineral density.
Patients and methods: This cross-sectional study was conducted at Geriatric inpatient and outpatient clinic, Mansoura university Hospitals. This study was conducted on 45 elderly males (60 years and above) and postmenopausal females aged 50 years or above having one or more clinical risk factors for osteoporosis.
Results: Regarding the validity of Trabecular bone score (TBS) in discriminating osteopenia/osteoporosis from normal, it was revealed that TBS at cutoff value of ≤ 1.422 can discriminate osteopenia/osteoporosis from normal with 86.4% sensitivity, and 43.5% specificity.
Conclusion: TBS has a limited association with direct measurements of bone micro-architecture, can't be used alone to diagnose primary osteoporosis and may be a useful adjunct to BMD, DEXA and QCT for evaluation of osteoporosis, fracture risk detection and prediction..

1. Introduction

Osteoporosis is defined as low bone mineral density caused by altered bone microstructure, ultimately predisposing patients to low-impact, fragility fractures. Osteoporotic fractures lead to a significant decrease in quality of life, increasing morbidity, mortality, and disability (Varacallo et al., 2021).

Over 200 million people have osteoporosis, and the incidence rate increases with age. Over 70% of those over age 80 are affected. It is more common in females than in males. In the developed world, 2% to 8% of males and 9% to 38% of females are affected. Worldwide, there are approximately 9 million fractures per year because of osteoporosis (Prince et al., 2019).

Primary osteoporosis is related to the aging process in conjunction with decreasing sex hormones. The bones demonstrate deterioration in microarchitecture, leading to loss of bone mineral density and increased risk of a fracture. If osteoporosis is detected early and treated, the outcomes are good. However, if the condition remains untreated, it can lead to chronic pain and fragility fractures, so it's important to screen and early diagnosis of osteoporosis (Porter and Varacallo, 2022).

The trabecular bone score (TBS), a newly developed tool scoring the DXA scan images using a gray scale analysis, has recently been proposed as a method for evaluating bone structure (Silva et al., 2014).

TBS is a textural index that evaluates pixel gray-level variations in the lumbar spine DXA image, providing an indirect index of trabecular microarchitecture (Bousson et al., 2012).

The following normal range for TBS values in postmenopausal women: TBS more or equal to 1.350 is normal; TBS between 1.200 and 1.350 is consistent with partially degraded microarchitecture; and TBS less than 1.200

defines degraded microarchitecture. These cutoff points were established by a working group of TBS users from different countries (Cormier et al., 2012).

Several studies have found that TBS could potentially complement a BMD in predicting fragility fractures. Most studies that have been summarized were conducted in postmenopausal women. It was found that those with low TBS were associated with 1.5 times higher risk of fracture compared with those with normal TBS. Also, it was found that TBS predicted vertebral as well as major osteoporotic fracture (MOF) (Kim et al., 2019).

2. AIM OF THE WORK

To evaluate the ability of lumbar spine TBS to assess osteoporosis independent of bone mineral density.

3. PATIENTS AND METHODS

This cross-sectional study was conducted at Geriatric inpatient and outpatient clinic, Mansoura university Hospitals. This study was conducted on 45 elderly males (60 years and above) and postmenopausal females aged 50 years or above having one or more clinical risk factors for osteoporosis.

Elderly males (60 years and above) and Postmenopausal females aged 50 years or above were included in the study. While patients who refused to participate in the study or have non-vertebral fractures, BMI < 15 Kg/m2 or > 35 Kg/m2, critical or terminal illness and those who presented evident vertebral morphological anomalies or had a T-score >1 between contiguous vertebrae were excluded from the study.

Research methodology conducted with respect to declaration of Helsinki. Informed written consent was obtained from every participant. For people who were unable to read or write for whatever reason, the study aims, and procedure was elaborated to them by the interviewer, and consent taken from patient's proxy.

We collected 45 participants; postmenopausal female (50 years or above) and elderly males (more than 60 years old) with one or more risk factors of osteoporosis, who are attending at our geriatric clinic and who are admitted to our geriatric inpatient. The primary investigator collected the cases conforming to our criteria, excluding cases with non-vertebral fracture, BMI < 15 Kg/m2 or > 35 Kg/m2, vertebral morphological anomalies or had a T-score >1 between contiguous vertebrae and have critical or terminal illness. Every participant in our study underwent a comprehensive geriatric assessment, including the risk factors of osteoporosis, geriatric assessment tools and examination. Laboratory data: routine laboratory data include CBC, blood glucose, albumin, serum creatinine, liver function tests, calcium, and phosphorus.

DEXA was done at different sites; at lumbar spine, neck of femur and lower end of radius and T-score was done. TBS on lumbar spine was done to every participant, at the same time as DEXA, one day a week to every participant and at another hospital which make it difficult to transfer inpatient participants. QCT provides volumetric density of the bone at lumbar spine and both neck femur to every participant, one day a week to every participant, at Mansoura university hospital, so it takes longer time to collect data of our participants.

All patients were subjected to detailed comprehensive geriatric history with special emphasize on Mini mental status examination (MMSE) to assess dementia, Geriatric Depression scale (GDS) to assess geriatric depression risk, Mini Nutritional Assessment (MNA), to assess nutritional status and risk of malnutrition, Activity of daily living (ADL) and Instrumental activity of daily living (IADL) to assess functional level, risk factors for osteoporosis and Fracture Risk Assessment Tool (FRAX) score, clinical examination and radiological assessment with special emphasis on dual-energy x-ray absorptiometry (DEXA) scan Trabecular Bone Score (TBS) using the TBS iNsight software Quantitative computed tomography (QCT) at lumbar spine and at neck femur.

4. STATISTICAL ANALYSIS:

Data were entered and analyzed using IBM-SPSS software (IBM Corp. Released 2019. IBM SPSS Statistics for Windows, Version 26.0. Armonk, NY: IBM Corp). Qualitative data were expressed as N (%). Quantitative data were initially tested for normality using Shapiro-Wilk's test with data being normally distributed if p>0.050. The presence of significant outliers (extreme values) was tested for by inspecting boxplots. Quantitative data were expressed as mean ± SD if normally distributed, or median and interquartile range (Q1 or 25th percentile – Q3 or 75th percentile), if not. Then appropriate statistical analyses were applied. For any

of the used tests, results were considered as statistically significant if p value ≤ 0.050.

5. RESULTS

Table (1): Categorical clinical data between the three groups as regard DEXA.

