JMS 2019;2(2):95-103
UDC:616.71-007.234-073.75:771.534.54

CLINICAL USE OF TRABECULAR BONE SCORE FOR THE DIAGNOSIS OF OSTEOPOROSIS: A REVIEW

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Abstract

Osteoporosis is a global pandemic affecting men and women of all ages and ethnicities. Not so long ago doctors had to rely on X- ray images for the diagnosis of osteoporosis. Dual-energy X-ray Absorptiometry (DXA) has been developed over the past half century to provide measurement of Bone Mineral Density for the purposes of clinical practice and research. BMD, measured by DXA has been the reference standard for osteoporosis diagnosis.

The *trabecular bone score (TBS)* is a new texture measurement that can be applied to any X-ray images including DXA images by quantifying local variations in gray level. Lumbar spine trabecular bone score (TBS) correlates with parameters of bone microarchitecture and can predict osteoporotic fractures independently of BMD and the WHO fracture risk assessment tool (FRAX) probability. It can be applied retrospectively to an existing DXA exam without the need of any further imaging and it can be compared directly with BMD because both evaluate the same region of bone. The importance of TBS in bone mineral densitometry for fracture risk assessment has been documented in a number of cross-sectional studies. We review relevant studies in order to evaluate the clinical use of this imaging tool. The clinical and scientific evidence supporting the use of TBS, makes TBS an attractive and useful clinical tool for physicians to improve patient management in osteoporosis

We conclude that when used correctly, this tool provides invaluable information for the diagnosis of osteoporosis and patient management in clinical practice.

Key words: Osteoporosis, Bone Density, Absorptiometry Photon, Trabecular Bone Score, Risk Assessment

Introduction

Osteoporosis is defined as a skeletal disease characterized by compromised bone strength and degradation of bone microarchitecture which leads to increased fracture risk, particularly at the hip, proximal humerus, vertebrae, and forearm[1]. Osteoporosis is a global epidemic affecting men and women of all ages and ethnicities. The fatality rate for hip fractures can exceed 20% , and all osteoporosis-related fractures can lead to significant long-term disability and decreased quality of life [2,3,4]. Worldwide, approximately nine million new osteoporotic fractures occur each year, with a global burden of osteoporosis projected to increase markedly over the next few decades as the number of elderly individuals increases [5]. Many fractures are preventable by identifying people at high risk for fracture and falls, and diagnosing those who already have osteoporosis, before they fracture.

Not so long ago clinicians had to rely on X- ray images for the diagnosis of osteoporosis. Today, osteoporosis is typically diagnosed from bone mineral density (BMD) measured with dual-energy X-ray absorptiometry (DXA) [6]. Bone-mineral density (BMD) is a measure of the inorganic mineral content in bone, and is one of the most informative assessments of bone quality in clinical studies and everyday

practice [7]. The World Health Organization (WHO) has devised an operational definition for osteoporosis of a BMD value of 2.5 standard deviations (SD) or more below the average young normal mean BMD value ($T \leq -2.5$ SD), based on a standardized reference site (the femoral neck) and reference population (National Health and Nutrition Examination Survey [NHANES] III data for White women aged 20–29 years) [8].

However, most fractures occur in individuals who have a BMD T-score above the cut-off defining osteoporosis, indicating that BMD alone is insufficient for identifying all individuals who will sustain fragility fractures. One potential explanation for this is that BMD is not the only structural determinant of bone strength [9,10]. Trabecular bone microarchitecture, for example, also appears to be a significant bone strength determinant and is complementary to bone density[11]. Another limitation of BMD measurements is that they disproportionately evaluate cortical bone, depending on the skeletal site measured, and cortical bone has a relatively slow rate of turnover relative to trabecular bone . Consequently, one must wait a long time (typically, years) between BMD measurements to be able to detect any meaningful changes, whether the change is related to the natural progression of aging or disease, or is the result of treatment [12]. Because of this increased rate of trabecular bone turnover, it is possible that evaluating the microarchitecture of trabecular bone could increase the accuracy and sensitivity of bone quality evaluations in clinical practice.

In recent years, a number of additional techniques have been developed for bone microarchitecture assessment [13,14]. Among the noninvasive techniques, (peripheral) quantitative computed tomography (pQCT, QCT) and magnetic resonance imaging (MRI)) allow for the direct measurement of bone microarchitecture [15]. However, these two techniques remain impractical for routine screening and clinical management owing to high costs and the inconvenience of having patients return to undergo another time-consuming assessment after DXA has been performed.

