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Original article

Trabecular bone score as an additional therapeutic decision tool in osteoporosis and osteopenia

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ABSTRACT

Objectives: To evaluate the role of trabecular bone score (TBS), in addition to bone mineral density (BMD), and to aid decision making to initiate anti-osteoporotic treatment in postmenopausal women with osteopenia.

Methods: TBS was assessed in a cohort of Thai postmenopausal women with BMD of femoral neck (FN), total hip (TH), and lumbar spine (LS) performed at the Police General Hospital, Bangkok, Thailand from July 2019 to October 2020. We retrospectively reviewed hospital database for underlying diseases, medication, and fractures, including relevant imaging and vertebral fracture assessment (VFA). Patients with previous osteoporosis treatment, skeletal malignancy, high-energy trauma, and uninterpretable BMD were excluded.

Results: In total there were 407 postmenopausal women, including 115 with osteoporotic fractures. The mean TBS of the cohort was 1.264 ± 0.005. The proportion of osteoporotic subjects ranged from 9.1% by TH BMD to 27.0% by lowest BMD. In fractured patients, 21.7%–54.8% were found to have osteoporosis while osteopenia was found in 37.4%–43.5%. Among subjects with osteopenia and degraded TBS, fractures ranged from 21.7 to 50.9%. Addition of osteopenic subjects with degraded microarchitecture yielded a significantly higher number of subjects eligible for treatment with 3.25-fold increase in non-fractured participants, and 7 to 11 additional osteopenic patients should be treated to detect 1 fracture.

Conclusions: Addition of TBS helped capturing osteopenic women with high risk of fracture. Decision to treat osteopenic women with degraded TBS increased the number of patients receiving treatment. We recommend evaluating TBS in osteopenic women without fractures to aid therapeutic decision on treatment initiation.

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1. Introduction

Osteoporosis is a condition with high risk of fragility fracture from low-energy trauma. It is caused by a reduction in bone mass and compromised bone quality. Traditionally, central bone mineral density (BMD), which includes the lumbar spine (LS), total hip (TH), and femoral neck (FN) measured by dual-energy X-ray absorptiometry (DXA), is widely performed to predict fracture risk and guide therapeutic management of osteoporosis [1–3]. However, BMD only accounts for 60–70% of bone strength. More than half of fragility fractures are found in postmenopausal women who have osteopenia or even normal BMD [4–7]. Hence, the microarchitecture also plays a crucial role in determining bone strength and fracture risk.

Trabecular bone score (TBS) is a measurement of the variation in gray-level texture between adjacent pixels in 2-dimensional projection images [8,9]. It can be interpreted from the same set of images obtained from DXA, yielding more information on bone quality without additional cost or radiation on the patients. TBS has been found to reflect bone microarchitecture, as it correlates with bone volume, connectivity density, trabecular number, and also cortical thickness [10,11]. In vivo studies also show its positive correlation with bone stiffness [12]. Lower TBS reflects poorer bone quality despite equal BMD [11,13,14].

Prospective studies have shown that TBS can be used to predict major osteoporotic fracture (MOF) risk with an odd ratio of having a fragility fracture of as high as 3.8 (95% CI, 2.2–6.7) per a 1-SD

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decrease in TBS [15–17]. Women with osteopenia or normal BMD, but with TBS in the lowest quartile, were significantly at higher risk of sustaining a fragility fractures [18], indicating the capability of TBS in assessing bone quality not captured by BMD. However, the same study showed that osteoporotic women with TBS below the threshold did not suffer more fractures. Hence, TBS may be valuable in determining fracture risk and also the threshold for treatment initiation in women with non-osteoporotic BMD.

As per national and international osteoporosis guidelines [1,19–21], there is currently no clear description on the complementary use of TBS as an indication to start osteoporosis treatment in patients with questionable BMD or fracture risk assessment tool (FRAX®) or in patients whose BMD is insufficient to stratify fracture risks. Generally, anti-osteoporotic agents are initiated in those with osteoporotic BMD or those with a history of fragility fractures or those with a high risk of fragility fractures determined by FRAX [1,3,21–23]. However, it is evident that an increase in fracture risk contributed to by degraded bone microarchitecture, especially in osteopenic women, cannot be underestimated. Hence, several experts have suggested considering anti-osteoporotic treatment in patients with degraded TBS with BMD in the osteopenic range [8,18,24].

