Original Article

Characteristics of Trabecular Bone Score [TBS] in Thai Osteopenic Postmenopausal Women

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Objective: To evaluate the characteristics and the correlation between trabecular bone score [TBS] and bone mineral density [BMD] in Thai osteopenic menopausal women.

Materials and Methods: A cross-sectional study of one hundred twenty Thai postmenopausal women aged 50 to 75 years old, who visited the menopause clinic in Ramathibodi Hospital between April 1 to September 30, 2015, with lumbar spine BMD [LS BMD] T-score between -1 and -2.5 and femoral neck BMD [FN BMD] T-score more than -2.5 were sent to evaluate the TBS of lumbar spine. The correlation analysis was performed to compare the TBS and BMD.

Results: One hundred fifty eight women were enrolled to study. The mean ± SD of age and years since menopause were 56.48±2.96 and 7.98±3.14 years, respectively and the median (range) body mass index was 23.96 kg/m^2 (17.09 to 34.80). The median LS BMD, FN BMD, and TBS of lumbar spine were 0.824 g/cm^2 (0.725 to 0.885), 0.652 g/cm^2 (0.548 to 0.838), and 1.272 (1.08 to 1.42), respectively. The correlation between TBS and LS BMD was minimal (R^2 0.134, adjusted R^2 0.127).

Conclusion: The correlation of TBS and axial BMD is minimal in Thai osteopenic women. The study confirmed these two parameters reflect the different properties of bone density and bone quality. For further study, the integration of TBS of lumbar spine, axial BMD, and clinical risk factors could be applied for more precisely fracture prediction and better management in osteopenic patient.

Keywords: Trabecular bone score, TBS, Bone mineral density, BMD, Osteopenia, Postmenopause

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Osteoporosis is a skeleton disorder characterized by compromised bone strength. Bone strength primarily reflects the integration of bone density and bone quality that results in bone fragility, susceptible to fracture(1). This is a burden in elderly because it is an asymptomatic disease that can lead to osteoporotic fractures. The fractures cause many of significant physical morbidity and associations with later mortality. The common sites of osteoporotic fracture are spine, hip, and forearm in which hip fracture is the greatest morbidity that lead to highest direct costs for health service all over the world(2). Osteoporosis is an important health problem worldwide and its complications are as prevalent as other common chronic diseases such as hypertension and diabetes, which is following the growth of the aging population.

It is estimated that there are 200 million osteoporosis patients worldwide, resulting in approximated nine million new osteoporotic fractures per year(3,4). From the National Health and Nutrition Examination Survey [NHANES] study in 2005 to 2010, the prevalence of osteopenia and osteoporosis in women older than 50 years old were 51.4% and 15.4%, respectively(5). In Thailand, data from a nation-wide survey between 2000 and 2001 revealed that the prevalence of osteoporosis in Thai women aged 40 to 80 years was 13.6% for femoral neck and 19.8% for lumbar spine. The age-specific prevalence of osteoporosis was more than 50% among Thai postmenopausal women older than 70 years(6). Additionally, the age-adjusted incidence of osteoporotic hip fracture was 289 women per 100,000 women(7). The consequence of hip fractures is a high mortality rate, irrespective of age, of around 17% in

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the first year that is caused by infection, especially septicemia, and pneumonia[8].

Osteoporosis diagnosis is defined by the World Health Organization [WHO] as a bone mineral density [BMD] of 2.5 standard deviation [SD] or less than the mean peak bone mass of the young female adult (T-score ≤-2.5), measured by dual-energy X-ray absorptiometry [DXA][9]. BMD from DXA evaluation calculated as the ratio of bone mineral content to the scanned area (express as g/cm^2), represents only bone density but do not provide any information about bone quality. In fact, areal bone density accounts for only 60% to 70% of the variation in bone strength[10]. The limitations of bone density assessment by DXA is that it does not precisely detect the fragility fractures[11,12]. Therefore, numerous bone quality assessment tools were developed to increase the precision in fragility fracture prevention, such as high-resolution peripheral quantitative computed tomography [HR-pQCT], high resolution magnetic resonance imaging [MRI], magnetic resonance spectroscopy, multi-detector computed tomography [MDCT] with finite element analysis [FEA], and trabecular bone score [TBS][13].