The concept of Trabecular Bone Score

The trabecular bone score (TBS) is a new texture measurement that can be applied to any X-ray images including DXA images by quantifying local variations in gray level [16]. TBS uses experimental variograms of 2D projection images to differentiate between 3D microarchitectures that exhibit the same BMD but different trabecular characteristics[17]. Large differences of grey levels in adjacent areas suggest decreased trabecular density, decreased trabecular volume, more “rod-like” rather than “plate-like” trabecular shape and decreased trabecular connectivity (Image 1). In simple words, TBS using DXA imaging “might not be able to detect each individual tree but can find the clearings within a forest”. The “more clearings and less areas of thick woods”, the larger and more frequent the differences in grey level and the poorer the microarchitecture [18]. Since it is constrained by neither the size nor shape of the region measured, TBS can be applied to small and/or irregular surfaces, such as the standard regions of measurement used in DXA

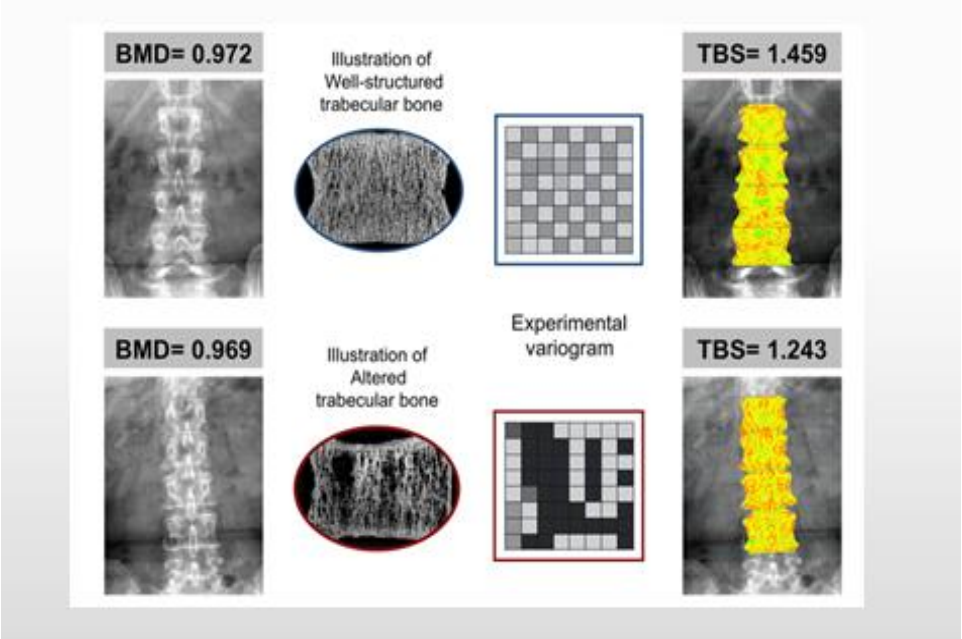

Image 1. Principles of TBS score and example of two normal BMD values with different TBS scores- TBS independent of BMD (from Silva et al. JBMR 2014). More numerous and connected and less sparse trabeculae translate into a high TBS value, whereas a low trabecular number and connectivity and high trabecular separation translate into a low TBS.

TBS can be applied retrospectively to an existing DXA exam without the need for any further imaging and can be compared directly with BMD because both evaluate the same region of bone. Higher scores in TBS reflect stronger and more fracture-resistant microarchitecture, whereas lower scores indicate bone that is weaker and more susceptible to fracture (Image 2). Although the TBS result is given for each vertebra, the TBS value reported represents the average of L_1 to L_4. The following normal range for TBS values in postmenopausal women has been proposed: TBS ≥1.350 is considered to be normal; TBS between 1.200 and 1.350 is considered to be consistent with partially degraded microarchitecture; and TBS ≤1.200 defines degraded microarchitecture (figure 1). These cutoff points were established by a working group of TBS users from different countries , by analogy with the three BMD categories, ie, normal bone mass, osteopenia, and osteoporosis[19].

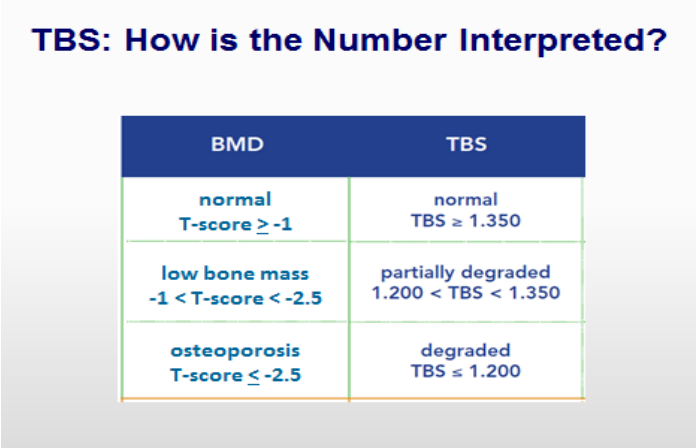

Figure 1. Interpretation of TBS score compared to BMD values and diagnosis (from Silva et al, JBMR 2014)

