Original Article

The Correlation between Trabecular Bone Score and Lumbar Spine Bone Mineral Density in Patients with Normal and High Body Mass Index

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Received: 18 November 2017
Revised: 14 February 2018
Accepted: 04 March 2018

Abstract

Background: Trabecular bone score (TBS) measures the underlying quality of bone texture using dual-energy X-ray absorptiometry (DXA) images. The present study aimed to investigate the correlation between lumbar spine bone mineral density (BMD) and TBS, and subsequently determine whether the association varies with the body mass index (BMI).

Methods: Data from 548 patients were collected and categorized into three groups according to the relationship between BMD and age. BMD of the lumbar spine (LS) using DXA and TBS from DXA images were measured. Pearson's correlation coefficient (SPSS software, version 24.0) was used to investigate the association between LS-BMD and TBS, as well as the effect of BMI and age on these parameters. $P<0.05$ was considered statistically significant.

Results: The total mean TBS was 1.31 ± 0.12. LS-BMD and TBS values significantly decreased with age in both sexes. A statistically significant correlation was found between TBS and LS-BMD ($r=0.601$). An increase in BMI was associated with a higher LS-BMD score and a lower TBS level. The correlation coefficient between LS-BMD and TBS reduced as the BMI increased. By comparing TBS with BMD, the majority of the patients with osteopenia and osteoporosis had fully degraded and partially degraded TBS, respectively.

Conclusion: TBS was positively correlated with LS-BMD and decreased with age. Moreover, the extent of the correlation varied with respect to BMI.

What's Known

• It has been shown that body mass index (BMI) is positively correlated with bone mineral density (BMD) and negatively correlated with trabecular bone score (TBS). However, the complex associations between BMI, TBS, and BMD are unclear.

What's New

• For the first time, a systematic evaluation of BMI, TBS, and BMD has been performed in Iran.
• TBS correlated positively with BMD and decreased with age. In addition, the association between LS-BMD and TBS varies depending on the BMI value.

Introduction

Osteoporosis is a skeletal disease characterized by impaired skeletal strength, increased bone fragility, and excessive susceptibility to fractures due to low bone mass and abnormalities in the bone micro-architecture.[1] However, fractures could occur at different locations in the skeletal system; more commonly in the vertebrae, proximal femur, and distal forearm. Osteoporotic fractures occur frequently with a worldwide annual prevalence of up to 9 million (i.e., one fracture every 3 seconds) and are expected to rise over the next decades.[2] Disability, substantial pain, mortality rates up to 20%, and costs are some of the

burdens imposed by osteoporosis-related and fragility fractures.[3] A study has reported that the peak bone mass in a healthy Iranian population in Tehran was lower than in their European or American counterpart.[4] Several factors such as sex, age, weight, height, and body mass index (BMI) influence bone mineral density (BMD) and the possibility of osteoporotic fractures.[5]

Before the onset of fractures, osteoporosis can be easily diagnosed with the use of non-invasive bone mineral measurements.[6] The BMD is a useful diagnostic tool for the prediction of osteoporotic fracture risk and the dual-energy X-ray absorptiometry (DXA) measurement is the widely accepted technique.[3] A working group of the World Health Organization (WHO) has recommended the BMD test as the gold standard method for the diagnosis of osteoporosis; expressed by the T-score formula.[7] However, the BMD test does not provide any information about bone quality. In addition, evaluation of the micro-architecture of bone tissue (an important component of bone strength) is not possible with this method.[8] Only 70-75% of the variance in bone strength can be defined with the BMD test and the remaining 25-30% could be related to other factors such as micro-fractures, abnormal bone remodeling, altered bone micro-architecture, and the effect of other skeletal risk factors.[1]

Recently, several techniques have been developed to assess bone micro-architecture. Among the non-invasive methods, magnetic resonance imaging (MRI) and quantitative computed tomography (QCT) provide a direct measurement of bone micro-architecture. These techniques are useful due to their image characterization and technology. However, they are impractical for clinical management and routine screening because of the higher radiation dose, costs, and the fact that the patients must undergo additional assessments after DXA has been performed.[9]