Characteristic	Group			Total	p-value
	Normal	Osteopenia	Osteoporosis		
Sex Male Female	 7(30.4%) 16(69.6%)	 4(25%) 12(75%)	 0(0%) 6(100%)	 11(24.4%) 34(75.6%)	0.492
Education level Illiterate <12 years >12 years	 7(30.4%) 8(34.8%) 8(34.8%)	 7(43.8%) 5(31.3%) 4(25%)	 2(33.3%) 2(33.3%) 2(33.3%)	 16(35.6%) 15(33.3%) 14(31.1%)	0.960
Marital status Unmarried Married	 3(13.0%) 20(87.0%)	 3(18.8%) 13(81.3%)	 1(16.7%) 5(83.3%)	 7 (15.6%) 38(84.4%)	0.860
Current smoking	5(21.7%)	3(18.8%)	0(0%)	8 (17.8%0	0.660
Diabetes	8(34.8%)	11(68.8%)	6(100.0%)	25(55.6%)	0.006
Hypertension	12(52.2%)	14(87.5%)	6(100.0%)	32(71.1%)	0.018
IHD	3(13.0%)	7(43.8%)	3(50.0%)	13(28.9%)	0.038
Chronic constipation	7(30.4%)	9(56.3%)	1(16.7%)	17(37.8%)	0.168
Osteoarthritis	10(43.5%)	10(62.5%)	10(66.7%)	10 (53.3%	0.414
RA	0(0%)	1(6.3%)	1(16.7%)	2 (4.4%)	0.112
CKD	2(8.7%)	3(18.8%)	3(50%)	8 (17.8%)	0.079
CLD	4(17.4%)	1(6.3%)	0(0%)	5 (11.1%)	0.538
Thyroid status Hypothyroidism Hyperthyroidism	 4(17.4%) 0(0%)	 4(25%) 1(6.3%)	 4(66.7%) 0(0%)	 12(26.7%) 1 (2.2%)	0.070
Parathyroid status Hypoparathyroidism Hyperparathyroidism	 0(0%) 1(4.3%)	 1(6.3%) 1(6.3%)	 0(0%) 3(50%)	 1 (2.2%) 5 (11.1%)	0.019
Polypharmacy	7(30.4%)	12(75%)	6(100%)	25(55.6%)	0.001
Anti-epileptic drugs	3(13%)	3(18.8%)	4(66.7%)	10(22.2%)	0.025
PPI use	6(26.1%)	5(31.3%)	4(66.7%)	15(33.3%)	0.212
Parental hip fracture	5(21.7%)	6(37.5%)	3(50%)	14(31.1%)	0.293
History of fall	2(8.7%)	8(50%)	3(50%)	13(28.9%)	0.005
MMSE (Mini Mental State Examination) Normal Mild dementia Moderate dementia	 22(95.7%) 0(0%) 1(4.3%)	 12(75%) 4(25%) 0(0%)	 4(66.7%) 2(33.3%) 0(0%)	 38(84.4%) 6 (13.3%) 1 (2.2%)	0.019
MNA (Mini Nutritional Assessment) Normal At risk of malnutrition Malnourished	 21(91.3%) 2(8.7%) 0(0%)	 10(62.5%) 5(31.3%) 1(6.3%)	 1(16.7%) 4(66.7%) 1(16.7%)	 32(71.1%) 11(24.4%) 2 (4.4%)	0.002
IADL (Instrumental Activity of Daily Living) Independent Assisted	 20(87%) 3(13%)	 10(62.5%) 6(37.5%)	 5(83.3%) 1(16.7%)	 35(77.8%) 10(22.2%)	0.215
GDS (Geriatric depression risk)	4(17.4%)	3(18.8%)	4(66.7%)	11(24.4%)	0.043

Notes: Data is N (%). Test of significance is Fisher's exact test.

This table shows a statistically significant difference between the three groups as regards DM, hypertension, IHD, polypharmacy, hyperparathyroidism, mild dementia by MMSE, at risk of malnutrition by MNA, and GDS, anti-epileptic use, and history of fall. DM, hypertension, IHD, polypharmacy, anti-epileptic use, hyperparathyroidism, mild dementia by MMSE, at risk of malnutrition by MNA, and GDS were all higher in osteoporosis > osteopenia > normal. However, post-hoc tests revealed that these differences achieved statistical significance between osteoporosis vs. normal as regards DM, antiepileptic use, hyperparathyroidism, at risk of

malnutrition by MNA, GDS, polypharmacy, mild dementia by MMSE, and history of fall, and between osteopenia vs osteoporosis. polypharmacy, mild dementia by MMSE, and history of fall.

Table (2): Quantitative clinical and laboratory data between the three groups as regard DEXA.

Characteristic	Group			Total	p-value
	Normal	Osteopenia	Osteoporosis		
Age (years)	63.1±6.1	68±9.9	63±3.46	64.8±7.7	0.115
Body weight (kg)	87.9±13 a	81.5±13 a, b	66.5±13.3 b	82.8±14.6	0.003
Height (cm)	158.4±9.5	156.6±8.2	152.7±6.4	157 ± 6.7	0.368
BMI (kg/m^2)	35.3±6.2	33.5±6.1	28.9±7.7	33.8 ± 6.6	0.100
Serum total calcium (mg/dl)	8.5±0.4 a	8.2±0.5 b	7.8±0.3 b	8.29 ± 0.5	0.001
Serum phosphorus (mg/dl)	4.1±0.5	4.2±0.9	3.6±1	4.07±0.72	0.209

Notes: Data is mean ± SD. Test of significance is one-way ANOVA. Post-hoc (Tukey HSD) tests were presented as letters (if similar = insignificant difference, and if different = significant difference).

This table shows a statistically significant difference in body weight and serum calcium between the three groups. Post-hoc tests revealed that body weight was statistically significantly lower in osteoporosis vs. normal, and that serum calcium was statistically significantly lower in both osteoporosis and osteopenia vs. normal.

Table (3): DEXA, BMD at spine, femur, and forearm, FRAX, FRAX TBS, and QCT scores at spine and femur in the three TBS categories.

Measurement	Normal	Partially degraded	Degraded	H [2]	p-value
DEXA at spine	-0.55 (-1.975 to 0.025)	-1.10 (-2.20 to -0.450)	-1.70 (-2.15 to -0.325)	1.77	0.412
BMD at spine	1.128 (0.953-1.23)	1.08 (0.926-1.15)	0.98 (0.95-1.16)	1.239	0.538
FRAX	8.30 (5.93-11.25)	10 (6.9-17)	5.85 (4.37-11)	3.496	0.174
FRAX TBS	6.70 (4.83-9.28)	11 (7.7-16.5)	7.80 (5.65-12.25)	6.728	0.035
qCT L1	207 (168.3-297)	186 (144.5-260.5)	186.5 (108.3-267.5)	3.006	0.223
qCT L2	191 (171.5-303.7)	164 (140-240)	198.5 (126.3-272.3)	2.442	0.295
qCT L3	199 (162.3-231.7)	180 (150-213)	215 (1.56.5-243.5)	1.005	0.605
qCT L4	185 (170.3-276.3)	192 (158.5-242.5)	149.5 (77-223.8)	3.019	0.221
qCT L5	198 (167-244.8)	160 (137-252)	197.5 (150.3-237)	1.505	0.471
AqCT spine	207 (171-252)	198 (156-229)	192.5 (141.5-253)	1.477	0.478
qCT right femur	256.5 (165.7-315.3)	250 (142-299)	230 (94.7-270.7)	1.923	0.382
qct left femur	215 (163.3-270)	185 (116-1)	193.5 (85.3-251)	1.126	0.570
AqCT femur	242 (169.8-325)	228 (136.5-315)	212 (89.8-260.8)	1.778	0.441
DEXA at femur	-1.35 (-1.83 to -0.68)	-1.40 (-2.30 to -1.00)	-1.35 (-1.78 to -0.650)	1.491	0.475
BMD at femur	0.840 (0.763-0. 910)	0.813 (0.741-0.863)	0.830 (0.767-0.969)	1.469	0.480
DEXA at forearm	-2.10 (-3.0 to -0.68)	-1.60 (-2.55 to -0.70)	-1.30 (-2.52 to -0.80)	0.332	0.847
BMD at forearm	0.726 (0.572-0.824)	0.763 (0.625-0.824)	0.801 (0.656-0.847)	1.251	0.533

