

Review of the Clinical Applications of Trabecular Bone Score

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Assessment of bone health is essential in many different diseases and conditions, including osteoporosis and fragility fracture. Although bone mineral density (BMD) has a well-established role in measuring bone quantity, it is unable to determine bone quality. Recently, the trabecular bone score (TBS) was developed as a valuable approach to determining bone quality by evaluating the microarchitecture of a bone. TBS data is of critical importance, particularly in conditions in which BMD is falsely elevated or has not yet decreased significantly. The current review has collected current evidence regarding the clinical applications of TBS in various disorders, such as osteoporosis, fracture, diabetes, chronic kidney disease, and degenerative bone diseases.

Keywords: Bone, Microarchitecture, Osteoporosis, Trabecular bone score

Introduction

Bone mineral density (BMD) is a valuable tool for determining bone quantity, but it is flawed by the inability to assess bone quality. Trabecular bone score (TBS) is a new bone evaluating measure that provides valuable information about bone microarchitecture [1]. It is an analytical tool that quantifies variation in grey-level texture on the standard lumbar spine BMD [2]. This feature allows better evaluation of bone status, thereby easing therapeutic decision-making for responsible physicians. Combining TBS with the fracture risk assessment tool (FRAX) has also been successful in estimating the risk of fracture [3]. Due to the importance of bone quality in the prediction of fracture risk, TBS is continuously drawing the attention of professionals in the assessment of bone health. In particular, it is suggested for use in conditions in which BMD is not capable of accurately measuring bone health, such as in patients with degenerative bone diseases [4].

The excitement of researchers and clinicians has led to an increasing number of publications about the application of TBS in a variety of diseases and conditions. This article aims to review the wide range of TBS applications in medical conditions.

TBS Definition

TBS is captured from the gray-level variation of pixels on DXA images as a higher number, and the homogeneity

of these pixels indicates a better microarchitecture and bone quality [5] (Figure 1). Although the TBS range for normal and abnormal values is still an open research question, there is greater consensus on the following [1]:

Normal (not degraded): >1.31

Borderline (partially degraded): ≤ 1.31 and >1.23

Abnormal (degraded): ≤ 1.23

Nevertheless, a recent study on an Iranian population has suggested microarchitecture degradation cut-offs of ≤ 1.23 and ≤ 1.29 in men and women, respectively [6].

Fracture Prediction

FRAX is an online system developed by the World Health Organization (WHO) that is used extensively to estimate the probability of future fragility fractures. Despite the valuable information it provides, until recently, it was only based on the mineral density of bone. Therefore, a great deal of information regarding the bone quality was missed. After the development of TBS, FRAX incorporated the TBS data into BMD information, thereby providing a fracture risk assessment based on both bone quality and quantity. This feature allows a more accurate estimation of bone health and provides better identification of at-risk populations requiring therapeutic intervention for fracture prevention [7]. The literature review suggests that

TBS alone is capable of fracture prediction independent of BMD. However, its combination with BMD results in a more accurate assessment. Moreover, recent evidence suggests that TBS may even be superior to FRAX in fracture prediction in situations where BMD alone is unreliable and not of great help [8].

A recent study in Japan on more than 1500 adults and a follow-up of 10 years concluded that TBS score alone could be used for fracture prediction, and adding TBS to FRAX resulted in a more accurate fracture prediction [9]. The meta-analysis of McCloskey et al. on a pooled population of 17,809 adults concluded that TBS could predict fracture independently of FRAX, and when it is used conjunct with FRAX, the accuracy of prediction is increased [10].

The study of Mirzaei et al. on 358 postmenopausal Iranian women did not show any significant clinical benefit of TBS adjusted FRAX on improving fracture prediction or therapeutic decision-making. They concluded that TBS evaluation is more valuable for patients with borderline risk of major osteoporotic and hip fracture, as the choice of therapeutic intervention in these patients is more probable to change after FRAX adjustment with TBS. In addition, their study showed that TBS evaluation is of great value for patients with severe osteophytes in their spine X-rays, because BMD results are falsely normal in these patients [11].

Holloway et al. reported similar findings on the value of FRAX adjustment with TBS in an Australian population [12]. Future research will provide more precise evidence for the TBS application in daily routine practice and will identify the population who will take the most benefit from this tool. Moreover, TBS measurement shows technical variations, and with the newly published study of Shafiee et al. on the reference value of TBS in an Iranian population, further research is needed [6].