Bone density measurement is a diagnostic method for osteoporosis and only assesses the bone mass but does not provide any information about bone quality. A new technique for the assessment of trabecular bone micro-architecture in the lumbar spine (LS) is the trabecular bone score (TBS), which is independent of BMD.[3] TBS is a new textural index that provides an indirect index of trabecular bone micro-architecture by evaluating changes in the gray-level texture from DXA images of LS. Since both the BMD and TBS evaluate the same region of the bone, TBS could be retrospectively applied to an existing DXA image without the need for any additional assessments.[10] In other words, TBS is an indirect measurement of bone micro-architecture that calculates the overall rate of local variations in gray levels through the projection of the 3D structure onto a 2D plane.[11] An experimental variogram is built by the transformation of gray-level variations (pixels) in several random directions; TBS is the slope at the origin of this variogram.[12]

Several studies have reported that information about the structural condition of bone micro-architecture could be obtained from TBS. Higher TBS values reflect a dense, strong, and fracture-resistant micro-architecture with tiny spaces between spans. On the other hand, a low TBS value means a weak and fracture-prone micro-architecture with large spaces between spans. TBS may be related to bone strength as a trabecular pattern index of the measured bone. Some human studies have noted a negative correlation between BMI and TBS, whereas a positive association between BMI and LS-BMD has been shown.[13, 14] Therefore, the complex associations between TBS, LS-BMD, and BMI remain unclear. The present study aimed to investigate the correlation between LS-BMD and TBS, and subsequently determine whether the association varies with BMI.

Patients and Methods

Patients

Data from 600 patients who referred to Tehran Resalat Hospital (Tehran, Iran) were collected and analyzed during January-August 2015. Demographic data included age, weight, height, BMI, menopausal status, habitual physical activity, alcohol consumption, and smoking. Note that menopause was defined as the permanent end of menstrual bleeding for at least one year. The BMI was calculated based on the measured weight (kg) and height (cm) using a stadiometer and a standardized balance-beam scale, respectively. All patients underwent BMD testing.

The exclusion criteria were BMI>37, a history of amenorrhea or oligomenorrhea before the age of 40, conditions affecting bone metabolism (e.g., thyroid and parathyroid disorders, liver or kidney disease, hematologic diseases; oophorectomy, malignant tumors, malabsorption syndrome, diabetes mellitus; ankylosing spondylitis, hyperprolactinemia, rheumatoid arthritis, cerebral infarction; angiopathy, hypertension, coronary artery diseases, infectious diseases, and myocardial infarction), previous pathological fractures, traumatic fractures within the previous year, and treated with specific medications (thyroid hormone, calcitonin, estrogens, glucocorticoids,

bisphosphonate, thiazide diuretics; parathyroid hormone, barbiturates, fluoride, and anti-seizure drugs). Based on these criteria, 52 individuals were excluded and the remaining 548 patients, aged 20-90 years, were evaluated.

Vertebral fractures were evaluated using the assessment software provided with the DXA device (Lunar Prodigy, GE Medical Systems, Madison, WI, USA). BMI (kg/m^2) was categorized according to the WHO classification as underweight (BMI<18.5), normal weight (18.5≤BMI<25), overweight (25≤BMI<30), or grade 1 obesity (30≤BMI<35). An additional group with 35≤BMI≤37 was defined since those with a BMI higher than 37 were excluded from the study.[15] Furthermore, the patients were categorized according to the relationship between BMD and age. Accordingly, three age groups were defined, namely group A: 20-40 years, group B: 41-60 years, and group C: older than 60 years. In doing so, the BMD after the age of 60 was significantly reduced.

Written informed consent was obtained from all the participants. The study protocol was approved by the Research Ethics Committee of Tehran Resalat Hospital, Tehran, Iran (IR. SBMU.RETECH.REC.1397.691).