Notes: Data is median (Q1-Q3). The test of significance is Kruskal-Wallis H-test. Pairwise comparisons with Bonferroni correction for multiple tests is presented as letters.

This table shows a statistically significant difference in FRAX TBS score between the three groups. Pairwise comparison reveals a statistically significantly higher score in partially degraded versus normal.

Table (4): Correlations between TBS, DEXA and BMD at lumbar spine, neck femur and Forearm.

Measurement	Trabecular bone score category	
	r_s	p-value
DEXA t-score at lumbar spine	0.265	0.079
BMD of lumbar spine	0.243	0.108
DEXA t-score at neck femur	0.199	0.190
BMD of neck femur	0.186	0.221
DEXA t-score at forearm	0.047	0.761

BMD of forearm	-0.013	0.935

Notes: r_s = Spearman's correlation coefficient.

This table shows that: No Statistically significant correlation between TBS, DEXA t-score at lumbar spine, BMD of lumbar spine, DEXA t-score at femoral neck, BMD of femoral neck, DEXA t-score at forearm and BMD of forearm, emphasized by low strength of association.

Table (5): Correlations between TBS and QCT at lumbar spine and neck femur.

Measurement	Trabecular bone score category	
	r_s	p-value
QCT at L1	0.160	0.29
QCT at L2	0.098	0.521
QCT at L3	0.040	0.793
QCT at L4	0.192	0.206
QCT at L5	0.094	0.540
Average QCT at spine	0.112	0.465
QCT at RT neck femur	0.213	0.161
QCT at LT neck femur	0.085	0.577
Average QCT at neck femur	0.193	0.204

Notes: r_s = Spearman's correlation coefficient.

This table shows no statistically significant correlation between TBS and QCT at lumbar spine and at neck femur.

Table (6): Correlations between TBS and different measurements.

Measurement	Trabecular bone score category	
	r_s	p-value
Age(years)	-0.175	0.251
Body weight(kg)	0.163	0.285
Height(cm)	-0.396	0.007
BMI (kg/m^2)	0.334	0.025
Serum total Calcium(mg/dl)	0.226	0.135
Serum phosphorus(mg/dl)	0.056	0.714

Notes: r_s = Spearman's correlation coefficient.

This table shows statistically significant positive correlation between TBS and BMI (kg/m^2) and statistically significant negative correlation with height (cm). Also, there was no statistically significant correlation with other measurement.

Table (7): Predictors of BMD Categories {osteopenia/ osteoporosis (N=22) vs. normal (N=23)}

Risk factor	Univariate			Multivariate (Step 5)		
	p-value	COR	95% CI	p-value	AOR	95% CI
Diabetes Absent Present	0.006	r(1) 6.4	r(1) 1.7 – 23.8	0.072	r(1) 9.1	r(1) 0.82 – 100.9
Hypertension Absent Present	0.009	r(1) 9.2	r(1) 1.7 – 48.6			
IHD Absent Present	0.023	r(1) 5.6	r(1) 1.3 – 24.3	0.021	r(1) 52.3	r(1) 1.8 – 1507
Polypharmacy No Yes	0.001	r(1) 10.3	r(1) 2.5 – 41.8	-	-	-
History of fall	0.006			0.032		

No Yes		r(1) 10.5	r(1) 2 - 56		r(1) 22.5	r(1) 1.31 – 388
Body weight >85 kg ≤85 kg	0.005	r(1) 7	r(1) 1.8 – 27.5	-	-	-
Serum calcium >8.4 kg ≤8.4 kg	0.001	r(1) 10.3	r(1) 2.5 – 41.8	-	-	-
TBS >1.422 ≤8.1.422	0.035	r(1) 4.87	r(1) 1.12 – 21.2	0.015	r(1) 31.4	r(1) 1.9 – 511.8
QCT at lumbar spine >189 ≤189	0.001	r(1) 9.6	r(1) 2.45 – 37.6	0.004	r(1) 93.5	r(1) 4.3 – 2020.8

Notes: COR = crude odds ratio. AOR = Adjusted odds ratio. CI = confidence interval. r(1) = reference category. Test of significance is binary logistic regression (Backward elimination). Step 5 was reported.

This table shows the results of binary logistic regression, which was run to ascertain the effects of DM, hypertension, IHD, polypharmacy, history of fall, body weight ≤85 kg, and serum calcium ≤8.4 mg/dl, TBS ≤1.422, and qCT at lumbar spine ≤189 on the likelihood that geriatric participants will exhibit either osteopenia or osteoporosis. On univariate analysis, all these predictor variables were statistically significant. Accordingly, all these risk factors were entered in a multivariate analysis through binary logistic regression model using backward elimination. The model correctly classified 86.7% with 86.4% sensitivity, and 80% specificity. The model was statistically significant (χ^2 [5] = 37.920, P<0.001). Of the 9 predictor variables, only 4 were statistically significant independent predictors of osteopenia or osteoporosis, which are IHD, history of fall, TBS ≤1.422, and QCT at lumbar spine ≤189. Geriatric participants with IHD, history of fall, TBS ≤1.422, and QCT at lumbar spine ≤189 have 52.3-, 22.5-, 31.4-, and 93.5-times higher odds to exhibit osteopenia or osteoporosis.

Table (8): TBS, FRAX, and QCT scores in the three BMD categories at whole body.

