BALNEO RESEARCH Balneo and PRM Research Journal
English Edition
e ISSN 2734 - 8458 p ISSN 2734 - 844X ROMANIAN ASSOCIATION OF BALNEOLOGY

Research article

Trabecular bone score – the newest diagnostic tool for patients with osteoporosis and osteopenia from different pathologies

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Citation: Abdula I., Ungureanu A.E., Vîlcea L.C., Stanciu L.E., Azis O., Iliescu M.G. - Trabecular bone score – the newest diagnostic tool for patients with osteoporosis and osteopenia from different pathologies
Balneo and PRM Research Journal ***2023****, 14(4): 625*

Academic Editor(s):
Constantin Munteanu

Reviewer Officer:
Viorela Bembea

Production Officer:
Camil Filimon

Received: 20.11.2023
Accepted: 04.12.2023
Published: 20.12.2023

Reviewers:
Sinziana Calina Silisteanu
Carmen Nistor Cseppento

Publisher's Note: Balneo and PRM Research Journal stays neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Abstract: The trabecular bone score (TBS) is a recently developed instrument that performs gray-level bone texture measurements on dual X-ray absorptiometry (DXA) images of the lumbar spine and thus captures data on trabecular microarchitec-ture. This paper highlights a review of the scientific literature, using PRISMA methodology. A low TBS value is associat-ed with an increase in both prevalent and incident fractures, which is partially independent of both clinical risk factors and areal BMD (aBMD) at the lumbar spine and proximal femur. TBS is related to bone microarchitecture and provides skeletal information that is not captured by standard bone mineral density (BMD) measurements. A low TBS value cor-relates with poor skeletal microstructure; an increased TBS value correlates with better skeletal microstructure. Based on these data, TBS at the lumbar spine is promising as an emerging technology that could become a valuable clinical tool in diagnosing osteopenia and osteoporosis and assessing fracture risk.

Keywords: trabecular bone score, fracture risk, bone mineral density

1. Introduction

The gold standard method now available for estimating bone mineral density (BMD), which is the primary factor in the diagnosis of osteoporosis and the prediction of fragility fracture risk, is dual-energy X-ray absorptiometry (DXA). First however, BMD only evaluates the quantity of bone and, hence, its significance in determining bone strength are restricted. Two DXA scans represent the three-dimensional (3D) bone as two-dimensional (2D) projections, organization, converting a 2D representation of a bone into the 3D structure it represents, which is a mathematical problem that would yield further information about bone quality and strength. A decade ago, the development of trabecular bone score (TBS) addressed both of these issues the difficult assessment of BMD in osteoporosis diagnosis and fracture risk prediction of the real-world 3D bone structural characteristics from the 2D DXA images.

Trabecular microarchitecture is indirectly indexed by TBS, a textural characteristic. Research has conclusively demonstrated that TBS distinguishes between and forecasts osteoporotic fractures in spite of clinical risk factors (CRFs) and body mass index (BMD) [1].

Recent decades have seen a huge explosion of information in medicine, and the evolution of electronic, computerised and computerised technology, presentation and display has increased the visibility, accessibility and therefore the speed of dissemination of the extremely new data. This context brings with it two more difficult issues: the first is the difference between what is new, modern, directly applied by clinics and medical centres in different parts of the world and what is offered to each of us by everyday medical practice as diagnostic and therapeutic resources. The second concerns the difficulty faced by the doctor or medical technician in choosing a particular diagnostic method or therapeutic protocol when there are several insufficiently stratified options [1].

Overlaid on this context is the problem of an increasingly common disease, namely osteoporosis. There are many diagnostic, preventive and therapeutic resources for this condition, but despite this visible progress, more than half of the total population at risk is not identified and therefore not sufficiently treated to reduce the risk of fracture [2].

The newest method of identifying these patients is the trabecular bone score (TBS). It represents a unique reflection of medicine to date by recording certain data related to bone quality [1].