Similar to those of other countries, Thai national guidelines does not incorporate the use of TBS, possibly due to its lack of evidence in Thai population [3]. Therefore, we aim to evaluate the role of TBS to enhance decision making whether to initiate treatment in those traditionally ineligible for anti-osteoporotic treatment according to the guidelines but are at potentially high risk of fractures, which are osteopenic women with degraded bone microarchitecture in a cohort of Thai postmenopausal women with and without fragility fractures.

2. Methods

This study was performed in a cohort of Thai postmenopausal women with BMD measurement performed at the Police General Hospital, Bangkok, Thailand from July 1, 2019 to October 31, 2020. The study was approved by the institutional ethical committee (Ethical approval number Dh300796/63).

2.1. Subjects

We conducted a retrospective analysis within the cohort of postmenopausal women visiting the Police General Hospital for DXA scan. The DXA was either requested as a check-up program or after an osteoporotic fracture as a part of the hospital fracture liaison service. Patients were eligible if there were over 50 years of age, and had interpretable DXA images. The main exclusion criteria were previous or current use of anti-osteoporotic medication, and diseases that could lead to secondary osteoporosis, which included primary hyperparathyroidism, hyperthyroidism, hypogonadism, inflammatory bowel disease, and rheumatoid arthritis. We also excluded patients with skeletal malignancy, bone metastasis, previous spinal surgery including decompressive surgery, fixation, cement augmentation or intervertebral disc replacement.

2.2. Data extraction

2.2.1. Participant's characteristics

After informed consent, the hospital electronic database was thoroughly searched to gather required information of each participant, including age, weight, height, underlying diseases, and medication use. Personal history on cigarette use and alcohol abuse was also obtained. Estimated glomerular filtration rate (eGFR), and serum 25-hydroxy vitamin D (25(OH)D) were also collected if available. If the required information was absent from the database, the researchers would contact the participants by telephone to gather the missing information. The research was reviewed by Police General Hospital ethical committee.

2.2.2. Fracture evaluation

Each participant's medical record was analyzed for history of previous fragility fractures of the hip, spine, proximal humerus, and distal radius, either as coded ICD-10, narrated medical records, X-rays, computed tomography (CT), or magnetic resonance imaging (MRI). When available, vertebral fracture assessment (VFA) obtained during DXA was also examined for presence of vertebral compression fracture (VCF) defined as a collapse of more than 25% of vertebral height, which was defined as moderately (reduction of 26–40% of height) or severely (reduction of > 40% of height) deformed vertebral compression fracture by Genant's semi quantitative classification [25]. When evidence of fracture was marked in the ICD-10 or narrated medical records, relevant imaging was again checked to confirm the diagnosis. Fracture from high-energy trauma was excluded.

2.2.3. Bone densitometry

DXA scans of all subjects were performed using HORIZON A Hologic bone densitometry (Marlborough, MA, USA) by a single certified technologist, following recommendations from the International Society for Clinical Densitometry (ISCD). The DXA was calibrated by the manufacturer. Daily quality check was performed by the technologist. The least significant change (LSC) of the DXA at the institution was 0.022 g/cm^2, 0.029 g/cm^2, and 0.027 g/cm^2 for the LS, FN, and TH BMD, respectively. BMD were measured at LS, TH, and FN. The level of lumbar spine used for interpretation of BMD should not contain obvious artifacts or fractures. Any suspected level with BMD T-score of more than 1 standard deviation (SD) different from an adjacent vertebra was excluded from analysis. At least 2 vertebrae were needed for analysis.

2.2.4. TBS analysis

TBS was calculated by TBS iNsight version 3.0.2.0 from the slope of log-log transform 2-dimesional variograms projected from antero-posterior (AP) spine DXA image. To minimize inaccuracy from severe arthritis or fracture [26], we used the same region of interest (ROI) as LS BMD. Mean TBS was calculated from the selected vertebral levels. Degraded TBS was defined as TBS value less than or equal to 1.23 (TBS $\leq$ 1.23), partially degraded as TBS more than 1.23, but less than or equal to 1.31 (1.23 < TBS $\leq$ 1.31), and normal as TBS more than 1.31 (TBS >1.31) [8].