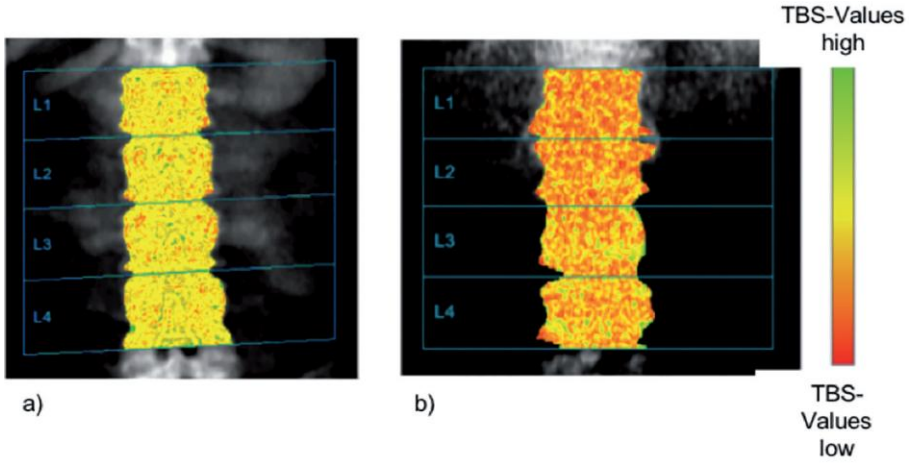

Image2. Example of normal TBS (**a**) and very low TBS (**b**). The male in image a) had a DXA bone assessment because of a possible endocrine disorder but had normal BMD for his age (Z-scores around 0.0). The male in image b) is multi-morbid with renal, cardiac and rheumatologic diseases and has severe secondary osteoporosis (lowest Z-score -3.5). The individual in image a) has TBS of 1.551, well above the cut-off of 1.31 for normal trabecular microarchitecture. The individual in image b) has a TBS of 0.734, well below the cut-off of 1.20 for degraded microarchitecture. (from J.J. Carey, B. Buehring. Clin Exp Rheumatol 2018)

This review wishes to address the clinical use of TBS for fracture risk prediction. Therefore, we need to examine the scientific background on the improved fracture risk prediction through the TBS, combined with DXA and as independent measurement.

TBS combined with Dual X-ray Absorptiometry

The added value of TBS in bone mineral densitometry for fracture risk assessment has been documented in several cross-sectional studies [20,21]. We review two of the most important. In the study by Rabier B et al., authors have examined 42 postmenopausal women with osteoporosis-related vertebral fractures (31 with osteoporosis confirmed by DXA and 11 with osteopenia) and compared them with 126 age-matched women without any fractures (86 with osteoporosis and 40 with osteopenia). Unfortunately, this study lacked the numbers to identify any similar, statistically significant relationships in that segment of the postmenopausal population for whom the combination might have the greatest utility, those whose BMD falls in the osteopenia range.

The second study was intended to address this issue of how valuable the TBS is in women whose BMD falls in the osteopenia, rather than the osteoporosis range. They only analyzed postmenopausal women whose T-score fell between -1.0 and -2.5 and included in the analysis 81 such women with fractures and 162 age-matched osteopenic controls, versus the 11 and 40 osteopenic subjects recruited in the fracture and nonfracture groups in the previous study.

What they found was that the combination of BMD + TBS was better than either test alone, in terms of correctly classifying patients overall and tended toward being superior in terms of classifying by fracture status. The combination also was statistically more specific than either test used alone.

In conclusion of these two studies, TBS has been found:

1. To be lower in postmenopausal women with a past osteoporotic fracture compared with age- and BMD-matched women without fracture,
2. To give an incremental increase in the odds ratio for spine fracture when combined with spine BMD. and 3. To be lower in women with (versus without) fractures irrespective of whether their BMD met the criteria for osteoporosis or osteopenia.

TBS independent of BMD

The objective of this study by Hans et al (The so called Manitoba study) was to determine whether TBS can predict osteoporosis-related fractures independent of BMD in a large cohort of postmenopausal women. In this retrospective historical cohort study, 2D gray-scale DXA images of the lumbar spine, collected from a large cohort of postmenopausal women (29,407 women) from the Canadian Province of Manitoba, were sent to the University of Lausanne, Switzerland, for the calculation of spine TBS. The Manitoba Bone Density Program is a targeted case-finding clinical program[22]. The associated database has shown to exceed 99% in terms of completeness and accuracy[23]. All women 50 years of age or older who had undergone BMD measurement of the spine and hip by DXA were eligible for inclusion. All TBS measurements were performed with The TBS iNsight software. The software uses the anteroposterior spine raw image(s) from the densitometer, including the BMD region of interest (ROI) and edge detection, so that the TBS calculation is performed over exactly the same ROI as the BMD measurement.