		Lumbar spine			
Measurement	Normal	Osteopenia	Osteoporosis	H [2]	p-value
Trabecular bone score (TBS)	1.38 (1.28-1.49)	1.31 (1.17-1.40)	1.33 (1.25-1.38)	4.113	0.128
FRAX score	7.00 (5.30-11.00) a	9.90 (6.45-13.7) a, b	17.0 (14.0-20.75) b	13.880	0.001
FRAX TBS	6.50 (5.10-8.80) a	9.05 (7.02-15.25) b	16.5 (11.5-20.0) b	15.931	<0.001
qCT at lumbar spine	226 (198.0-238.0)	172 (156.7-231.5)	164.0 (131.5-218.5)	6.931	0.031
		Neck femur			
Trabecular bone score (TBS)	1.45 (1.32-1.49)	1.33 (1.23-1.41)	1.28 (1.23-1.31)	5.459	0.065
FRAX score	5.50 (4.25-7.15) a	10.0 (7.0-13.5) b	17.0 (8.65-21.75) b	13.139	0.001
FRAX TBS	5.05 (3.42-6.42) a	8.90 (7.15-12.0) b	16.5 (9.55-21.5) b	16.004	<0.001
qCT at neck of femur	241.5(153.5-302.8)	236 (166.5-322.5)	128 (52.3-235.3)	3.367	0.186
		Forearm			
Trabecular bone score (TBS)	1.32 (1.20-1.47)	1.33 (1.24-1.42)	1.36 (1.29-1.44)	0.491	0.782
FRAX score	5.20 (4.37-7.50) a	10.0 (6.50-12.5) b	12.5 (7.87-18.5) b	16.006	<0.001
FRAX TBS	5.60 (3.87-7.80) a	8.80 (7.15-11.5) b	10.9 (7.55-16.3) b	11.302	0.004

Notes: Data is median (Q1-Q3). The test of significance is Kruskal-Wallis H-test. Pairwise comparisons with Bonferroni correction for multiple tests is presented as letters (similar letters = insignificant difference, different letters = significant difference)

Table (9): Pairwise comparisons for significantly different parameters of the whole body.

	Lumbar spine					
Pair	FRAX		FRAX TBS		qCT at lumbar spine	
	Unadjusted p	Adjusted p	Unadjusted p	Adjusted p	Unadjusted p	Adjusted p
Normal vs. osteopenia	0.075	0.226	0.016	0.049	0.681	1.000
Normal vs. osteoporosis	<0.001	0.001	<0.001	0.001	0.045	0.135
Osteopenia vs. osteoporosis	0.022	0.067	0.050	0.150	0.027	0.080
		Neck femur				
	Unadjusted p	Adjusted p	Unadjusted p	Adjusted p		
Normal vs. osteopenia	0.002	0.005	0.001	0.002		
Normal vs. osteoporosis	0.003	0.009	0.001	0.003		
Osteopenia vs. osteoporosis	0.225	0.674	0.163	0.490		
		Forearm				
	Unadjusted p	Adjusted p	Unadjusted p	Adjusted p		
Normal vs. osteopenia	0.006	0.019	0.011	0.033		
Normal vs. osteoporosis	<0.001	<0.001	0.001	0.004		
Osteopenia vs. osteoporosis	0.166	0.497	0.418	1.000		

Notes: p-values are adjusted by Bonferroni correction for multiple tests.

Tables (8) and (9) show:

1- At lumbar spine: A statistically significant difference between the three groups as regards FRAX score, FRAX TBS score, and QCT score at lumbar spine. Pairwise comparisons revealed a statistically significantly higher FRAX in osteoporosis vs. normal bone density (p=0.001) but not between osteopenia vs. normal (p=0.226) and osteoporosis (p=0.067).

- Pairwise comparisons also revealed a statistically significantly higher FRAX TBS score in osteoporosis vs. normal bone density (p=0.001) and between osteopenia vs. normal (p=0.0.049) but not between osteopenia vs. osteoporosis (p=0.150). On the other hand, pairwise comparisons with Bonferroni correction for multiple tests revealed no statistically significant difference in QCT score at lumbar spine between normal bone density vs. osteoporosis vs. (p=0.135), normal bone density vs. osteopenia (P=0.080), and between osteopenia vs. osteoporosis (p=1.000).

2- At neck femur: a statistically significant difference between the three groups as regards FRAX and FRAX TBS scores.

- Pairwise comparisons revealed a statistically significantly higher FRAX and FRAX TBS scores in osteopenia and osteoporosis vs. normal bone density. p-values for FRAX: Osteopenia vs. normal = 0.005, and osteoporosis vs. normal = 0.009), and p-values for FRAX TBS: Osteopenia vs. normal = 0.002, and osteoporosis vs. normal = 0.003), while there was no statistically significant difference between osteopenia vs. osteoporosis as regards FRAX score (P=0.674) and FRAX TBS (P=0.490).

3- At forearm: a statistically significant difference between the three groups as regards FRAX and FRAX TBS scores.

- Pairwise comparisons revealed a statistically significantly higher FRAX and FRAX TBS scores in osteopenia and osteoporosis vs. normal bone density. p-values for FRAX: Osteopenia vs. normal = 0.019, and osteoporosis vs. normal = 0.001), and p-values for FRAX TBS: Osteopenia vs. normal = 0.033, and osteoporosis vs. normal = 0.004), while there was no statistically significant difference between osteopenia vs. osteoporosis as regards FRAX score (P=0.497) and FRAX TBS (P=1.000).

Table (10): Correlations between FRAX score and FRAX (TBS) score with different measurements:

Measurement	FRAX score		FRAX (T.B.S) score	
	r_s	p-value	r_s	p-value
DEXA t-score at lumbar spine	-0.586	<0.001	-0.639	<0.001
BMD of lumbar spine	-0.587	<0.001	-0.632	<0.001
DEXA t-score at femoral neck	-0.700	<0.001	-0.683	<0.001
BMD of femoral neck	-0.712	<0.001	-0.697	<0.001
DEXA-t-score at forearm	-0.564	<0.001	-0.501	<0.001
BMD of forearm	-0.613	<0.001	-0.544	<0.001
QCT at L1	-0.436	0.003	-0.436	0.003
QCT at L2	-0.389	0.008	-0.355	0.017
QCT at L3	-0.510	<0.001	-0.469	0.001
QCT at L4	-0.352	0.018	-0.358	0.016
QCT at L5	-0.307	0.040	-0.318	0.033
Average QCT at lumbar spine	-0.468	0.001	-0.440	0.002
QCT at right femoral neck	-0.102	0.503	-0.138	0.365
QCT at left femoral neck	-0.073	0.636	-0.061	0.692
Average QCT at femoral neck	-0.067	0.660	-0.104	0.495
Age (years)	0.208	0.170	0.196	0.196
Body weight (kg)	-0.347	0.019	-0.381	0.010
Height (cm)	-0.203	0.181	-0.087	0.569
BMI (kg/m^2)	-0.171	0.262	-0.265	0.079
Serum total calcium (mg/dl)	-0.403	0.006	-0.427	0.003
Serum phosphorus (mg/dl)	-0.234	0.122	-0.286	0.057

Notes: r_s = Spearman's correlation coefficient.