The TBS is a textural marker consisting of different shades of grey that are obtained directly from lumbar DXA acquisition images. TBS has the property of providing a prediction of the risk of osteoporotic fractures without actually establishing the diagnosis of osteoporosis. Thus, it is the newest method used to routinely assess the skeleton for risk of minimal trauma (fragility) fracture [3].

2. Results

The general search revealed a number of 456.728 articles in total: 3.751 in PubMed and 452.977 in Springer. 3210 papers remained after the removal of duplicates. After screening the titles and abstracts, 3129 studies were excluded, resulting in 52 articles. 16 articles were left after excluding the papers that discussed the clinical correlation with other patologies. Of these, 6 articles that were published between 2015 and 2022 were chosen in final (Figure 1).

Articles have been sorted using the following criteria for inclusion: population: patients suffering from osteopenia and osteoporosis. Only articles from 2015 to 2022, written in English were elected. Exclusion criteria for this review were articles written in other language than English, books, book chapters and conference abstracts, articles regarding TBS in conjunction with pathologies other than osteopenia and osteoporosis.

The titles and abstracts of the selected articles were evaluated by two reviewers, and if the two could not reach consensus, a third reviewer was consulted.

Two reviewers will independently the data from the articles, namely: participants, study design, intervention, methodological quality from the included studies, outcome measures.

The resulting six papers are listed in the table below, along with information about the authors, the country and year in which they were published and references (Table 2).