2.3. Statistical analysis

The demographic data of the subjects in the cohort were presented as frequency with percentage, and mean ± SD, depending on the type of variables. Subgroup analysis was done to compare the subjects with and without history of fragility fracture using Pearson's chi-square test, Fischer's exact test, or Student's *t*-test. After categorization of subjects into groups based on BMD and TBS, the percentage of subjects eligible for treatment was determined and compared between the traditional method using BMD alone, and

BMD with TBS. Additional patients with osteopenia and degraded TBS to be treated to capture 1 fractured patient =

$$\frac{1}{\left(\frac{\text{Number of fractured patients with osteoporosis}}{\text{Number of all patients with osteoporosis}}\right) - \left(\frac{\text{Number of fractured patients with osteoporosis OR osteopenia with degraded TBS}}{\text{Number of all patients with osteoporosis OR osteopenia with degraded TBS}}\right)}$$

We performed the same calculation using different sites of BMD and lowest BMD. All statistical analysis was performed using standard software package (Stata, version 13.0; StataCorp LLC, College Station, TX, United States).

3. Results

The cohort consisted of 407 Thai postmenopausal women. The mean age of the cohort was 68.1 ± 0.5 years old. The mean body mass index of the cohort was 24.2 ± 5.2 kg/m^2. Dyslipidemia, type 2 diabetes mellitus, and chronic kidney disease were present in 17.4%, 12.0%, and 18.7% of the cohort, respectively. History of fragility fracture was present in 115 (28.3%). The most common fracture was vertebral fracture (N = 62 (53.9%)), followed by hip (N = 35 (30.4%)), distal radius (N = 16 (13.9%)), and humeral fracture (N = 2 (1.7%)). The cohort has a mean LS, FN, and TH BMD of 0.868 ± 0.008, 0.638 ± 0.006, 0.763 ± 0.010. The mean BMD was significantly lower in the fracture group at all sites. The mean TBS of the whole cohort, the fracture group, and the non-fracture group was 1.264 ± 0.005, 1.244 ± 0.101, and 1.272 ± 0.099, respectively. The TBS was significantly lower in the fracture group (P = 0.011). The characteristics of the subjects with and without history of fragility fracture are described in Table 1.

3.1. Categorization of patients with BMD

We categorized patients into patients with normal BMD, osteopenia (−1.0 > BMD T-score > −2.5), and osteoporosis (BMD T-score ≤ −2.5) using either LS, FN, TH BMD, and the lowest central BMD for each patient. Of 407 subjects, 67(16.5%), 82(20.1%) and 37(9.1%) were classified as osteoporosis by LS, FN, TH BMD, respectively. Using the minimal BMD of each participant resulted in 110 (27.0%) of the cohort having osteoporosis. Subgroup analysis of subjects with previous fragility fracture, 38 (33.0%), 50 (43.5%), 25 (21.7%), and 63 (54.8%) were found to have osteoporosis according to their LS, FN, TH, and lowest BMD, while osteopenia was found in 44 (38.3%), 50 (43.5%), 48 (41.7%), and 43 (37.4%), respectively. From 292 women in the non-fracture group, osteoporosis was found in 29 (9.9%), 32 (11.0%), 12 (4.1%), and 47 (16.1%) by LS, FN, TH, and lowest BMD, respectively. The fracture group had the largest proportion of osteoporotic patients regardless of BMD sites considered. Categorization of the overall cohort, subjects with and without fragility fracture by each site of BMD is shown in Figs. 1-3.

3.2. Categorization of patients with BMD

TBS was used to classify the participants into 3 groups with normal, partially degraded, and degraded microarchitecture in Figs. 1-3. The individuals with normal TBS constituted 30.0% of the whole cohort, while it only made up 17.4% of the fracture group. Partially degraded group were similarly distributed in both fractured and non-fractured participants (34.8% and 33.9% respectively). In contrast, divergence can be seen in the degraded TBS group with 35.9% in the whole cohort, 47.8% in fractured and 31.2% in the non-fractured group.