This table shows that statistically significant negative correlation FRAX score and DEXA t-score at lumbar spine, BMD of lumbar spine, DEXA t-score at femoral neck, BMD of femoral neck, DEXA t-score at forearm, BMD at forearm, QCT at L1, L2, L3, L4, L5 and average QCT at lumbar spine, Body weight (kg) and Serum total calcium (mg/dl). Also, there was statistically significant negative correlation between and FRAX T.B.S score and DEXA t-score at lumbar spine, BMD of lumbar spine, DEXA t-score at femoral neck, BMD of femoral neck, DEXA t-score at forearm, BMD at forearm, QCT at L1, L2, L3, L4, L5 and average QCT at lumbar spine, Body weight (kg) and Serum total calcium (mg/dl).

Table (11): Trabecular bone score (TBS) and DEXA T-score at lumbar spine Crosstabulation.

Trabecular bone score	DEXA T-score at lumbar spine			
	Normal	Osteopenia	Osteoporosis	Total
Normal	14 (31.1%)	5 (11.1%)	3 (6.7%)	22 (48.9%)
Partially degraded	8 (17.8%)	6 (13.3%)	3 (6.7%)	17 (37.8%)
Degraded	1 (2.2%)	5 (11.1%)	0 (0%)	6 (13.3%)
Total	23 (51.1%)	16 (35.6%)	6 (13.3%)	45 (100%)

This table shows that there is poor agreement between TBS and DEXA T-score at spine. This explained by there are 14 (31.1%) of participants are normal by TBS and DEXA T-score, 6 (13.3%) of participants are partially degraded by TBS and osteopenia by DEXA and no participants have osteoporosis by TBS and DEXA, so, there are only 20 (44.4%) of participants have an agreement between TBS and DEXA for evaluation of osteoporosis.

6. DISCUSSION

This cross-sectional study was conducted at Geriatric inpatient and outpatient clinic, Mansoura university Hospital. This study was conducted on 45 elderly males (60 years and above) and postmenopausal females aged 50 years or above having one or more clinical risk factors for osteoporosis.

The main aim of this study was to evaluate the ability of lumbar spine TBS to assess bone microarchitecture and osteoporosis independent of bone mineral density.

The main results of this study were as follows:

The current study showed that there was a significant association between BMD and DM, as 55.6% of elderly people have diabetes. In agreement with the current study Yao et al. (2020) showed that bone metabolism can be influenced by type 2 diabetes mellitus and there was significant correlation between type 2 diabetes with BMD.

The current study showed that there was a significant association between low BMD and hypertension, there were 77.1% of elderly have hypertension. Consistent with the current study several studies (Cappuccio et al., 1999 and Yang et al., 2014). Their results found that women with hypertension had lower BMD at the femoral neck than those without hypertension.

The current study showed that there was a significant association between low BMD and IHD, there were 28.9% of elderly have IHD. In concordance with our results Paccou et al. (2015) showed that IHD is associated with lower BMD of the distal radius.

The current study showed that there was a significant association between low BMD and polypharmacy. In agreement with the current study Huang et al. (2019) showed that there was significant association in middle-aged and elderly men between low BMD and polypharmacy. In contrast with our results Shepperd (2013) showed that there was also no correlation between BMD and polypharmacy.

In this study we revealed that there was a significant association between low BMD and anti-epileptic drugs (AEDs) use. In line with the current study Meier & Kraenzlin (2011) stated that AEDs are associated with significant side effects such as decreased bone mineral density, altered bone turnover, and increased risk of fracture.

This study demonstrated that there was a significant association between low BMD and hyperparathyroidism. In harmony with the current study Jones et al. (2022) showed that Individuals with primary hyperparathyroidism have reduced bone mineral density according to DEXA.

The current study showed that there was a significant association between low BMD and dementia. In line with the current study Laudisio et al. (2016) showed that there was a significant association between BMD and dementia in elderly women. Also, Kang et al. (2018) concluded that Low BMD is correlated with cognitive impairment in community-dwelling adults aged 50 years and above.

The current study showed that there was a significant association between low BMD and malnutrition. This comes in agreement with Chen et al. (2019) who revealed that good nutrition resulted in higher BMD among elderly patients.

The present study showed that there was a significant association between low BMD and depression. This comes in agreement with Oh et al. (2012) who revealed that Depression was significantly associated with lower BMD in Korean older men. Although it remains unclear whether depression and osteoporosis share a biological pathway or there are some common risk factors (Oh et al., 2012).

In the present study it was revealed that there was a statistically significant difference in body weight and serum calcium between Normal, Osteopenia and Osteoporosis groups. Post-hoc tests revealed that body weight was statistically significantly lower in osteoporosis, and serum calcium was statistically significantly lower in both osteoporosis and osteopenia.

This comes in agreement with Hariri et al. (2019) and Chen et al. (2018) who revealed that low body mass is correlated with reduced BMD and an increased risk of osteoporosis.

Moreover, other studies explained that such relationship exists because heavy body weight could result in bone remodeling to compensate for the heavy mechanical load (Kang et al., 2014). Another study suggested that an increased BMI could subsequently increase the levels of leptin, which contributes to the relationship by promoting osteoblast production and functions (Russell et al., 2010). Other studies showed that early postmenopausal women with a low BMI have low BMD compared with women with a higher BMI, further supporting the positive relationship between the two variables (Bjarnason & Christiansen, 2000).

Also, in concordance with the present study Rai & Anand (2015) showed that there was significant association between BMD and serum calcium levels in elderly patients. Also, Alghadir et al. (2016) showed that there was significantly positive correlation between BMD and serum calcium levels.

Regarding the correlation between the three TBS categories regarding (DEXA, BMD at spine, femur, and forearm), (FRAX and FRAX TBS), and (QCT scores at spine and femur), the present study showed that there was statistically significant difference in FRAX TBS score between the three groups.

This was supported by the findings of the meta-analysis by McCloskey et al. (2016) concluded that TBS is a significant predictor of fracture risk independently, addition of TBS to FRAX didn't improve the fracture prediction significantly.

However, Leslie et al. (2013) showed that a combination of TBS and FRAX may yield an improvement in the predictive ability of osteoporotic fractures over using either of these alone. However, many of the risk factors included in FRAX were significantly associated with TBS.

Regarding the correlations between TBS and (DEXA and BMD at lumbar spine, neck femur and Forearm), it was revealed that there was no statistically significant correlation between TBS and DEXA t-score and BMD of different sites.

This was supported by Kim et al. (2018) who revealed that there was no significant correlation between TBS and areal bone mineral density (aBMD) in postmenopausal patients under thyrotropin suppressive therapy. Also, there was no significant difference in TBS according to DXA, BMD status.

In agreement with Leib et al. (2014) who revealed that in several cross-sectional studies on elderly women in Europe, North America and Asia, there was a weak correlation between TBS and BMD values.