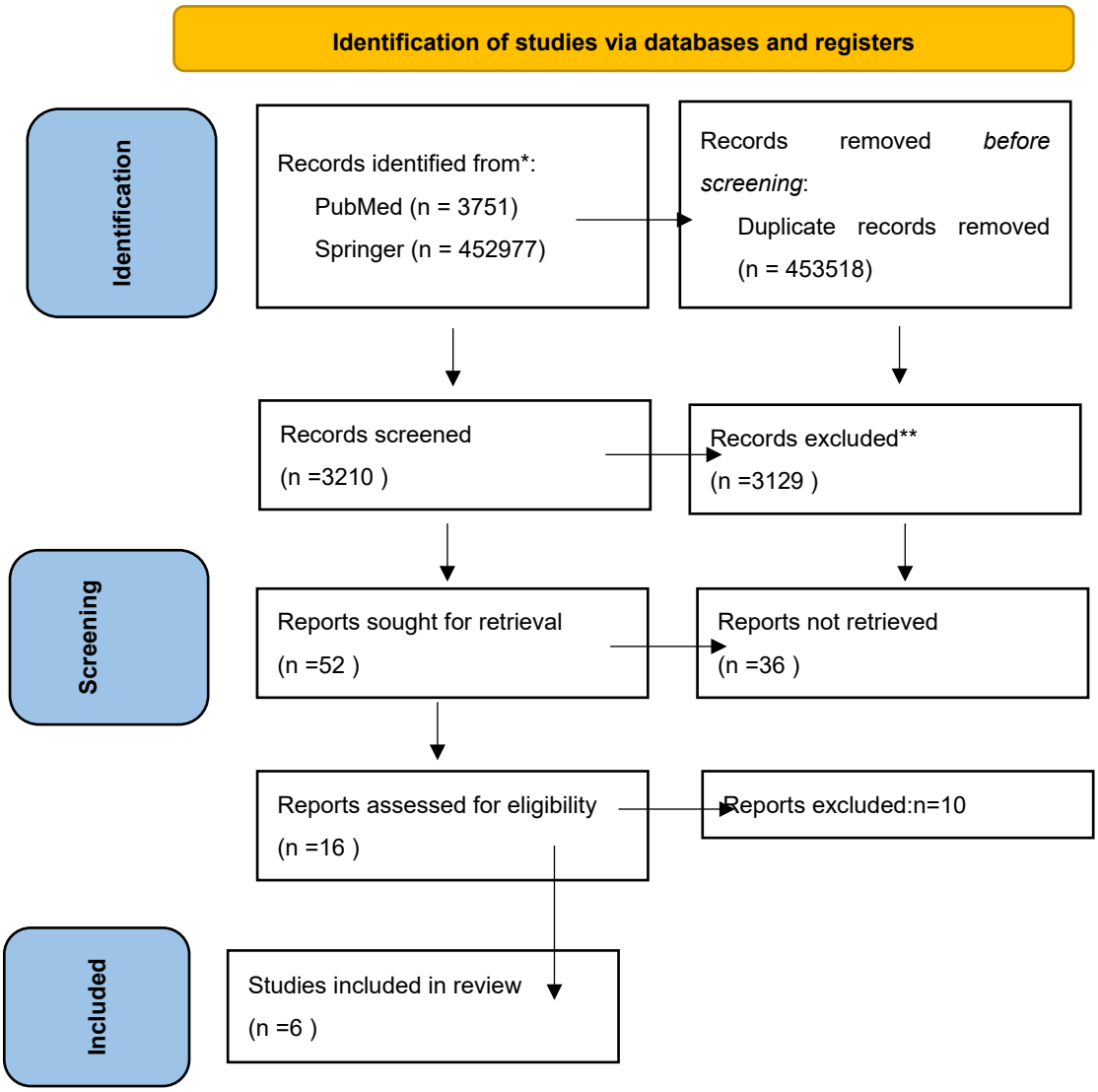

Fig.1. PRISMA adapted type of the flow diagram

Authors	Year	Country	References
Bazzocchi et al.	*2015*	*Italy*	*37*
Popp et al.	*2015*	*Germany*	*43*
McCloskey et al	*2015*	*SUA*	*64*
Ripamonti et al.	*2018*	*Italy*	*22*
Messina et al.	*2019*	*Italy*	*21*
Therdiothin et al	*2022*	*Thailand*	*30*

Table 2. Distribution of the articles

The review highlights the importance of the trabecular bone score for diagnosing osteopenia and osteoporosis. The description of the study included can be found below.

In 2015, Bazzocchi et al. examined the importance of trabecular bone score in a study of 250 people. The main objective of the paper was to report on trabecular bone score (TBS)

by dual-energy X-ray absorptiometry (DXA) in healthy Italian individuals. The second objective was to study the relationship between TBS and conventional bone and body composition parameters by DXA. Two hundred and fifty individuals from 5 age groups (ranging from 18 to 70 years, equally distributed in both age and sex) were recruited in a prospective study. A DXA scan of the lumbar spine (LS) (Lunar iDXA™; GE Healthcare, Madison, WI) was acquired for each subject and subsequently analyzed with the latest version of TBS iNsight v. 2.1 software (Med-Imaps, France, Pessac). LS bone mineral density (LS BMD), T-score, Z-score and TBS values were obtained. A significant reduction in TBS and LS BMD was recorded with age in both men (mean TBS from 1.486 to 1.374; mean LS BMD values from 1.219 to 1.187) and women (mean TBS values from 1.464 to 1.306; mean LS BMD values from 1.154 to 1.116). There was a significant correlation between LS BMD and TBS values in both sexes ($r = 0.555$-0.655, $p < 0.0001$). BMI determined LS BMD but not TBS. TBS values were inversely correlated with some adipose mass indicators, especially visceral adipose tissue (in men: $r = -0.332$, $p < 0.001$; in women: $r = -0.348$, $p < 0.0001$). No correlation was identified between TBS and total lean mass, contrary to BMD LS (in men: $r = 0.418$, $p < 0.0001$; in women: $r = -0.235$, $p < 0.001$).This study represents an attempt to initiate the creation of a database for healthy people in Italy that would provide age and sex reference curves for TBS. This could help clinicians to improve patient management in terms of detecting affected bone mineral status and monitoring bone developments [4].