The advantages of TBS for bone quality assessment are low cost, comfortable, no additional operated time, and retrievable to any DXA image obtained from GE Lunar (Prodigy and iDXA; Medison, WI, USA) and Hologic (Dephi, QDR4500 and Discovery; Waltham, MA, USA) densitometers without any additional radiation exposure[14-17].

The objective of this study was to determine the characteristic of TBS in Thai osteopenic postmenopausal women and explore the correlation of TBS to the BMD. Furthermore, this present study is the first study of TBS in Thai osteopenic postmenopausal women.

Materials and Methods

Patients

The study included Thai postmenopausal women aged 50 to 75 years old, who visited the menopause clinic, Ramathibodi Hospital between April 1 and September 30, 2015 and received a BMD examination by DXA with a lumbar spine [LS] BMD T-score between -1 and -2.5 and femoral neck [FN] BMD T-score of more than -2.5. The patients were excluded if they had a history of lumbar or hip fractures, history of drug used that affected bone metabolism within one year, history of osteoarthritis or rheumatoid arthritis or others causes secondary osteoporosis, such as hyperthyroidism and hyperparathyroidism, and body mass index [BMI] of more than 35 kg/m^2. The study was approved by Ramathibodi Hospital Ethics Committee on Human research, Faculty of Medicine, Ramathibodi Hospital by IRB. Number (MURA) 2015/70 (3-9-2015).

Methods

All of the patients signed the informed consent before being enrolled to the study. One hundred twenty women that met the eligibility criteria were interviewed for baseline data and investigated for LS BMD, FN BMD, and TBS by DXA images. LS BMD and FN BMD were assessed using a fast area mode Hologic Discovery WDXA scanner (Hologic, Bedford, MA). All measurement procedures were performed according to the International Society for Clinical Densitometry [ISCD] recommendations by ISCD-certified densitometer technologists. Quality assurance procedures using a spine phantom were performed daily. The LS BMD root mean square [RMS] coefficient of variation and RMS SD were 0.69% and 0.006 g/cm^2, respectively. TBS assessment used TBS iNsight software version 2.1 (medimaps, Mérignac, France). TBS was measured on the same regions of interest [ROI] used for LS BMD and calculated as the mean value of the individual measurements for each vertebra and for every combination of ROI from L1 through L4 vertebrae. The TBS RMS SD and RMS coefficient of variation were 0.026 and 2.05%, respectively.

After 2008, TBS was introduced for assessing bone quality in part of skeletal microarchitecture. It used conventional DXA images of the lumbar spine to extract the gray-level texture of each lumbar vertebra, providing an indirect index of trabecular microarchitecture by the projection of the 3D structure onto a 2D plane. TBS is calculated as the slope of the log-log transform of the 2D variogram, where the slope characterizes the rate of gray-level amplitude variation. A steep variogram slope with a high TBS value is associated with better bone structure. In human cadavers' study[15], the significant correlations have been identified between TBS and 3-Dimension parameters of bone microarchitecture. Higher TBS scores reflects stronger and more fracture-resistant microarchitecture, whereas lower scores indicate weaker and more susceptible to fracture[16].

Statistical analysis

The correlation sample size was calculated using the correlation between LS BMD and TBS in prior study[10] in 2014 (r = 0.28), alpha error 0.05 (two

tailed), beta error 0.2. Statistical analysis was analyzed by using Stata version 14 (College Station, Texas: StataCrop LP, USA). The descriptive statistics were presented as the mean ± SD or median (minimum value to maximum value) in continuous data and the percentage in categorical data. Pearson's correlation coefficient was used to investigate whether there was a correlation between BMD and TBS. The statistical significant was assigned as *p*-value lower than 0.05.

Results

One hundred fifty-eight Thai postmenopausal women that had LS BMD T-score between -1 to -2.5 and FN BMD T-score more than -2.5 were enrolled. Thirty-eight women were excluded because they did not meet the inclusion criteria as they had underlying disease of hyperthyroid and were currently using of medications that affected bone metabolism, either raloxefene, tamoxifen, bisphosphonate, or anti-epileptic drugs. Therefore, 120 postmenopausal osteopenic women were eligible for the study. Baseline characteristics of the patients are summarized in Table 1. The mean age of the subjects was 56.48±2.96 years, median age of menopause was 49 years (range from 38 to 55 years), mean time since menopause was 7.98±3.14 years, and median BMI was 23.96 kg/m^2 (range from 17.09 to 34.80 kg/m^2).