Also, Hassan et al. (2014) revealed that comparing subjects suffering from osteopenia or osteoporosis with those with normal BMD; using DEXA at lumbar site; there were highly statistically significant differences were found in BMD and its T-score by using DXA, QCT or even OST.

Also, the current study showed that there was no statistically significant correlation between TBS and QCT at lumbar spine and neck femur.

This was supported by Langsetmo et al. (2016) revealed that no significant correlations between TBS and lumbar spine volumetric BMD assessed by QCT in older men especially with high body mass index.

However, Amstrup et al. (2016) revealed that Correlations between distal and central site measurements of the hip and of the tibia and radius showed weak to moderate correlation between volumetric BMD by spine and hip- peripheral QCT (HR-pQCT) and QCT. TBS correlated with QCT at the lumbar spine and to trabecular indices of HR-pQCT at the radius and tibia in post-menopausal women.

While Brunerova et al. (2016) showed that TBS was significantly correlated with QCT parameters in hemodialysis patients, the disagreement with the current study was due to the difference in inclusion criteria.

The current study showed that there was statistically significant negative correlation between TBS score and FRAX-TBS score.

In concordance with the current study Kim et al. (2016) showed that there was statistically significant negative correlation between TBS score and FRAX-TBS score. Also, McCloskey et al. (2016) concluded that TBS is a significant predictor of fracture risk independently. Also, Shevroja et al. (2023) showed that TBS is a significant predictor of fracture risk independent of FRAX and that the adjustment of FRAX for TBS resulted in a small but significant increase in fracture risk prediction.

The current study showed that there was statistically significant negative correlation between TBS with height. Consistent with the current study Stachowska et al. (2021) revealed that TBS was significantly correlated with height. Also, Pouillès et al. (2021) found significant negative correlation between TBS with height in postmenopausal women. However, Kim et al. (2016) observed a significant positive correlation between height and TBS in female group, and in the male group a significant negative correlation between weight and TBS was observed.

The current study showed that there was statistically significant positive correlation between TBS and BMI

(kg/m2). In agreement with the current study Torgutalp et al. (2019) showed that there was significant positive correlation between TBS and BMI, the same results were reported by Bonaccorsi et al. (2020). Moreover, Adel et al. (2020) showed that Lumbar spine TBS was directly correlated with BMI in Egyptian male patients with ankylosing spondylitis. In contrast, Olmos et al. (2020) reported that TBS values correlated negatively with BMI.

Regarding the validity of predictors in TBS categories, QCT at L1 at cutoff value of ≤158 can discriminate partially degraded/degraded from normal with 43.5% sensitivity, and 90.9% specificity.

Our results consistent with Rehman et al. (2002) showed that QCT at L1 at cutoff value for lumbar spine BMD values 93% specificity and 46% sensitivity.

Regarding the predictor variables of osteopenia/ osteoporosis, the results of binary logistic regression, which was run to ascertain the effects of DM, hypertension, IHD, polypharmacy, history of fall, body weight ≤85 kg, and serum calcium ≤8.4 mg/dl, TBS ≤1.422, and QCT at lumbar spine ≤189 on the likelihood that participants will exhibit either osteopenia or osteoporosis.

In agreement with our study, Khinda et al. (2022) in univariable and multivariable regression analysis, showed that variables independently influencing the risk of osteoporosis and osteopenia was higher systolic blood pressure and higher body mass index was observed to be a significant protective factor against the risk of osteoporosis and osteopenia.

As well, Bilha et al. (2021) showed that in multiple regression analysis, diabetes duration negatively predicted femoral neck BMD in T1D, while BMI was a positive predictor for lumbar spine and femoral neck BMD in T2DM.

Also, Huang et al. (2019) showed that polypharmacy is associated with low BMD and osteoporosis in elderly men.

In agreement with our study, Lin et al., (2014) history of fall is strongly associated with osteoporosis in elderly women.

The present study showed that 1-at lumbar spine: A statistically significant difference between the three BMD groups as regards FRAX score, FRAX TBS score and QCT score at lumbar spine.

Our results consistent with Pepe et al. (2021) who aimed to test if FRAX, without or with BMD values, also adjusted for trabecular bone score (TBS) was able to identify subclinical carotid atherosclerosis, as compared to DEXA values. They found that at lumbar spine: the prevalence of osteoporosis and FRAX BMD, TBS-adjusted FRAX both were higher in group A compared to group B.

2-at neck femur: a statistically significant difference between the three groups as regards FRAX and FRAX TBS scores.

Osteoporosis and osteopenia both lead to an increased risk of hip fractures in patients, which can lead to disability. Tomasevic et al. (2018) compared the fracture risk at neck femur (FRAX) between these 2 conditions, finding that patients suffering from osteopenia at neck femur had a significantly higher fracture risk because of their weight compared to those with osteoporosis, whereas patients with osteoporosis had a higher fracture risk because of previous hip fractures compared to those with osteopenia.

3- at forearm: a statistically significant difference between the three groups as regards FRAX and FRAX TBS scores.

This was supported by Øyen et al. (2011) who revealed that the prevalence of osteoporosis in patients with distal radial fractures is high compared with that in control subjects, and osteoporosis is a risk factor for distal radial fractures in both women and men.

FRAX score is a commonly used as a Fracture Risk Assessment tool, the above results showed that the Fracture Risk was significantly higher in Osteopenia and osteoporosis cases compared to matched controls.

Also, Li et al. (2021) concluded that fracture risk using FRAX score increases with decreasing BMD measurement parameters and anthropometric indicators.

The present study shows a statistically significant negative correlation between FRAX score, FRAX TBS and (DEXA t-score and BMD of lumbar spine, femoral neck and forearm), QCT at lumbar spine, Body weight and Serum total calcium.

In agreement with the current study, Silva et al. (2013) showed that Lumbar spine abnormal BMD was positively correlated with all QCT volumetric BMD measures at lumbar spine, femoral neck. The strongest association was with QCT trabecular volumetric BMD at lumbar spine. The strength of the association between Femoral neck integral volumetric BMD by QCT and TBS was greater than that between femoral neck integral volumetric BMD by QCT and lumbar spine abnormal BMD.

Moreover, Shin et al. (2019) showed that TBS was positively correlated with all BMD values, but the correlation coefficients were lower than the r values between the femur and the lumbar spine BMD values. We observed a moderate correlation between TBS and lumbar spine BMD and negative correlations between TBS and age or BMI.

Our study shows that, there is poor agreement between TBS and DEXA T-score at spine, this explained by there are only 14 (31.1%) of participants are normal by TBS and DEXA T-score, 6 (13.3%) of participants are partially degraded by TBS and osteopenia by DEXA and no participants have osteoporosis by TBS and DEXA, so, there are only 20 (44.4%) of participants have an agreement between TBS and DEXA for evaluation of osteoporosis.