3.3. Identifying fracture in osteopenic subjects with degraded microarchitecture

After categorization of subjects by BMD and TBS, we calculated the proportion of fractured participants in each category. From Fig. 2, a considerable proportion of osteopenic individuals with degraded bone microarchitecture had fractures regardless of BMD site measurement, with fractures identified in 22/75 (29.3%), 22/67 (32.8%), 28/55 (50.9%), and 15/69 (21.7%) for diagnosis made by LS, FN, TH, and lowest BMD, respectively.

3.4. Decision to treat with BMD and TBS

Figs. 1-3 also categorizes subjects according to their TBS. Addition of osteopenic subjects with degraded microarchitecture yields a higher number of subjects eligible to start anti-osteoporotic

Table 1
Characteristics of the cohort, participants with MOF, and participants without MOF.

	Total (N = 407)	Fracture (N = 115)	Non-fracture (N = 292)	P-value
Number of participants (%)	407 (100%)	115 (28.3%)	292 (71.7%)	
Age, yrs	68.1 ± 0.5	73.4 ± 10.0	66.0 ± 8.6	< 0.001
BMI, kg/m^2	24.2 ± 5.2	23.4 ± 4.2	24.5 ± 5.5	0.050
DLP, %	71 (17.4%)	23 (20%)	48 (16.4%)	0.394
DM Type 2 (%)	49 (12.0%)	22 (19.1%)	27 (9.3%)	0.006
CKD stage 3 or worse (%)	76 (18.7%)	37 (32.2%)	39 (13.4%)	< 0.001
Steroid use[a] (%)	16 (3.9%)	4(3.5%)	12 (4.1%)	0.768
Anticonvulsant/Antidepressant/Antipsychotics use[b] (%)	17(4.2%)	7(6.1%)	10(3.4%)	0.227
Trabecular bone score	1.264 ± 0.005	1.244 ± 0.101	1.272 ± 0.099	0.011
LS BMD, g/cm^2	0.868 ± 0.008	0.817 ± 0.184	0.887 ± 0.159	< 0.001
FN BMD, g/cm^2	0.638 ± 0.006	0.558 ± 0.126	0.669 ± 0.112	< 0.001
TH BMD, g/cm^2	0.763 ± 0.010	0.665 ± 0.188	0.801 ± 0.188	< 0.001

MOF, major osteoporotic fracture; BMI, body mass index; 25(OH)D, 25-hydroxyvitamin D; DLP, dyslipidemia; DM, diabetes mellitus; CKD, chronic kidney disease; LS, lumbar spine; FN, femoral neck; TH, total hip; BMD, bone mineral density.
[a] Steroid use is the use of an equivalent dose of 5 mg per day of prednisolone for 3 months or longer.
[b] Anticonvulsant, antidepressant or antipsychotics use is defined as a regular use of the aforementioned medication for three months or longer.

LS BMD					
TBS		Normal	Osteopenia	Osteoporosis	Total
	Normal	88 (21.62%) 1.376 ± 0.006	29(7.12%) 1.355 ± 0.006	5 (01.22%) 1.446 ± 0.107	122(29.97%) 1.374 ± 0.006
	Partially degraded	50(12.28%) 1.279 ± 0.003	75(18.42%) 1.271 ± 0.003	14(3.43%) 1.251 ± 0.003	139(34.15%) 1.272 ± 0.002
	Degraded	23(5.65%) 1.173 ± 0.009	75(18.42%) 1.165 ± 0.009	48(11.79%) 1.162 ± 0.007	146(35.87%) 1.165 ± 0.005

FN BMD					
TBS		Normal	Osteopenia	Osteoporosis	Total
	Normal	55)13.51%(1.385 ± 0.008	61)14.98%(1.356 ± 0.005	6(1.47%) 1.450 ± 0.086	122(29.97%) 1.374 ± 0.006
	Partially degraded	35(8.59%) 1.283 ± 0.003	76(18.67%) 1.271 ± 0.003	28(6.87%) 1.261 ± 0.005	139(34.15%) 1.272 ± 0.002
	Degraded	31(7.61%) 1.155 ± 0.017	67(16.46%) 1.168 ± 0.007	48(11.79%) 1.167 ± 0.006	146)35.87%(1.165 ± 0.005