Another 2015 study led by McCloskey et al. shows that TBS is an independent predictor of bone mineral density (BMD) for fracture risk. The aim of this meta-analysis was to find out whether TBS predicted fracture risk independently of FRAX probability and to check their combined performance by correcting FRAX probability for TBS. Individual-level data from 17,809 men and women in 14 prospective population-level cohorts were used. TBS and FRAX risk variables were entered as the basis of the assessment, and outcomes during the follow-up period (mean 6.7 years) included major osteoporotic fractures. The correlation between TBS, FRAX probabilities and fracture risk was analysed using an extension of a Poisson regression model in each cohort and at the level of each sex and was displayed as a risk gradient. FRAX probabilities were assessed as a function of the risk variable (GR; risk ratio for each 1 SD change in the risk variable in the direction of increasing risk). Overall, the GR of TBS in major osteoporotic fracture was 1.44 (95% confidence interval [CI] 1.35-1.53) when adjusted for age and time since baseline and was similar in men and women ($p > 0.10$). When additionally adjusted for FRAX 10-year estimate of the probability of a major osteoporotic fracture, TBS still remained a significant and independent predictor for fracture (GR = 1.32, 95% CI 1.24-1.41). Adjusting FRAX probability for TBS resulted in a non-significant increase in GR (1.76, 95% CI 1.65-1.87 vs. 1.70, 95% CI 1.60-1.81). There was a smaller change in GR for hip fracture (FRAX probability for hip fracture GR 2.25 vs. 2.22). TBS is a significant predictor of fracture risk independent of FRAX. The results support the use of TBS as a potential adjustment for FRAX probability [5].

A study conducted in Germany by Popp et al. predicted fracture risk in a specific sample of postmenopausal women with the aim of establishing the estimated predictive value of vertebral trabecular bone score (TBS), individually or in addition to bone mineral density (BMD). Retrospective analysis of the relative contribution of BMD (measured at femoral neck (FN), total hip (TH) and lumbar spine (LS) levels) and TBS to the risk of incident clinical fracture in a representative cohort of postmenopausal female patients who had previously participated in the Swiss Evaluation of the Methods of Measurement of Osteoporotic Fracture Risk study. Mean age 76.1 years, LS BMD 0.863 g/cm2 and TBS 1.195. LS BMD and LS TBS were moderately associated ($r 2 = 0.25$). After a mean of 2.7 ± 0.8 years of follow-up, the frequency of fragility fractures was 9.4%. Age- and BMI-adjusted hazard ratios (95% confidence intervals) on standard deviation subtraction were 1.58 (1.16-2.16), 1.77 (1.31-2.39) and 1.59 (1.21-2.09) for LS, FN and TH BMD, respectively, and 2.01 (1.54-2.63) for TBS. While 58 and 60% of fragility fractures occurred in females

with a T BMD score ≤-2.5 and TBS <1.150, respectively, combining these two limits identified 77% of all females with an osteoporotic fracture. TBS, alone or in combination with BMD at the lumbar spine, predicted frailty bills in a cohort of postmenopausal women [6].

A 2018 retrospective, case-control study examines the ability of TBS to predict fragility spine fractures (FFS) in postmenopausal women with and without known osteoporosis (diagnosed by T-score≤-2.5). TBS and LS-BMD were determined at the L1-L4 lumbar spine. Statistical analysis was performed on the entire group of 699 women, both women with osteoporosis (osteoporosis subgroup) (n. 253) and women without osteoporosis (non-osteoporosis subgroup) (n. 446). In the unpaired t-test, both LS-BMD and TBS (p≤0.001) were lower in women with LFS (n.62) of the total group. Within the non-osteoporosis subgroup, TBS (p≤0.009) was lower in women with LFS (n.29). Within the osteoporosis subgroup, LS-BMD (p≤0.003) was lower in women with LFS (n.33). Considering TBS and LS-BMD taken separately in a block logistic regression, TBS was associated with LFS in the whole group (odds ratio (OR): 1.599, 95% confidence interval (CI): 1.021-2. 128) and in the non-osteoporosis subgroup (OR: 1.725, 95% CI:1.118-2.660), while LS-BMD was associated with LFS in the whole group (OR: 1.611, 95% CI: 1.187-2.187) and in the osteoporosis subgroup (OR: 2.383, 95% CI: 1.135-5.003). After direct logistic regression, introducing TBS, LS-BMD and disturbance factors as predictors, LS-BMD in the whole group (OR: 1.620, 95% CI: 1.229-2.135) and in the osteoporosis subgroup (OR: 2.344, 95% CI: 1.194-4.600) and TBS in the non-osteoporosis subgroup (OR: 1.685, 95% CI: 1.131-2.511) were the only predictors of LFS. In the whole group, TBS predicted SFFs as well as LS-BMD, but not independently of it. TBS, but not LS-BMD, predicted SFFs in the non-osteoporosis subgroup [7].