Body Mass Index (BMI) Effect on TBS

TBS is directly affected by abdominal soft tissue that influences the grey-level pixels, and thus, TBS is negatively affected by fat tissue. Langsetmo et al. revealed that the association between BMD and TBS is affected by BMI. They recommended limiting the application of TBS in men with BMI higher than 37 kg/m², particularly those with abdominal obesity [13]. Conversely, Shayganfar et al. studied 1054 postmenopausal women in Iran and concluded that BMI had no significant association with TBS [14]. Interestingly, Kim et al. reported that although higher BMI was related to lower TBS both in men and women, height was directly associated with TBS in women, and weight was directly associated with TBS in men [15]. This might be due to the different patterns of fat tissue accumulation in men and women. Central obesity is more prevalent in men than in women, and abdominal fat tissue may significantly influence TBS obtained from lumbar spine BMD.

TBS Application in Diabetes

Diabetes mellitus (DM) adversely affects bone health with several mechanisms such as vasculopathy,

inflammation, hyperglycemia, and altered metabolism. Reduced bone turnover and microarchitecture degradation are eventually presented as bone fragility [16]. Although epidemiologic studies suggest that diabetics, especially elderly people, are more prone to osteoporosis and fractures [17], other studies have reported that BMD in DM patients is not reduced and is even above the normal average [18-20]. Still other studies suggest that diabetes mostly affects bone quality and not its density [21]. In that case, TBS evaluation in diabetic patients would be of critical value, and for this reason, interest in applying TBS in DM cases is increasing.

In several studies, TBS has been successful in assessing bone quality and in predicting fracture risk in DM patients [22, 23]. It has also been shown to be negatively correlated with DM risk factors, including high hemoglobin A1c and fasting glucose [24]. In a recent meta-analysis of 12 studies with a pooled population of 4962 men and 35,546 women, TBS was significantly lower in diabetics, and the difference was greater in women [25]. In addition, TBS was significantly lower in prediabetics compared to the healthy population [25], which may be related to microarchitecture degradation as a key mechanism in DM [21]. Despite the result of this meta-analysis and other original studies, some investigations have reported that TBS was not significantly different between diabetics and healthy people [24, 26]. This discrepancy may be attributable to the difference in DM duration and the therapeutic regimen used by patients [25]. Overall, BMD and FRAX are tools of great help in osteoporosis and fracture management for DM patients, and TBS could improve these tools [27]. Future studies will provide a more precise understanding of the role of TBS in DM patients.

TBS Application in Chronic Kidney Disease (CKD) and Kidney Transplant Recipients (KTR)

Osteoporosis and fractures are prevalent in CKD patients, and guidelines recommend BMD as a routine clinical practice for assessing bone health in these patients [28]. However, BMD is not reliable enough for fracture prediction in these patients compared to healthy people [29], mostly due to calcifications of joints and arthritic vasculatures [30]. For this reason, imaging methods that provide information on bone microarchitecture, including magnetic resonance imaging (MRI), high-resolution peripheral quantitative computed tomography (HR-pQCT), and TBS, are now under investigation to enhance current bone densitometry techniques. TBS has been shown to be significantly reduced in end-stage renal disease (ESRD) patients [31-34] and has successfully predicted fractures in CKD patients [33, 35]. Furthermore, it has been reported to be correlated with estimated glomerular filtration rate (eGFR); lower TBS was seen in patients with eGFR ≤ 60 mL/min/1.73 m² [36]. Nevertheless, the application of TBS in CKD patients resulted in a significant alteration in the number of patients receiving osteoporosis treatment [37].

Aortic calcification in KTR patients is an important cause of falsely elevated BMD. Luckman et al. concluded

that TBS was superior to spine BMD in predicting fractures and could successfully monitor the loss of bone quality in the first year following transplantation. These observations reveal that TBS may be of considerable value to reporting early bone loss in KTR patients, when the reduced quantity of bone is not yet detectable on BMD [38]. However, there is an evidence gap on this research topic, and further large-scale prospective studies are needed to investigate the change of TBS following a kidney transplant in early and long-term follow-up. Still, the current evidence suggests that TBS may be of use in KTR patients [39].