TH BMD					
TBS		Normal	Osteopenia	Osteoporosis	Total
	Normal	95(23.34%) 1.375 ± 0.005	22(5.40%) 1.374 ± 0.024	5(1.22%) 1.360 ± 0.023	122(29.97%) 1.374 ± 0.006
	Partially degraded	90)22.11%(1.277 ± 0.002	39)9.58%(1.266 ± 0.004	10)2.45%(1.247 ± 0.005	139(34.15%) 1.272 ± 0.002
	Degraded	69)16.95%(1.164 ± 0.009	55)13.51%(1.168 ± 0.006	22)5.40%(1.162 ± 0.010	146)35.87%(1.165 ± 0.005

Lowest BMD					
TBS		Normal	Osteopenia	Osteoporosis	Total
	Normal	51)12.53%(1.388 ± 0.008	61)14.98%(1.358 ± 0.005	10)2.45%(1.398 ± 0.054	122(29.97%) 1.374 ± 0.006
	Partially degraded	20)4.91%(1.286 ± 0.003	85)20.88%(1.273 ± 0.003	34)8.35%(1.259 ± 0.004	139(34.15%) 1.272 ± 0.002
	Degraded	11)2.70%(1.175 ± 0.011	69)16.95%(1.163 ± 0.009	66)16.21%(1.166 ± 0.006	146)35.87%(1.165 ± 0.005

■ = Very high risk, ■ = High risk, ■ = Intermediate risk, ■ = Low risk

(Risk stratification modified from [16])

BMD, bone mineral density; TBS, trabecular bone score; LS, lumbar spine; FN, femoral neck; TH, total hip

Fig. 1. Categorization of the cohort by BMD and TBS.
BMD, bone mineral density; TBS, trabecular bone score; LS, lumbar spine; FN, femoral neck; TH, total hip.

medication regardless of site of BMD measured, and history of fracture (all P-values < 0.05). In the whole cohort, TBS increases the decision to treat from 67(16.5%) to 142(34.9%), 82(20.1%) to 149(36.6%), 37(9.1%) to 92(22.6%) and 110(27.0%) to 179(44.0%) when osteoporosis and osteopenia was categorized by LS, FN, TH, and lowest BMD, respectively. In the fracture group, the addition of TBS resulted in a similar finding, but was less pronounced, especially when the lowest BMD was used with an increase from 63(54.8%) to 78(67.8%) (P-value 0.042) and a proportion of additional treatment of 1.24. Decision to treat in the non-fracture group also increased significantly when osteopenic subjects degraded TBS were included. The proportion of treated patients increased 3.25 folds TH BMD was applied, increasing from 12 (4.1%) to 39 (13.4%). The change was less obvious with lowest BMD with an increase

LS BMD					
TBS		Normal	Osteopenia	Osteoporosis	Total
	Normal	12 (10.43%) 1.364 ± 0.009	6 (5.21%) 1.366 ± 0.015	2 (1.73%) 1.635 ± 0.236	20 (17.39%) 1.392 ± 0.026
	Partially degraded	16 (13.91%) 1.281 ± 0.006	16 (13.91%) 1.269 ± 0.007	8 (6.96%) 1.250 ± 0.005	40 (34.78%) 1.271 ± 0.004
	Degraded	5 (4.35%) 1.169 ± 0.016	22 (19.13%) 1.178 ± 0.011	28 (24.35%) 1.167 ± 0.008	55 (47.82%) 1.171 ± 0.006

FN BMD					
TBS		Normal	Osteopenia	Osteoporosis	Total
	Normal	6 (5.21%) 1.367 ± 0.018	11 (9.56%) 1.358 ± 0.006	3 (2.60%) 1.567 ± 0.152	20 (17.39%) 1.392 ± 0.026
	Partially degraded	4 (3.47%) 1.275 ± 0.007	17 (14.78%) 1.276 ± 0.006	19 (16.52%) 1.263 ± 0.006	40 (34.78%) 1.271 ± 0.004
	Degraded	5 (4.34%) 1.138 ± 0.029	22 (19.13%) 1.179 ± 0.009	28 (24.34%) 1.172 ± 0.008	55 (47.82%) 1.171 ± 0.006