Bone Mineral Density Measurement

BMD (g/cm^2) of the LS (L1–L4) was measured and analyzed using the Hologic QDR 4500A DXA device (Hologic, Bedford, MA, USA) and its corresponding software (version 12.60). A single device was used throughout the study and all DXA measurements were performed by the same skilled operator. The vertebrae body including posterior arches were scanned in the lateral and anteroposterior projections in the array and single-beam modes, respectively. All fractured vertebrae or those affected by arthritis were excluded from the analysis. Using the scanner software in default mode, the density was calculated. In accordance with the WHO classification criteria, based on the lower values of BMD at the LS, a T-score≤-2.5 SD (standard deviation) was considered osteoporosis. Osteopenia was defined as −1≥T-score>−2.5 SD and T-score>-1 SD was considered normal.[7]

Trabecular Bone Score Evaluation

TBS was evaluated by reanalyzing the anteroposterior DXA LS (L1-L4) scans using the TBS iNsight software version 2.10 (Medimaps, Pessac, France). The regions used for the TBS evaluation were the same as those used for the BMD measurement. TBS was calculated as the mean value of the individual measurements for each vertebra (L1-L4) and their combinations,

excluding any fractured vertebrae or those affected by arthritis. Based on the TBS scores, the patients were categorized into three groups, namely normal micro-architecture (NM) group (TBS³1.35), partially degraded micro-architecture (PDM) group (1.2<TBS<1.35), and fully degraded micro-architecture (FDM) group (TBS£1.20).[11]

Statistical Analysis

All variables were analyzed quantitatively and qualitatively using SPSS statistical software package (version 24.0). Descriptive statistics were expressed as means±SD. The Chi-square test was used for categorical variables. TBS, LS-BMD, and BMI were normally distributed in our study population. Since the dependent variables were continuous, linear regression was performed to determine the correlation between the dependent variables (BMD and TBS) and independent variables (BMI, sex, and age). Pearson's correlation coefficient was used to compare quantitative variables. P<0.05 was considered statistically significant.

Results

Of the 548 participants, 64 (11.7%) and 484 (88.3%) were male and female patients, respectively. At the time of the BMD measurements, the mean age of the participants was 57.26±14.06 years. By associating the BMD with the three age groups (A-C), the BMD after the age of 60 years was significantly reduced. Most of the younger individuals refused participation in the study, resulting in a lower number of patients in the age group A (>40 years) than other groups (table 1). The total mean BMI was 27.68±4.79 kg/m^2. The total mean LS-BMD was -1.01±1.39 g/cm^2 with its maximum in the 20-40 years age group and a significant reduction beyond the age of 60. The total mean TBS was 1.31±0.12 with its maximum in the 20-40 years age group and a decreased value for all other age groups.

Since the dependent variables were continuous, linear regression was performed to determine the correlation between the dependent variables (BMD and TBS) and independent variables (BMI, sex, and age). The results showed a significant positive correlation between BMI and BMD (B=0.10, CI [0.078, 0.123], P<0.001), while there was a significant negative correlation between BMD and age (B=-0.04, CI [-.0.049, -0.034], P<0.001), as well as between BMD and sex (B=-0.55, CI [-0.87, -0.23], P<0.001). This meant, provided that other variables were fixed, a 1-unit increase in BMI produced 0.1-unit increase in BMD.