TBS Application in Ankylosing Spondylitis (AS) and Rheumatoid Arthritis (RA)

Arthritis adversely affects bone, cartilage, and joints, and the presence of osteophytes and falsely increases BMD syndesmophytes. However, since this osteoproliferation affects only the quantity and not the quality of bone, TBS provides a more accurate measurement of bone health in these patients [40]. According to Bréban et al., TBS successfully detected vertebral fractures among RA patients, and the number of these fractures was associated with lower TBS [41]. Based on the report of Choi et al., this association is even more prominent in RA patients receiving glucocorticoids [42]. Kim et al. reported that TBS more precisely predicts fractures compared to BMD, especially in RA patients receiving glucocorticoids [43]. Nam et al. reported that TBS is useful in predicting fractures and measuring bone quality, even with the presence of osteoproliferation [44]. Other studies have also report that TBS accurately diagnosed axial osteoporosis in the early stages of AS, while BMD is not a reliable tool. Moreover, TBS is reported to be capable of predicting spine fractures independent of FRAX in AS patients [45-47].

TBS Application in Osteoarthritis (OA)

TBS application in OA patients is not yet well studied. Kolta et al. revealed that patients with lumbar spine OA have a higher BMD than those without it. In contrast, spine TBS is not affected by the presence of OA. This data suggested a more reliable implication of TBS than BMD in patients with lumbar spine OA [48]. The study of Padlina et al. on a cohort of 1443 women revealed that despite the increase in BMD at the age of 62.5 years, TBS drops each year. Accordingly, they concluded that TBS is not influenced by degenerative diseases of bone [49]. Although the evidence of TBS application in OA is still limited, interest in TBS in future research will increase, because TBS is not influenced by spondylosis [50].

TBS and Treatment with Glucocorticoids

Glucocorticoids are among the most prescribed medications worldwide and a major cause of secondary osteoporosis with a significant risk of fracture in the long-term [51]. BMD is valuable in providing a baseline measurement before the initiation of glucocorticoid therapy, and FRAX could be used to estimate the initial risk of fracture. However, despite a daily dose of glucocorticoids, the length of the treatment and the cumulative dose is not considered in this algorithm [52].

Since microarchitecture degradation is one of the mechanisms involved in glucocorticoid-induced osteoporosis [53], TBS may be a beneficial tool for the evaluation of bone health in this population. Nonetheless, evidence of TBS application for glucocorticoid-induced osteoporosis management is limited, and there are discrepancies among the published articles. One study reports that TBS predicts and diagnoses fractures, especially vertebral fractures, in glucocorticoid-induced osteoporosis [54]. Other studies, however, report TBS as not being capable of fracture risk assessment independently, but having added value when used in combination with FRAX [55]. TBS is capable of monitoring treatment response; because glucocorticoids mostly reduce bone formation, anabolic agents (teriparatide) show more desirable clinical outcomes in glucocorticoid-induced osteoporosis compared to antiresorptive agents (alendronate). Thus, TBS could be a sensitive tool in distinguishing between different treatments [56]. Overall, TBS adjunct to FRAX is useful for fracture prediction in patients receiving glucocorticoids. However, future studies are needed to shed more light on TBS application in the management of glucocorticoid-induced osteoporosis.

TBS Application in Bariatric Surgery

Bariatric surgery is an effective treatment for morbid obesity, yet it has many potential long-term complications. This surgery adversely affects bone health through the nutritional and hormonal changes that result in reduced bone turnover and degraded microarchitecture [57]. Current evidence suggests that BMD alone is not a precise measure for bone changes after bariatric surgery, and quantitative computed tomography (QCT) or HR-pQCT are studied to predict fracture risk. However, there is limited evidence regarding the application of TBS for such purpose [58]. In one randomized clinical trial with two years of follow-up, TBS was reduced during the first six months after bariatric surgery and then remained unchanged after interventions such as vitamin D and exercise. However, the change in BMD between intervention and observation groups was not significant [59]. Another study revealed similar findings after three years of follow-up, although TBS did not change FRAX data significantly [60].

TBS Application in Breast Cancer

Aromatase inhibitors (AIs) are among first-line therapies in breast cancer, but they may cause osteoporosis and increase the risk of fracture by reducing bone turnover [61]. TBS, as an adjunct to BMD, has been investigated by some researchers for screening osteoporosis and its management in breast cancer patients under treatment with AIs. According to these studies, TBS improves BMD and FRAX evaluation in these patients; therefore, adding TBS to FRAX could be helpful in maximizing the identification of at-risk patients before, during, or after AIs treatment [62-64].