TH BMD					
TBS		Normal	Osteopenia	Osteoporosis	Total
	Normal	13 (11.30%) 1.364 ± 0.009	5 (4.34%) 1.456 ± 0.104	2 (1.73%) 1.415 ± 0.016	20 (17.39%) 1.392 ± 0.026
	Partially degraded	16 (13.91%) 1.278 ± 0.006	15 (13.04%) 1.273 ± 0.007	9 (7.82%) 1.248 ± 0.006	40 (34.78%) 1.271 ± 0.004
	Degraded	13 (11.30%) 1.170 ± 0.015	28 (24.34%) 1.176 ± 0.008	14 (12.17%) 1.163 ± 0.012	55 (47.82%) 1.171 ± 0.006

Lowest BMD					
TBS		Normal	Osteopenia	Osteoporosis	Total
	Normal	6 (5.21%) 1.367 ± 0.018	11 (9.56%) 1.358 ± 0.006	3 (2.60%) 1.567 ± 0.152	20 (17.39%) 1.392 ± 0.026
	Partially degraded	2 (1.73%) 1.280 ± 0.017	17 (14.78%) 1.278 ± 0.006	21 (18.26%) 1.261 ± 0.006	40 (34.78%) 1.271 ± 0.004
	Degraded	1 (0.86%) 1.138 ± 0.000	15 (13.40%) 1.176 ± 0.013	39 (33.91%) 1.170 ± 0.007	55 (47.82%) 1.171 ± 0.006

■ = Very high risk, ■ = High risk, ■ = Intermediate risk, ■ = Low risk
(Risk stratification modified from [16])

BMD, bone mineral density; TBS, trabecular bone score; LS, lumbar spine; FN, femoral neck; TH, total hip

Fig. 2. Categorization of fractured participants by BMD and TBS.
BMD, bone mineral density; TBS, trabecular bone score; LS, lumbar spine; FN, femoral neck; TH, total hip.

from 47 (16.1%) to 101 (34.6%) or 2.15 times. However, the proportion of additional subjects eligible for treatment was still higher than the fracture group. The percentages of subjects eligible for treatment using BMD and BMD and TBS are shown in Table 2, along with the proportion of subjects additionally receiving treatment when TBS was taken into consideration. To capture 1 patient with fragility fracture in osteopenic individuals with degraded TBS, the numbers of additional patients in this group to be prescribed anti-osteoporotic mediation are 7, 8, 11, 8 patients based on LS, FN, TH, and lowest BMD, respectively.

LS BMD					
TBS		Normal	Osteopenia	Osteoporosis	Total
	Normal	76 (26.02%) 1.378 ± 0.006	23 (7.87%) 1.353 ± 0.007	3 (1.02%) 1.321 ± 0.005	102 (34.93%) 1.370 ± 0.005
	Partially degraded	34 (11.64 %) 1.278 ± 0.004	59 (20.20%) 1.271 ± 0.003	6 (2.05%) 1.252 ± 0.005	99 (33.90%) 1.273 ± 0.002
	Degraded	18 (6.16%) 1.174 ± 0.011	53 (18.15%) 1.160 ± 0.011	20 (6.84%) 1.155 ± 0.007	91 (31.16%) 1.161 ± 0.007

FN BMD					
TBS		Normal	Osteopenia	Osteoporosis	Total
	Normal	49 (16.78%) 1.388 ± 0.008	50 (17.12%) 1.356 ± 0.006	3 (1.02%) 1.334 ± 0.003	102 (34.93%) 1.370 ± 0.005
	Partially degraded	31 (10.61%) 1.284 ± 0.004	59 (20.20%) 1.269 ± 0.003	9 (3.08%) 1.257 ± 0.006	99 (33.90%) 1.273 ± 0.002
	Degraded	26 (8.90%) 1.158 ± 0.019	45 (15.41%) 1.164 ± 0.009	20 (6.84%) 1.160 ± 0.010	91 (31.16%) 1.161 ± 0.007

TH BMD					
TBS		Normal	Osteopenia	Osteoporosis	Total
	Normal	82 (28.08%) 1.376 ± 0.006	17 (5.82%) 1.350 ± 0.007	3 (1.02%) 1.324 ± 0.005	102 (34.93%) 1.370 ± 0.005
	Partially degraded	74 (25.34%) 1.276 ± 0.003	24 (8.21%) 1.262 ± 0.004	1 (0.34%) 1.242 ± 0.000	99 (33.90%) 1.273 ± 0.002
	Degraded	56 (19.17%) 1.162 ± 0.011	27 (9.24%) 1.161 ± 0.009	8 (2.73%) 1.158 ± 0.020	91 (31.16%) 1.161 ± 0.007