Approximately, all studies using TBS and DEXA disagree with this poor agreement and showed that there is a good agreement and positive association between TBS and DEXA.

It's considered a limitation in our study, as there is poor agreement between TBS and DEXA for evaluation of osteoporosis and that explained by small sample size. So, TBS alone can't be used and not favorite on DEXA in assessing osteoporosis as DEXA is still the gold standard for diagnosis osteoporosis.

To the best of our knowledge this is the first study assessing the utility of TBS discriminating osteopenia/ osteoporosis and assessing bone microarchitecture from normal elderly individuals.

Our study is limited by small sample size, being a single center study and being the first study to use TBS, DEXA and QCT for evaluating osteoporosis.

7. CONCLUSION

TBS has a limited association with direct measurements of bone micro-architecture, can't be used alone to diagnose primary osteoporosis and may be a useful adjunct to BMD, DEXA and QCT for evaluation of osteoporosis, fracture risk detection and prediction. TBS score is lower in older male than postmenopausal female. No correlation between DEXA or BMD and TBS score in evaluation of osteoporosis and there is no association between TBS and QCT in evaluation of bone microarchitecture and osteoporosis. The current study was limited by small sample size, being a single center study and relatively no follow up period. Further studies with larger sample size and longer follow-up are needed to confirm our results and to identify risk factors of fracture.

References:

[1] Adel Y, El Adalany MA, Bassiouni SARAK (2020): Performance of bone mineral density and trabecular bone score in assessment of bone quality in Egyptian male patients with ankylosing spondylitis. Egyptian Rheumatology and Rehabilitation; 47: 1-8.

[2] Alghadir AH, Gabr SA, Al-Eisa ES, Alghadir MH (2016): Correlation between bone mineral density and serum trace elements in response to supervised aerobic training in older adults. Clinical interventions in aging 2016; 265-273.

[3] Amstrup AK, Jakobsen NFB, Moser E, Sikjaer T, Mosekilde L, Rejnmark L (2016): Association between bone indices assessed by DXA, HR-pQCT and QCT scans in post-menopausal women. Journal of bone and Mineral Metabolism, 34: 638-645.

[4] Bilha SC, Leustean L, Preda C, Branisteanu DD, Mihalache L, Ungureanu MC (2021): Bone mineral density predictors in long-standing type 1 and type 2 diabetes mellitus. BMC Endocrine Disorders, 21, 1-9.

[5] Bjarnason NH, Christiansen C (2000): The influence of thinness and smoking on bone loss and response to hormone

replacement therapy in early postmenopausal women. The Journal of Clinical Endocrinology & Metabolism, 85(2): 590-596.

[6] Bonaccorsi G, Cafarelli FP, Cervellati C, De Guio F, Greco P, Giganti M, Guglielmi G (2020): A new corrective model to evaluate TBS in obese post-menopausal women: a cross-sectional study. Aging Clinical and Experimental Research, 32: 1303-1308.

[7] Bousson V, Bergot C, Sutter B, Levitz P, Cortet B (2012): Trabecular bone score (TBS): available knowledge, clinical relevance, and future prospects. Osteoporos Int.; 23(5): 1489– 501.

[8] Brunerová L, Ronová, P, Verešová, J, Beranová, P, Potoèková, J, Kasalický P, & Rychlík, I (2016): Osteoporosis and impaired trabecular bone score in hemodialysis patients. Kidney and Blood Pressure Research, 41(3), 345-354.

[9] Cappuccio FP, Meilahn E, Zmuda JM, Cauley JA (1999): High blood pressure and bone-mineral loss in elderly white women: a prospective study. The Lancet, 354(9183): 971-975.

[10] Chen S C, Chung, W S, Wu, P Y, Huang, J C, Chiu, Y W, Chang, J M, & Chen, H C (2019): Associations among geriatric nutrition risk index, bone mineral density, body composition and handgrip strength in patients receiving hemodialysis. Nutrition, 65, 6-12.

[11] Chen Y Y, Fang, W H, Wang, C C, Kao, T W, Chang, Y W, Wu, C J, & Chen, W L (2018). Body fat has stronger associations with bone mass density than body mass index in metabolically healthy obesity. PloS one, 13(11), e0206812.

[12] Cormier C, Lamy O, Poriau S (2012): TBS in routine clinial practice: proposals of use Internet. Plan-les-Outes, Switzerland: Medimaps Group.

[13] Hariri AF, Almatrafi MN, Zamka AB, Babaker AS, Fallatah TM, Althouwaibi OH, Hamdi AS (2019): Relationship between body mass index and T-scores of bone mineral density in the hip and spine regions among older adults with diabetes: A retrospective review. Journal of obesity; 22:20-29.

[14] Hassan NE, El-Masry SA, El-Banna RA, El Hussieny MS (2014): Different tools for the assessment of bone mass among Egyptian adults. Open Access Macedonian Journal of Medical Sciences, 2(4), 557-561.

[15] Huang CF, Liu DY, Yang SH, Mao TY (2019): The Effects of Polypharmacy on Bone Mineral Density in Middle-Aged and Elderly Men. International Journal of Gerontology, 13.

[16] Jones AR, Simons K, Harvey S, Grill V (2022): Bone Mineral Density Compared to Trabecular Bone Score in Primary Hyperparathyroidism. Journal of clinical medicine, 11(2), 330.

[17] Kang D, Liu Z, Wang Y, Zhang H, Feng X, Cao W, Wang P (2014): Relationship of body composition with bone mineral density in northern Chinese men by body mass index levels. Journal of endocrinological investigation, 37, 359-367.

[18] Khinda R, Valecha S, Kumar N, Walia JPS, Singh K, Sethi S, Singh A, Singh M, Singh P, Mastana S (2022): Prevalence and Predictors of Osteoporosis and Osteopenia in Postmenopausal Women of Punjab, India. International journal of environmental research and public health, 19(5), 2999.

[19] Kim D, Cho SK, Kim JY, Choi YY, Sung YK (2016): Association between trabecular bone score and risk factors for fractures in Korean female patients with rheumatoid arthritis. Modern rheumatology, 26(4):540-545.

[20] Kim H-A, Lee HY, Jung J-Y, Suh C-H, Chung Y-S, Choi YJ (2019): Trabecular bone score is a useful parameter for the prediction of vertebral fractures in patients with polymyalgia rheumatica? J Clin Densitom. 2019

[21] Kim K, Kim IJ, Pak K, Kim SJ, Shin S, Kim BH, Kim SS, Lee BJ, Jeon YK (2018): Evaluation of bone mineral density using DXA and cQCT in postmenopausal patients under thyrotropin suppressive therapy. The Journal of Clinical Endocrinology & Metabolism; 103(11):4232-40.