The characteristics of TBS of Thai osteopenic of lumbar spine were 1.27 (1.08 to 1.42) [median (ranges)]. The present study found less correlation among TBS and LS BMD (R^2 0.134) and FN BMD (R^2 0.013) as shown in Table 2, Figure 1 and 2. The adjusted R^2 of correlation were 0.127 and 0.004 for LS BMD and FN BMD, respectively as shown in

Table 1. Baseline characteristics of osteopenic postmenopausal women

Subject characteristics	n (%) (total 120 cases)
Age (years), mean ± SD	56.48±2.96
Body weight (kg), mean ± SD	57.37±8.52
Height (cm), mean ± SD	154.45±5.03
BMI (kg/m^2), median (range)	23.96 (17.09 to 34.80)
Time since menopause (years), mean ± SD	7.98±3.14
Age of menopause (years), median (range)	49 (38 to 55)
History of MHT	29 (24.2)
MHT duration (month), median, (range)	6 (1 to 102)
Exercise	43 (35.8)
Exercise duration (minute/week), median (range)	30 (15 to 420)
LS BMD (g/cm^2), median (range)	0.824 (0.725 to 0.885)
FN BMD (g/cm^2), median (range)	0.652 (0.548 to 0.838)
TBS, median (range)	1.272 (1.088 to 1.424)

BMI = body mass index; MHT = menopausal hormonal therapy; LS BMD = lumbar spine bone mineral density; FN BMD = femoral neck bone mineral density; TBS = trabecular bone score

Table 2. Outcomes and correlations of LS BMD, FN BMD, and TBS

	Measurement result			Correlation with TBS	
	Median	Minimum	maximum	R^2	Adjusted R^2
TBS	1.272	1.088	1.424	-	-
LS BMD (g/cm^2)	0.824	0.725	0.885	0.134	0.127
FN BMD (g/cm^2)	0.652	0.548	0.838	0.013	0.004

TBS = trabecular bone score; LS BMD = lumbar spine bone mineral density; FN BMD = femoral neck bone mineral density

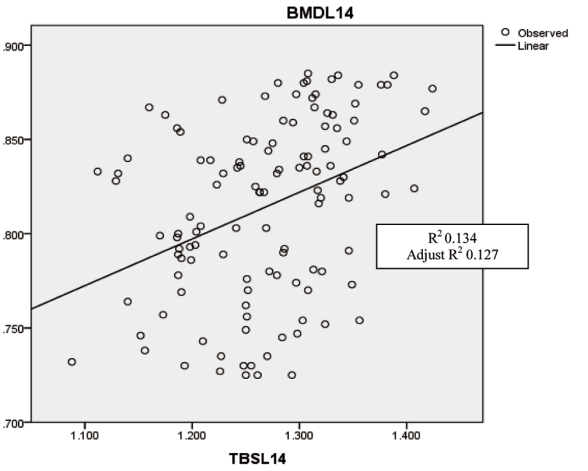

Figure 1. Correlation between lumbar spine bone mineral density [BMD] L1-4 and trabecular bone score [TBS] L1-4.

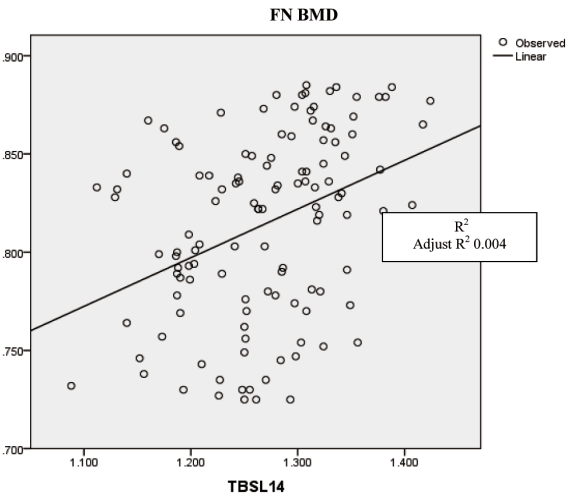

Figure 2. Correlation between femoral neck bone mineral density [FN BMD] and trabecular bone score [TBS] L1-4.