Lowest BMD					
TBS		Normal	Osteopenia	Osteoporosis	Total
	Normal	45 (15.41%) 1.391 ± 0.009	50 (17.12%) 1.359 ± 0.006	7 (2.39%) 1.326 ± 0.004	102 (34.93%) 1.370 ± 0.005
	Partially degraded	18 (6.16%) 1.287 ± 0.004	68 (23.28%) 1.272 ± 0.003	13 (4.45%) 1.255 ± 0.004	99 (33.90%) 1.273 ± 0.002
	Degraded	10 (3.42%) 1.179 ± 0.012	54 (18.49%) 1.160 ± 0.011	27 (9.24%) 1.159 ± 0.009	91 (31.16%) 1.161 ± 0.007

■ = Very high risk, ■ = High risk, ■ = Intermediate risk, ■ = Low risk
(Risk stratification modified from [16])

BMD, bone mineral density; TBS, trabecular bone score; LS, lumbar spine; FN, femoral neck; TH, total hip

Fig. 3. Categorization of non-fractured participants by BMD and TBS.
BMD, bone mineral density; TBS, trabecular bone score; LS, lumbar spine; FN, femoral neck; TH, total hip.

4. Discussion

BMD, measured by DXA is globally used nowadays as a gauge to evaluate fracture risk, diagnose osteoporosis, and start anti-osteoporotic medication in the absence of major osteoporotic fracture, due to its availability and non-invasiveness [23,27]. BMD, however, does not fully explain why a person fractures and others do not. For example, not all osteoporotic patients under the World Health Organization's (WHO) criteria suffer from fractures, while over half of patients with fractures have BMD within the normal to

Table 2
Comparison of number of subjects eligible for anti-osteoporotic treatment when BMD alone and BMD with TBS were used as therapeutic decision.

	Number of subjects eligible for treatment			Increment of eligible subjects by BMD plus TBS (Fold)
	BMD alone	BMD plus TBS	P-value	
Cohort (N = 407)				
LS BMD	67 (16.5%)	142 (34.9%)	< 0.001	2.12
FN BMD	82 (20.1%)	149 (36.6%)	< 0.001	1.82
TH BMD	37 (9.1%)	92 (22.6%)	< 0.001	2.49
Lowest BMD	110 (27.0%)	179 (44.0%)	< 0.001	1.63
Fracture (N = 115)				
LS BMD	38 (33.0%)	60 (52.2%)	0.003	1.58
FN BMD	50 (43.5%)	72 (62.6%)	0.004	1.44
TH BMD	25 (21.7%)	53 (46.1%)	< 0.001	2.12
Lowest BMD	63 (54.8%)	78 (67.8%)	0.042	1.24
Non-fracture (N = 292)				
LS BMD	29 (09.9%)	82 (28.1%)	< 0.001	2.83
FN BMD	32 (11.0%)	77 (26.4%)	< 0.001	2.41
TH BMD	12 (4.1%)	39 (13.4%)	< 0.001	3.25
Lowest BMD	47 (16.1%)	101 (34.6%)	< 0.001	2.15

BMD, bone mineral density; TBS, trabecular bone score; LS, lumbar spine; FN, femoral neck; TH, total hip.

osteopenic range [6,28]. Therefore, a more comprehensive risk stratification is needed to capture more individuals with higher risk of fractures in order to prevent fragility fractures and the burden they bear, especially in those with osteopenia. In our study, the percentage of fractured participants with osteopenic BMD ranged from 37.4% to 43.5%, depending on the site of BMD measured. The number is consistent previous large prospective studies, the Rotterdam study [4] and the OFELY study [18].

TBS is one of non-invasive predictors of fracture risk, independent of BMD. Studies have found a consistent inclination toward lower TBS in subjects with fragility fractures [16]. The largest prospective study on TBS was in the Manitoba cohort, which demonstrated a hazard ratio of a hip and MOF of 1.44 (95% CI, 1.28–1.62) and 1.42 (95% CI, 1.33–1.53) per 1 SD decrease in TBS. Studies in Asian populations resulted in a similar trend. A cohort of 665 Japanese women had a hazard ratio of VCF per 1 SD decrease in TBS of 1.98 (95% CI, 1.56–2.51) [17].