[22] Laudisio A, Fontana DO, Rivera C, Ruggiero C, Bandinelli S, Gemma A, Ferrucci L, Antonelli Incalzi R (2016): Bone mineral density and cognitive decline in elderly women: results from the InCHIANTI study. Calcified tissue international; 98:479-88.

[23] Leib E, Winzenrieth R, Aubry-Rozier B, Hans D (2014): Vertebral microarchitecture and fragility fracture in men: a TBS study. Bone 62:51–55.

[24] Leslie W D, Krieg, M A, Hans, D, & Manitoba Bone Density Program (2013): Clinical factors associated with trabecular bone score. Journal of Clinical Densitometry, 16(3), 374-379.

[25] Li H L, Shen, Y, Tan, L H, Fu, S B, Dai, R C, Yuan LQ, & Wu X Y (2021). Relationship between bone mineral density and fragility fracture risk: a case-control study in Changsha, China. BMC Musculoskeletal Disorders, 22(1), 1-8.

[26] Lin MR, Hwang HF, Lin PS, Chen CY (2014): Relations of osteoporosis and follow-up duration to recurrent falls in older men and women. Osteoporosis International, 25, 863-871.

[27] McCloskey E V, Odén, A, Harvey, N C, Leslie, W D, Hans, D, Johansson, H, & Kanis, J A (2016): A meta-analysis of trabecular bone score in fracture risk prediction and its relationship to FRAX. Journal of bone and mineral research, 31(5), 940-948.

[28] Meier C, Kraenzlin ME (2011): Antiepileptics and bone health. Therapeutic advances in musculoskeletal disease, 3(5), 235-243.

[29] Oh SM, Kim H C, Ahn, S V, Rhee, Y, & Suh, I (2012): Association between depression and bone mineral density in community-dwelling older men and women in Korea. Maturitas, 71(2), 142-146.

[30] Øyen J, Brudvik, C, Gjesdal, C G, Tell, G S, Lie, S A, & Hove LM (2011): Osteoporosis as a risk factor for distal radial fractures: a case-control study. JBJS, 93(4): 348-356.

[31] Paccou J, Edwards, M H, Ward, K A, Jameson, K A, Moss, C L, Harvey NC, Cooper C (2015): ischemic heart disease is associated with lower cortical volumetric bone mineral density of distal radius. Osteoporosis International, 26: 1893-1901.

[32] Pepe J, Della Grotta, G, Santori, R, De Martino, V, Occhiuto, M, Cilli, M, & Cipriani, C (2021): Lumbar spine bone mineral density and trabecular bone score-adjusted FRAX, but not FRAX without bone mineral density, identify subclinical carotid atherosclerosis. Journal of Endocrinological Investigation, 44: 1989-1995.

[33] Porter JL, Varacallo M (2022): Osteoporosis. Updated 2022 Feb 12. In: StatPearls Internet. Treasure Island (FL): StatPearls Publishing; 2022 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK441901/

[34] Pouillès JM, Gosset A, Breteau A, Trémollieres FA (2021): TBS in early postmenopausal women with severe vertebral osteoporosis. Bone, 142, 115698.

[35] Prince RL, Lewis JR, Lim WH, Wong G, Wilson KE, Khoo BC, Zhu K, Kiel DP, Schousboe JT (2019): Adding Lateral Spine Imaging for Vertebral Fractures to Densitometric Screening: Improving Ascertainment of Patients at High Risk of Incident Osteoporotic Fractures. J Bone Miner Res; 34(2):282-289.

[36] Rai SP, Anand BK (2015): Correlation Between Bone Mineral Density and Serum Calcium Level in Urban Clinic. Asian Journal of Pharmaceutical and Health Sciences, 5(1).

[37] Rehman Q, Lang T, Modin G, Lane NE (2002): Quantitative computed tomography of the lumbar spine, not dual x-ray absorptiometry, is an independent predictor of prevalent vertebral fractures in postmenopausal women with osteopenia receiving long-term glucocorticoid and hormone-replacement therapy. Arthritis & Rheumatism, 46(5): 1292-1297.

[38] Shepperd KN (2013): Relationship Between Bone Mineral Density & Muscle Strength Related to Protein Intake & Polypharmacy: Elderly, Greater than 55 Years of Age (Doctoral dissertation, Texas Woman s University).

[39] Shevroja E, Reginster JY, Lamy O, Al-Daghri N, Chandran M, Demoux-Baiada AL, Harvey NC (2023): Update on the clinical use of trabecular bone score (TBS) in the management of osteoporosis: Epidemiology of Musculoskeletal Health and Aging. Osteoporosis International, 34(9), 1501-1529.

[40] Shin YH, Gong HS, Lee KJ, Baek GH (2019): Older age and higher body mass index are associated with a more degraded trabecular bone score compared to bone mineral density. Journal of Clinical Densitometry, 22(2), 266-271.

[41] Silva BC, Leslie WD, Resch H, Lamy O, Lesnyak O, Binkley N, McCloskey EV, Kanis JA, Bilezikian JP (2014): Trabecular bone score: a noninvasive analytical method based upon the DXA image. J Bone Miner Res; 29(3):518-30.

[42] Silva BC, Walker MD, Abraham A, Boutroy S, Zhang C, McMahon DJ, Bilezikian JP (2013): Trabecular bone score is associated with volumetric bone density and microarchitecture as assessed by central QCT and HRpQCT in Chinese American and white women. Journal of clinical densitometry, 16(4), 554-561.

[43] Stachowska B, Halupczok-Żyła J, Kuliczkowska-Płaksej J, Syrycka J, & Bolanowski M (2021): Decreased Trabecular Bone Score in Patients With Active Endogenous Cushing's Syndrome. Frontiers in endocrinology, 11, 593173.

[44] Tomasevic-Todorovic S, Vazic A, Issaka A, Hanna F (2018): Comparative assessment of fracture risk among osteoporosis and osteopenia patients: a cross-sectional study. Open access rheumatology: research and reviews, 61-66.

[45] Torgutalp S S, Babayeva, N, Kara, Ö S, Özkan, Ö, Dönmez, G, & Korkusuz, F (2019): Trabecular bone score of postmenopausal women is positively correlated with bone mineral density and negatively correlated with age and body mass index. Menopause, 26(10), 1166-1170.

[46] Varacallo M, Davis DD, Pizzutillo P (2021): StatPearls Internet. StatPearls Publishing; Treasure Island (FL): Aug 30, 2021. Osteoporosis in Spinal Cord Injuries.

[47] Yang S, Nguyen ND, Center JR, Eisman JA, Nguyen TV (2014): Association between hypertension and fragility fracture: a longitudinal study. Osteoporosis International; 25:97-103.

[48] Yao X, Xu X, Jin F, Zhu Z (2020): The Correlation of Type 2 Diabetes Status with Bone Mineral Density in Middle-Aged Adults. Diabetes, metabolic syndrome and obesity: targets and therapy; 13: 3269–3276.