Table 3. Subgroup analysis of interested factors, LS BMD, and TBS

Factors	n	LS BMD (g/cm^2)		TBS	
		Mean ± SD	*p*-value	Mean ± SD	*p*-value
BMI (kg/m^2)					
<19	9	0.798±0.552	0.374	1.302±0.865	0.250
≥19	111	0.815±0.046		1.265±0.068	
Time since menopause (year)					
<8	65	0.813±0.051	0.716	1.273±0.068	0.418
≥8	55	0.816±0.042		1.262±0.717	
Exercise duration (minute/week)					
<90	80	0.807±0.045	0.027	1.261±0.066	0.121
≥90	40	0.827±0.048		1.282±0.075	

BMI = body mass index; TBS = trabecular bone score; LS BMD = lumbar spine bone mineral density

Table 2. The subgroup analysis of interesting factors affecting BMD and TBS consisted of BMI, time since menopause, and exercise time. Later, we found that only exercise time factor had a significant difference of BMD (*p*-value 0.027) in the regular exercise group (exercise at least 90 minutes/week) compare to the non-regular exercise group (exercise less than 90 minutes/week group). However, there was no significant difference of TBS, as shown in Table 3.

Discussion

From the present study, the results showed that the BMD of lumbar spine and femoral neck of Thai osteopenic women had low correlation to the TBS of lumbar spine, which is relevant to prior study[18-22]. Briot et al (2013)[18] demonstrated in the Osteoporosis and Ultrasound Study [OPUS], a multicenter prospective study of risk factors for postmenopausal osteoporotic fracture consisting of 2,409 European women, showed that performance of TBS was significant better than LS BMD for predicting the incidence of clinical osteoporotic fractures. The combination of TBS and LS BMD seem to be better for predicting the radiographic vertebral fractures. However, TBS had a low correlation with LS BMD (r = 0.48), total hip BMD (r = 0.38), and FN BMD (r = 0.31). Hans et al[19] evaluated the ability of TBS to predict the osteoporotic fracture in 29,407 postmenopausal women, and found that combining TBS and BMD, including spine, total hip, and femoral neck, was superior to either measure alone. However, there was low correlation between LS TBS and LS BMD (r = 0.48), total hip BMD (r = 0.26), and FN BMD (r = 0.27). Furthermore, Krueger et al[20] found that the TBS enhanced the BMD measurement for predicting osteoporotic fracture, even though, there was low correlation between LS BMD and TBS (r = 0.28).

Vasic et al[21], performed an Eastern European multicenter study. They revealed that the combination of BMD and TBS moderately improved the sensitivity and accuracy for osteoporotic diagnosis as compared to BMD alone. As expected, there was a low correlation between LS BMD, and TBS (R^2 0.19). Similarly, Popp et al[22] showed a low correlation between LS BMD and TBS (R^2 0.25) in a retrospective analysis study of 556 elderly women with a mean age of 76.1 years. Moreover, they also found the diagnostic performance of BMD (including at lumbar spine, femoral neck, and total hip) and TBS for osteoporotic fracture was improving when used in combination for LS BMD and TBS.

The "Os des Femmes de Lyon" cohort [OFELY study][23] showed moderate correlation of TBS and BMD. This might depend on the different ethnicity, mean age of study population, densitometer, or through TBS software as shown in Table 4. The OFELY study is a retrospective analysis of the determinants of bone loss in 1,039 volunteer women (aged 31 to 89 years) with an annual follow-up that assessed TBS in 560 postmenopausal women. They found that 35% of fracture occurred in osteopenic women with a low LS TBS threshold. They showed that the combination of LS BMD and TBS improved the prediction of osteoporotic fracture even in osteopenic women, even if the correlation of LS BMD and TBS was moderate (r = 0.58).

In the Asian populations, there was only the Japanese Population-based Osteoporosis [JPOS] study that was performed to find out the normative values of TBS in 4,550 women aged 15 to 79 years from seven areas throughout Japan[24]. The study showed that TBS of Japanese women decreased by 16.2% by age 63 and 19% by age 80 relative to that at age 45, which is consistent with the study in Caucasian women[25,26]. However, the mean TBS of Caucasian was higher than in Japanese. Furthermore, the correlation between TBS and BMD in postmenopausal women was low including LS BMD (r = 0.482) and FN BMD (r = 0.412).