Table 1: Characteristics of the patients in different age groups in terms of age and BMD classification. Data expressed as mean±SD

Age groups		Number	BMI	TBS	BMD
Years	Mean±SD				
20-40	32.53±0.00	75	23.96±3.82	1.44±0.01	-0.42±1.08
41-60	52.44±5.43	234	28.27±4.35	1.34±0.10	-0.73±1.35
61-90	69.74±6.77	239	28.28±4.97	1.25±0.10	-1.47±1.37
Total	57.26±14.06	548	27.68±4.79	1.31±0.12	-1.01±1.39

Similarly, a 1-unit increase in age produced 0.049-unit reduction in BMD. BMD was 0.55-unit lower in female than male patients. The results also showed a statistically negative correlation between TBS and BMI (B=-0.003, CI [-.0.051, -0.016], P<0.001); age (B=-0.005, CI [-0.0056, -0.0044], P<0.001); and sex (B=-0.046, CI [-0.071, -0.020], P<0.001). Provided that other variables were fixed, a 1-unit increase in BMI or age produced 0.003-unit and 0.005-unit reduction in TBS, respectively. TBS was 0.046-unit higher in male than female patients.

Of the 548 participants, the study sample included 209 (38.1%) patients with NM-TBS, 236 (43.1%) with PDM-TBS, and 103 (18.8%) with FDM-TBS. The patients with PDM-TBS had higher mean age, higher BMI, and lower LS-BMD compared to those with NM-TBS. Similar conditions were also observed between patients with FDM-TBS compared to those with PDM-TBS or NM-TBS (table 2).

Although there was no correlation between BMI and TBS, the increase in BMI was related to a lower TBS (r=-0.30, P<0.001). The LS-BMD and BMI were positively correlated such that an increase in BMI was related to a higher LS-BMD (r=0.28, P<0.001). There was a significant positive correlation between TBS and LS-BMD (r=0.601, P<0.001). Based on the Pearson's correlation coefficient, while these correlations were statistically significant (P<0.001), the correlation between TBS and LS-BMD (r=0.601, P<0.001) appeared stronger than between TBS and BMI (r=-0.30, P<0.001) or between BMI and LS-BMD (r=0.28, P<0.001).

The mean TBS and the probability of osteoporosis are shown in figures 1 and 2, respectively. The probability of osteoporosis, in descending order, was observed among postmenopausal women (20.4), men (14.1), and premenopausal women (1.6). The mean TBS in postmenopausal women (1.27) was the lowest compared to men (1.35) and premenopausal women (1.42).

A comparison between TBS and BMD is shown in table 3. The fully degraded category of TBS included six patients with normal BMD (6:221), 42 with osteopenia (42:234), and 55 with

Table 2: Baseline characteristics of the patients stratified by TBS category. Data expressed as mean±SD

Characteristics	NM-TBS (n=209)	PDM-TBS (n=236)	FDM-TBS (n=103)
Age (years)	49.10±13.28	59.42±11.69	68.89±10.10
BMI (kg/m^2)	26.70±4.26	27.88±4.94	29.22±5.04
LS-BMD (g/cm^3)	-0.13±1.20	-1.27±1.13	-2.22±1.13