Application of TBS in patients undergoing spine surgery

Patients with degenerative lumbar spine pathology who are eligible for spinal fusion surgery are at high risk of postoperative fracture. The use of BMD alone to diagnose osteoporosis in patients with lumbar spondylosis is not reliable and has provoked interest in additional methods of evaluating preoperative spinal bone health. Jeffery et al. aimed to determine which patients should be considered for preoperative bone health optimization to reduce the risk of postoperative fracture. According to this study, of the

patients not identified with osteoporosis using BMD, 70.4% had osteoporosis with expanded spine criteria, which included TBS. The authors suggested an expanded spine definition considering the TBS data to more comprehensively identify patients with poor bone health that could benefit from preoperative optimization. Nevertheless, this implication of TBS, similar to its other implications, needs further validation in future researches [50].

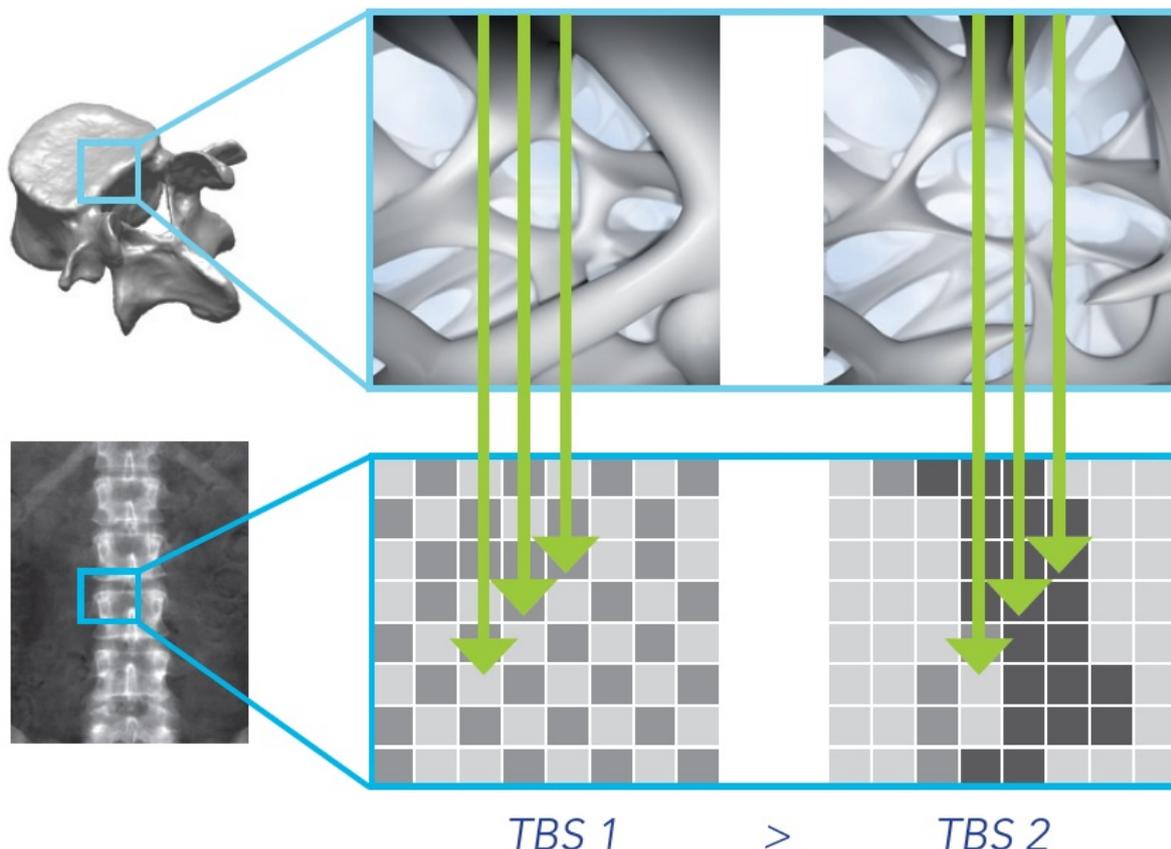


Figure 1: Comparison of normal (TBS1) and altered (TBS2) trabecular structure of bone (<https://www.roentgen-baden.at>)

Conclusion

Generally, TBS is useful for a variety of conditions, at least adjunct to BMD and FRAX. However, in some conditions such as osteoarthritis, TBS would be of more value, because the results of BMD are misleading. Future complementary research is needed to shed more light on the gaps in knowledge and to translate the application of TBS from research into clinical implications. While TBS is expected to attract more interest for the management of secondary osteoporosis, such as in ankylosing spondylitis, renal transplant recipients, or treatment with glucocorticoids, the limitations of TBS application should be properly addressed. For example, TBS is highly dependent on the quality of imaging, and conditions such as abdominal obesity may lead to false TBS results.

Conflict of interest

None to declare.

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