A study conducted in Italy in 2019 demonstrated that an increase in soft tissue thickness does not influence the reproducibility of TBS. It investigated the effect that increasing body mass index (BMI) and waist circumference had on the accuracy error of TBS in patients in relation to bone mineral density (BMD).A group of postmenopausal women was divided into 3 different BMIs (normal, overweight and class I obesity), in addition 2 other groups based on waist circumference diameter (≤88 cm and >88 cm, respectively). The coefficient of variation, percentage of least significant change and degree of reproducibility were calculated according to the guidelines of the International Society for Clinical Densitometry. Ninety-five women aged 66 ± 10 years (mean ± standard deviation) were included. No significant differences were found for both BMD and TBS accuracy errors, respectively, when comparing BMI and waist circumference groups. BMD reproducibility ranged from 95.9% (BMI > 30 kg/m2) to 97.5% (BMI < 25 kg/m2). TBS reproducibility ranged from 95.8% (BMI = 25-29.9 kg/m2, waist circumference > 88 cm) to 96.6% (BMI < 25 kg/m2). Apart from the obese group, there was a significant difference between BMD and TBS, with TBS being lower than BMD. There was a significant decrease in TBS values between normal and obese subjects and between waist circumference groups. The accuracy error of TBS is not influenced by the waist circumference value.The reproducibility of TBS was found to be lower than that of BMD, but this difference was attenuated in obese patients [8].

Another study in Thailand was done to detect osteopenic women with high fracture rates. A cohort of postmenopausal Thai women with BMD of femoral neck (FN), bilateral hip (TH) and L1-L4(LS) lumbar spine was evaluated at the General Police Hospital, Bangkok, Thailand. The hospital database for medication, underlying diseases and fractures, including relevant imaging and vertebral fracture assessment (VFA) was reviewed. Patients with prior treatment for osteoporosis, skeletal malignancies, trauma and uninterpretable BMD were excluded from the study.

Included in the study were 407 postmenopausal women, including 115 with osteoporotic fractures. The mean TBS of the group was 1.264 ± 0.005. The proportion of subjects with osteoporosis ranged from 9.1% after TH BMD to 27.0% after lowest BMD. Among patients with fractures, 21.7%-54.8% were found to have osteoporosis, while osteopenia was detected in 37.4%-43.5%. Among individuals with osteopenia and degraded BMD, fractures ranged from 21.7% to 50.9%. The addition of osteopenic subjects with impaired

microarchitecture resulted in a significantly higher number of treatable subjects, with a 3.25-fold increase in participants with no fracture and an additional 7-11 osteopenic patients who would need to be treated to detect 1 fracture.

TBS helped detect osteopenic women at increased risk of fracture. The decision to treat osteopenic women with degraded TBS increased the number of patients receiving treatment. Assessment of TBS in osteopenic women without any fracture is recommended to support the therapeutic decision to initiate treatment [9].

3. Discussion

Osteoporosis, the leading cause of brittle bone fractures, is a major public health problem primarily affecting postmenopausal women and older people of both sexes. In 1990, the incidence of fragility fractures was about 1.5 million worldwide and is expected to reach three million by 2025. Osteoporotic fragility fractures lead to severe mortality, a significant burden on society in general and a huge economic impact [10].

Currently, technologies used to detect skeletal microarchitectures, such as microCT biopsy analysis of the transiliac bone crest, MRI and high-resolution peripheral quantitative CT, are not routinely available [11,12].

As recommended by the World Health Organization (WHO) in 1994, bone mineral densitometry (BMD) measured at both the lumbar spine and proximal femur by dual X-ray absorptiometry (DXA) is the gold standard for diagnosing osteoporosis in postmenopausal women. Given all this, there is a large overlap in BMD values between people who will and will not have a fragility fracture, suggesting that BMD is not the main factor determining fracture risk. Other factors such as trabecular bone microarchitecture, bone mineralisation and turnover have been shown to play a significant role in bone quality [2,3].