The mean TBS in men and wemon
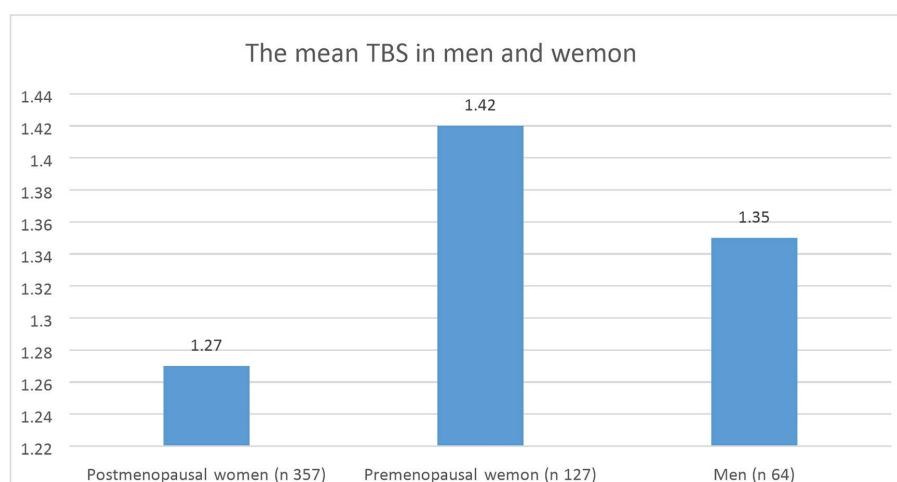
Figure 1: The mean TBS in men and women.
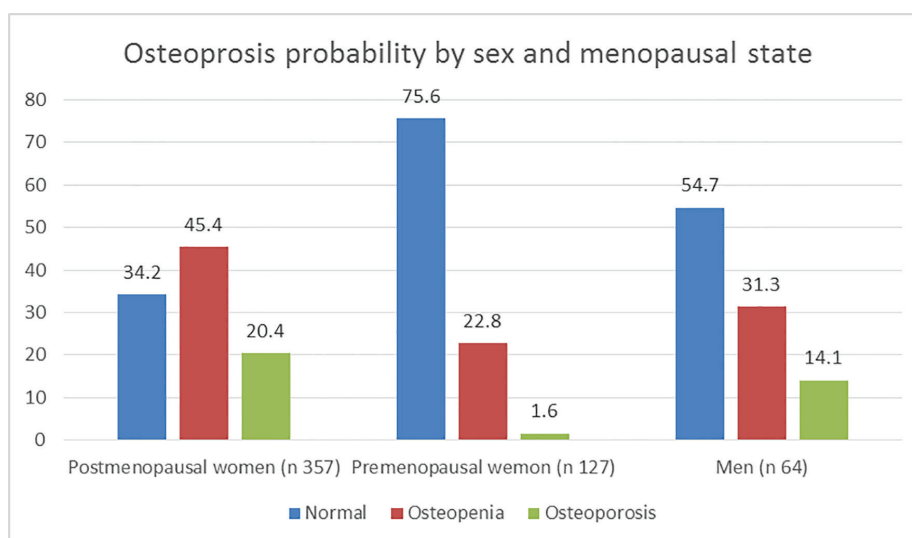
Figure 2: The probability of osteoporosis in terms of sex and menopausal status.

BMD	NM-TBS	PDM-TBS	FDM-TBS	Total [n (%)]
Table 3: The number of LS-BMD in different TBS categories				
Normal	157	58	6	221 (40.3%)
Low bone mass	49	143	42	234 (42.7%)
Osteoporosis	3	35	55	93 (17%)
Total [n (%)]	209 (38.2%)	236 (43%)	103 (18.8%)	548 (100%)

osteoporosis (55:93). Moreover, the TBS in 35 patients with osteoporosis (35:93) was partially degraded. Pearson's correlation coefficient indicated a strong correlation between TBS and LS-BMD (r=0.601, P<0.001).

Descriptive statistics and correlation between LS-BMD and TBS in different BMI groups are shown in table 4. An increase in BMI was correlated to a higher LS T-score, but lower TBS. Pearson's correlation coefficient between LS T-score and TBS was reduced as BMI increased.

Discussion

In the present cross-sectional study, the correlation between TBS and LS-BMD in patients aged 20-90 years was investigated. The results showed a significant negative correlation between TBS and age, and a significantly positive correlation between TBS and LS-BMD. The distribution of TBS varied by BMI such that

patients in the highest quintile of BMI had the lowest mean TBS. These findings provide useful information about TBS for clinicians to evaluate the risk of osteoporosis in individual patients.

The mean TBS in our study was 1.31±0.12, similar to a study conducted among healthy Chinese women (1.32±0.11).[1] The similarity could be due to the comparable study population (healthy individuals) and notable participation of women. The result of other studies in rheumatoid arthritis patients[1, 16] showed similar TBS values (1.13±0.19), which could be due to the effect the disease has on bone quality.