The most useful clinical implication of TBS is perhaps its ability to define individuals at higher risk of fractures whose BMD are above the osteoporotic range. In the Manitoba cohort, TBS was divided into tertiles, in which the lowest tertile was associated with higher risk of fracture in osteopenic women [16]. The OFELY study found that 58% of women with fracture either had LS BMD T-score in the osteoporotic range or TBS $\leq$1.2, while only 28% had osteoporotic BMD alone [18]. Similarly, in a study of 631 postmenopausal women, Lamy et al [29] showed an increased detection of fracture from 35 to 37% when only osteoporotic BMD was used to 54–60% when low TBS was also taken into consideration. Our study reported a similar number of osteoporotic participants in the fracture group of 33.0% using LS BMD, and 56.5% either had LS BMD T-score ≤ -2.5 or degraded TBS. Boutroy et al. [18] concluded that having TBS below the threshold more than doubled the risk of fracture, and was a significant predictor of fracture in non-osteoporotic women, but not in osteoporotic women, suggesting that TBS can help identify non-osteoporotic women with high fracture risk.

In our study, including osteopenic subjects with degraded TBS significantly increased the proportion of patients receiving treatment, especially in non-fracture subjects with over 3-fold increase when TH BMD was used for consideration. The increase was less obvious when only the fracture group was calculated. Following our approach to also treat osteopenia with degraded microarchitecture, we also found that in order to capture 1 patient with fragility fracture in osteopenic individuals with degraded TBS, we needed to treat 7 to 11 more patients.

While TBS should not be used alone in determining treatment decision of osteoporosis, TBS can be useful as a case-finding strategy and to aid therapeutic decision, in particular in osteopenic patients [30]. For example, patients with BMD T-scores below -2.5 SD or history of fragility fractures are already eligible for treatments without TBS, while TBS analysis from the obtained DXA image is used to further define osteopenic women with degraded microarchitecture without a history of fracture, in whom treatment should also be considered to hopefully reduce future fracture risk. However, evidence on the efficacy of anti-osteoporotic medication to prevent fracture in this particular group of patients is still lacking.

To date, the Thai national guideline for management of osteoporosis does not encompass the use of TBS [3]. Though our study found that TBS can be applied to identify osteopenic people with high risk of fracture with as few as 7 additional osteopenic patients with degraded microarchitecture treated to capture one fractured patient, long-term studies focusing on anti-fracture efficacy of anti-osteoporotic medication in osteopenic women with degraded TBS, along with its cost-effectiveness and national economical relevance are essential for TBS to be incorporated in the guideline.

The main limitation of our study is in its retrospective nature. The participants in the cohort would be subject to selection bias, since some of the participants originally visited the hospital because of a fracture. Bone turnover marker (BTM) was not available in this cohort, and the interaction of BTM and TBS would be valuable. Although we proposed the usage of TBS along with BMD to capture individuals at high risk of fracture, we could not confirm that prescribing anti-osteoporotic medication in osteopenic individuals with degraded TBS would help prevent fragility fractures. The strength of our study is in availability of all sites of BMD used in the analysis. The BMD and TBS was performed by a single technician using the same DXA. After all, this is the first study to explore the role of TBS in osteopenic individuals with and without MOF in Thailand. This study also highlighted the importance of using TBS in determining treatment initiation in osteopenic postmenopausal women, which would serve as a foundation for future studies and ultimately local and national policy changes.

5. Conclusions

Almost half of postmenopausal women with MOF had non-osteoporotic BMD. Addition of TBS helped capturing osteopenic women, who were at high risk of fracture. Decision to treat osteopenic women with degraded TBS increased the number of patients receiving treatment up to 3.25-fold in non-fracture subjects with 7–11 additional patients to be treated to capture 1 more fractured individual. Therefore, we recommend evaluating TBS in

osteopenic postmenopausal women without fracture to aid in therapeutic decisions about treatment initiation.

CRediT author statement

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Conflicst of interest

The authors declare no competing interests

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