Trabecular bone score (TBS) is an index of bone microarchitecture. It is a texture measure that quantifies variations in the gray level distribution of dual-energy X-ray absorptiometry (DXA) and correlates meaningfully with three-dimensional parameters of bone microarchitecture, independent of aBMD [11,12].

The clinical utility of a diagnostic test is to add more information to that derived from other techniques to improve overall diagnostic sensitivity [11,12].

In addition, it is important to appreciate that bone strength is also influenced by bone quality, an overall term describing a set of characteristics such as structural and the material properties of bone, both of which are affected by the rate of bone turnover. The structural properties of bone include the geometry and microarchitecture (thickness, connectivity, separation and number of trabeculae, and cortical thickness and porosity), while material properties include bone mineral content (crystal size and orientation) and collagen composition, as well as bone lesion accumulation [6,7].

The number of research evaluating the possible beneficial effect of TBS on the predictive value of FRAX for fracture is growing, but there is still a relatively new area of interest in the field of osteoporosis no agreement in this aspect [2].

A single metric is insufficient to fully describe bone quality. A complete understanding of bone quality could be obtained by combining ex vivo mechanical and compositional approaches with current noninvasive imaging methods. For the therapy of osteoporosis and fracture risk, combining the use of BMD, TBS, and clinical risk factors in clinical routine has shown to be effective. We can fine-tune the risk of fracture stratification, therapy choice, and disease management using this combination, whether or not FRAX is involved [13].

4. Materials and Methods

Experimental design

This review was designed using the "PRISMA" methodology- "Preferred Reporting Items for Systematic Reviews and Meta-Analysis"- the method accepted at the international level. For the selection of eligible articles for our research we scoped the following databases: Center for Biotechnology Information (NCBI) - PubMed and Springer. The following keywords were used initially to search the databases trabecular bone score, bone mineral density, fracture risk. (Table 1).

Key words	Pubmed	Sciencedirect	Total
Trabecular bone score	*31*	*14239*	*14270*
Bone mineral density	*3715*	*129839*	*133554*
Fracture risk	*5*	*308899*	*308904*

Table 1. Centralization of the keywords

5. Conclusions

The TBS determination is in fact an opportunity because no additional X-ray exposure of the patient is needed for another DXA acquisition and can be performed on an older determination of the same individual.

These studies show that the addition of TBS helped capture osteopenic women who were at high risk of fracture. The decision to treat osteopenic women with degraded TBS increased the number of patients receiving treatment. Therefore, we recommend the evaluation of TBS in postmenopausal osteopenic women without fracture to help make therapeutic decisions about initiating treatment.

TBS does alter with osteoporosis treatment, although not to the same extent as spine aBMD (areal BMD), and the relationship between TBS change and decreased fracture risk is unclear. In certain cases of secondary osteoporosis (such as diabetes, hyperparathyroidism, and glucocorticoid-induced osteoporosis), TBS may also be important in determining the risk of fracture. To sum up, TBS can be useful in assessing fracture risk when combined with aBMD and FRAX [14].

TBS assessment improves fracture risk prediction in primary and secondary osteoporosis and provides valuable information for treatment decision-making and monitoring when combined with FRAX and/or BMD [15].

Author Contributions: Conceptualization, I.A and M.G.I.; methodology, I.A. and L.E.S.; software, O.A.; validation, M.G.I. and L.E.S.; formal analysis, I.A.; investigation, O.A.; resources, A.E.U., L.C.V..; data curation, L.C.V.; writing—original draft preparation, I.A.; writing—review and editing, M>G.I..; visualization, I.A.; supervision, M.G.I. and L.E.S.; project administration, M.G.I. *All authors contributed equally in this paper.*

Funding: This research received no external funding.

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: Not applicable.

Acknowledgments: The study was realized in Reasearche Nucleus of Techirghiol Rehabilitation Sanatorium.

Conflicts of Interest: The authors declare no conflict of interest.

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