Recently, ISCD (2015) recommended to use combination of TBS with lumbar spine BMD to assess the major osteoporotic fracture risk in postmenopausal women including vertebral, hip, and major osteoporotic fracture. However, TBS should not be used alone to determine the osteoporosis treatment initiation or monitoring the treatment response[27].

In summary, the evidence suggested that TBS and BMD reflect the different properties of bone quality and

Table 4. Correlation of TBS and BMD of lumbar spine from various studies

Correlation strength	Citation	Population	Ethnicity	Age (year) mean ± SD	Densitometer	TBS iNsight software version
Moderate (r = 0.58)	OFELY study, 2013[23]	560 PMW	French	66.2±7.9	Hologic QDR 4500A	1.7
Low (r = 0.48)	JPOS study, 2014[24]	1,307 PMW	Japanese	NA	Hologic QDR 4500A	1.9.2
Low (r = 0.48)	OPUS study, 2013[18]	1,007 women age >50 years	European	65.9±6.9	Hologic QDR 4500	1.8
Low (r = 0.33)	Manitoba study, 2011[19]	29,407 women age ≥50 years	Canadian	65.4±9.5	Prodigy GE	1.8
Minimal (r = 0.28)	Krueger et al., 2014[20]	429 PMW	Caucasian	71.6±8.0	Prodigy/iDXA GE healthcare	1.8.2
Minimal (R^2 = 0.19)	Vasic et al., 2014[21]	1,031 women age 45 to 85 years	Eastern European	62.9±8.7	Hologic Discovery & Prodigy GE	1.9.2
Minimal (R^2 = 0.25)	SEMOF study, 2015[22]	556 PMW	Swiss	76.1±3.0	Hologic QDR 4500A	1.8.2
Minimal (R^2 = 0.134)	This study	120 PMW	Thai	56.48±2.96	Hologic Discovery WDXA	2.1

TBS = trabecular bone score; PMW = postmenopausal women

Classify the correlation strength to 5 levels as: r = 0.9 to 1 is very high correlation, 0.7 to 0.89 is high correlation, 0.5 to 0.69 is moderate correlation, 0.3 to 0.49 is low or modest correlation and 0.0 to 0.29 is minimal if any correlation

bone density. Besides, the combination of the BMD and TBS of lumbar spine improves the osteoporotic fracture prediction, including sensitivity and accuracy, when compared to the BMD of lumbar spine alone. In non-osteoporotic women, the lowest quartile of TBS of lumbar spine helped redefining a significant subset of a high-risk fracture group. Data from 272 osteopenic women of the OFELY study, mean age of 66±8.1 years, the incidence of fractures in women with the lowest quartile of LS TBS was statistically significant higher than women with the highest quartile of LS TBS (25% versus 13%, *p*-value 0.026).

This is the first study that described the TBS characteristics and TBS correlation to the axial BMD in Thai osteopenic women that had a positive dependence trend of minimal correlation between TBS and axial BMD. For further study, we recommend the combination of the TBS, axial BMD, and other clinical risk factors for predict the fracture risk in Thai postmenopausal women, especially in the osteopenic group where the fracture prediction is still imperfect and where it would be most helpful to be able to recognize early and prevent morbidity.

Conclusion

In Thai osteopenic women, the correlation of TBS and axial BMD is minimal. This confirmed that these two parameters reflect the different perspective properties of bone density and bone quality. In the future, it is promising to integrate the TBS of lumbar spine, the axial BMD, and clinical risk factors for more precisely fracture prediction in osteopenic group and to improve the osteopenia and osteoporosis management.

What is already known on this topic?

Bone strength is composed of bone density and bone quality. WHO criteria uses only bone density using DXA to diagnose osteoporosis. As such, more than half of the osteoporotic fractures occurred in non-osteoporotic population. Many parameters of bone quality assessment have been developed and applied for better prediction of the osteoporotic fracture.

TBS, a novel grey-level texture measurement on lumbar spine DXA image, reflects bone quality, especially the bone microarchitecture. TBS and BMD had minimal to moderate correlation. Combination of TBS and BMD improved the osteoporotic fracture prediction.

What this study adds?

This is the first analysis study of TBS in Thai osteopenic postmenopausal women and the correlation between TBS and BMD in Thai osteopenic postmenopausal women was minimal.

Potential conflicts of interest

The authors declare no conflict of interest.

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