What they found is significantly lower lumbar spine TBS and BMD scores in women with major osteoporotic fractures, spine fractures, and hip fractures. The correlation between spine BMD and spine TBS was modest. Spine TBS predicted fractures almost as well as lumbar spine BMD, and the combination was superior to either measurement alone ($p<0.001$). Incremental improvement in the performance of the combination of BMD and TBS remained significant even after adjustment for multiple clinical risk factors. These results do not support replacing BMD in favor of TBS. Rather, the authors discuss, there may be a role for using these two measurements in combination, especially in those at intermediate risk, such as individuals with BMD values in the osteopenic range. In principle, a protocol could be established to perform TBS only on scans with BMD values or risk scores within a specified range. This has the additional advantage over some other techniques of being potentially applicable to almost any bone site, including spine, femoral neck, hip, and forearm. Alternatively, if the information is easily extracted from DXA and is incremental to BMD, then it might be appropriate to use it in all cases. Such an approach could help to define the fracture risk profile by taking into account both the density and the microstructure of the bone.

Another issue needed to be addressed is that the DXA image quality degrades with increasing adiposity. To compensate for this effect on image texture, the TBS software includes an adjustment that is, in part, based upon body mass index (BMI) as a surrogate for abdominal soft tissue thickness. The original TBS algorithm (denoted TBS-v1) was optimized for women of average body size, and limitations were identified when used in men or extremes of BMI (manufacturer recommended range 15– 37 kg/m2) [24]. In particular, the original TBS algorithm gave paradoxically lower mean TBS measurements in men than women, despite their higher BMD, lower fracture risk, and the expectation of similar or better trabecular structure. The presumed explanation is that men tend to have more abdominal or truncal soft tissue than women for an equivalent BMI, which leads to an underestimation in TBS [25]. The TBS algorithm was updated (denoted TBS-v 2) to address these technical issues. The soft tissue adjustment was modified for female patients with extreme BMI measurements, and sex-specific differences in body morphometry were taken into account in order to perform the same level of soft tissue compensation for both men and women. This study by Schacter et al. compares the clinical performance of the original and updated TBS algorithms in terms of the effects of sex, BMI, and incident fracture risk stratification in women and men. Limitations of this study include the relative underrepresentation of men compared to women[26,27].

Their results showed that the updated TBS-v2 algorithm is less affected by soft tissue, gives higher results for men than women consistent with their lower fracture risk, and improves fracture risk stratification in both men and women compared with the original algorithm.

Conclusion

BMD, measured by dual-energy X-ray absorptiometry (DXA), has been the reference standard for osteoporosis diagnosis in the absence of established fragility fractures. Combined with fracture prediction tools such as Fracture Risk Assessment Tool (FRAX), which use a combination of clinical risk factors for fracture to provide a measure of risk, these elements have led to a fundamental change in the ability to diagnose osteoporosis and predict individuals who are at risk of fragility fracture. Still, there is considerable overlap in BMD values between individuals who develop fractures and those who do not.

Lumbar spine trabecular bone score (TBS) is a texture measurement derived from lumbar spine DXA images that correlates with parameters of bone microarchitecture and can predict osteoporotic fractures independently of BMD and the WHO fracture risk assessment tool (FRAX) probability. This review illustrates the potential utility of TBS as a clinical tool. One advantage of TBS over other proposed methods for assessment of bone microarchitecture is that the measurement can be extracted from previously obtained DXA images, unlike pQCT and MRI, which require a patient to return for further costly and time-consuming measurements.

This review shows that TBS holds promise as a low-cost and easily applied adjunct to BMD testing in the assessment of fracture risk.

The clinical and scientific evidence supporting the use of TBS, with the ability of this technology to be seamlessly integrated into a daily workflow, makes TBS an attractive and useful clinical tool for physicians to improve patient management in osteoporosis. Further research is ongoing and necessary to further clarify the role of TBS in additional specific disorders. TBS may improve fracture discrimination over DXA alone, but it remains to be seen whether osteoporosis treatment- related increase in TBS estimates antifracture effectiveness.

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27. Abbreviations: TBS= Trabecular Bone Score, DXA= Dual X-ray Absorptiometry, BMD= Bone Mineral Density