The correlation coefficient between TBS and LS-BMD among our female patients was 0.604, which was similar to reported values (0.580, 0.655) in some studies.[17, 18] However, some other studies reported lower values (0.320, 0.311), which could be due to the difference in the number of patients and the ratio between male and female participants.[19, 20] Note that in our study, the correlation coefficient between TBS

BMI	Number	TBS score*	LS T-score*	TBS vs. LS T-score**	P value
Table 4: Descriptive statistics and correlation between LS-BMD and TBS in different BMI groups					
<18.5	6	1.36±0.12	-1.95±1.36	1.0	<0.001
18.5-24.9	170	1.35±0.11	-1.30±1.29	0.680	
25-29.9	203	1.31±0.12	-1.10±1.40	0.739	
30-34.9	127	1.28±0.11	-0.68±1.35	0.702	
35-37	42	1.26±0.14	-0.32±1.40	0.521	

*Mean±SD, **Pearson's correlation coefficient

and LS-BMD values in male patients (0.576) was lower than in female patients (0.604). In a study by Bazzocchi and colleagues,[18] similar values were reported for male (0.555) and female (0.655) participants.

The two-dimensional DXA images include a superposition of cortical bone, trabecular bone, vertebral body, and posterior elements, and are impacted by soft tissues. Since BMI is suggestive of large body size, its effect on DXA images can affect TBS. Variation in soft tissue thickness influences the level of image noise, which analytically affects the initial slope of the variogram and in turn changes the TBS algorithm. The TBS algorithm has been modified to account for the possible effects of increased body mass on the accuracy of TBS measurement. However, TBS results from patients with BMI>37 kg/m^2 are still not considered valid.[21] Winzenrieth and colleagues studied the correlation between the 3-dimensional characteristics of trabecular bone micro-architecture. Based on the constructed DXA-like images from CT images, they showed that mathematically constructed Gaussian noise shifted the TBS scores downward while the rank order of the test samples was preserved.[22]

Our results showed a significant reduction (9%) in osteoporosis risk for a 1-unit increase in BMI. Other studies also indicated an association between BMI and osteoporosis, and reported a similar significant reduction (8%, 12%) in osteoporosis risk for a 1-unit increase in BMI. Moreover, a lower BMI was reported in women with osteoporosis compared to patients with normal BMD (23.7 versus 28.5 kg/m^2, P=0.001).[23]

The results of a comparison between BMD and TBS are shown in table 3. As shown, about 37% of osteoporosis diagnosed patients (based on their BMD) were in the PDM-TBS group. Also, 18% and 20% of the low bone mass reported patients had FDM-TBS and NM-TBS, respectively. These data indicated the need for TBS evaluation, especially when the BMD level points to osteopenia.

We found that an increase in BMI was related to a higher LS-BMD score, lower TBS, and a lower correlation between LS-BMD and TBS. A previous study also reported that an increase in BMI was associated with a lower correlation between LS-BMD and TBS.[21] Correlation between TBS and BMI is still the subject of controversy. In a study among 250 Italian women and men, no correlation was found between BMI and TBS.[18] Whereas another study reported a positive correlation between BMI and TBS in 1,474 postmenopausal Korean women.[24] In contrast, McCloskey and colleagues reported a weak negative correlation.[25] Consequently,

more studies are required to eliminate the existing uncertainties.

The main strength of our study was to demonstrate the potentials of TBS in diagnosing osteoporosis. In addition, for the first time, such a systematic evaluation of BMD, BMI, and TBS with a large sample size has been performed in Iran. Our data offer a valuable source of information to physicians to interpret a patient's TBS in their clinical management of osteoporosis. The main limitation of the study was the lack of evaluation of radiographic assessment of osteoarthritis. Worth mentioning, a previous study reported that TBS was unaffected by degenerative changes of the spine and their severity in radiologic images while affecting BMD measurement.[26] Finally, since the patients were recruited from a single center in Tehran, the results are not representative of the whole Iranian population.

Conclusion

TBS was positively correlated with BMD and decreased with age. The correlation between LS-BMD and TBS among patients varied depending on the BMI value. Further studies are required to determine whether the relationship between incident fractures and TBS also depends on BMI.

Conflict of Interest: None declared.

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