Accepted Article

Journal of Research and Practice on the Musculoskeletal System JRPMS

Review Article

Additional tools for the estimation of fracture risk using DXA method

Laoura R. Vako

Laboratory for the Research of Musculoskeletal Disorders, Medical School, National & Kapodistrian University of Athens, Greece

Abstract

As the world population grows, the life expectancy of the elderly will continue to grow. With the growing prevalence of various chronic diseases, the incidence of fragility fractures caused by osteoporosis is expected to further increase in the future. DXA is a simple, inexpensive and safe technique currently used for the diagnosis of osteoporosis, but numerous osteoporotic fractures also present in patients with osteopenia. Other techniques using the DXA technology also currently employed, such as the assessment of bone quality by analyzing bone microarchitecture with Trabecular Bone Score (TBS), or geometrical properties of the femur with Hip Structural Analysis (HSA) contribute to the prediction of fracture risk and bone strength, while Vertebral Fracture Assessment (VFA) serves in assessing prevalent vertebral fractures by replacing conventional X-ray.

Keywords: Dual-energy X-ray Absorptiometry, Hip Structural Analysis, Osteoporosis, Trabecular bone score, Vertebral Fracture Assessment

Introduction

Osteoporosis is mainly characterized by low bone mass as well as by bone microarchitectural deterioration, thus increasing the risk of fractures. Therefore, osteoporosis may cause a high fracture risk due to low intensity impact or loading forces. Patients at risk for fragility fractures may be identified by DXA and its T-score system.

DXA is a technique for measuring BMD, the major bone strength determinant, utilizing quantitative procedures. DXA scans produces bone mineral density reports in terms of [g/cm^2]. The bone mineral density that is derived, is equal to BMC (bone mineral content in [g]) by ROI (region of interest) scanned in [cm^2]. The results of DXA are reported as the SD (standard deviation) from mean BMD of a population of young healthy women, (T-score) and or an age-matched population (Z-score).

As defined by WHO (World Health Organization), based on the T-score of each person, osteoporosis is distinguished in the following four categories: normal bone density (T-score greater than or equal to -1.0 SD), osteopenia (T-score between -1,0 and -2,5 SD), osteoporosis (T-score less than or equal -2,5 SD) and established osteoporosis (T-score less than or equal -2,5 SD with one or more fragility fractures).

The World Health Organization's fracture risk assessment algorithm, which is well known as FRAX and is the most widely used tool, takes into consideration a very important risk factor such as Femoral neck BMD by DXA, but also includes risk factors such as age, sex, previous fragility, smoking, alcohol consumption, use of corticosteroids or history of rheumatoid arthritis. This well-studied tool has various country specific versions and the algorithms may give a 10 year probability of major osteoporotic and hip fractures.

Nevertheless, many people who lie within the normal range for bone density or slightly below in the osteopenic ranges still suffer fragility fractures. This suggests that there may be other factors to consider when attempting to predict risk for fractures, such as geometry of the bone, micro-architectural changes, accumulated microfractures, rate of bone remodeling and others. Taking into account

The author has no conflict of interest.

Corresponding author: *Laoura R. Vako, Nikis 2, Kifissia, 14561, Greece*

E-mail: *laouravako@gmail.com*

Edited by: *Konstantinos Stathopoulos*

Accepted *22 April 2021*

all of these factors, in addition to the aBMD, gives a much more comprehensive picture of the bone's overall health and therefore is a better risk indicator. Given this reality, efforts have been made in recent years to more accurately screen patients who may be at increased risk of fragility fractures by developing better assessment tools based on DXA, which is readily available. These adjunct techniques include VFA (vertebral fracture assessment), (TBS) trabecular bone score, as well as, DXA-derived hip structural analysis[1-6].

VFA

Vertebral fractures increase in direct correlation with age and have a direct impact on decreased quality of life and increased mortality and morbidity. It's therefore surprising that they remain frequently underdiagnosed, especially given their high value for in risk assessment for further fractures. Genant et al.[7] describe the visual SQ (semi-quantitative) assessment of typical radiographs, which is the most widely accepted method used to identify VF: grade one for an anterior, mid or posterior decrease in vertebral height between 20 to 25%, grade two for a decrease between 25 and 40% and grade three for a higher than 40% decrease.

Vertebral fracture assessment is a technique used for thoracic and lumbar spine imaging by DXA. This method is mainly used for detecting vertebral fracture and is accomplished using images acquired by bone densitometers in the same period as bone mineral density measurements have been carried out.

Vertebral fracture assessment compared to conventional radiography

VFA technique has several advantages for the patient over conventional radiographs. It can aid in the VF diagnosis during the same visit as a BMD measurement. Additionally, the radiation exposure for the patient is minuscule (roughly 3-40 μSv) compared to the exposure associated with a conventional lateral thoracic and lumbar spine radiograph (over 600μSv). The cost is potentially lower as well[8].

Based on available data[9], several clinical guidelines have already adopted VFA as their primary tool to assess prevalent vertebral fractures, and subsequently risk for fracture. In addition to the aforementioned advantages VFA has over conventional radiotherapy, it has been found that it comes with the trade-off of higher noise rates in the upper thoracic, between levels Th4 and Th6[10]. This problem also applies to X-ray, but to less extent[11]. In addition, according to available data[12,13], the inferior resolution is directly related to reduced accuracy in the grade 1, mild fractures diagnosis.

Recently, vertebral fracture assessment technological developments may further improve performance compared to conventional radiography. Buehring et al[14] found over 90 percent of all vertebrae to be evaluable on vertebral fracture assessment images using a newer Lunar-GE densitometer, compared to more than 75 percent on VFA images acquired on an older generation densitometer. According to a study[15], the most recently available Hologic vertebral fracture assessment technology also yields better images compared to elder Hologic densitometers. As a consequence, reported less than 2 percent of vertebrae not to be evaluable and for Genant SQ grade 2 or grade 3 prevalent vertebral fractures, vertebral fracture assessment was reported that has close to 100% specificity compared to radiographs and at least 93 percent sensitivity. This percentage may reach even higher values with the use of improved resolution technologies.

In addition, latest developments in image quality by new dual-energy X-ray absorptiometry devices may lead to higher accuracy of vertebral fracture assessment, further assisting mild VFs diagnosis[16,17]. As indicated in[17] vertebral fracture assessment by recent DXA devices showed high sensitivity and specificity in tremendous agreement with SQ assessment of spinal radiography, misclassifying only eleven vertebrae among more than 4500. Only three mild VF's identified by spinal radiography were not diagnosed by vertebral fracture assessment.

However, if there are two or more unavailable vertebrae below Th6, the presence of osteoarthritis[11], reduced visualization due to moderate to severe scoliosis[18] or a need to confirm possible (grade 1) vertebrae fractures, additional confirmatory spine radiography should be considered[19].

Indications for VFA

In 2019, the ISCD eased the indications in the diagnostic use of VFA using DXA spine images as a prospective alternative to typical radiography, in order to detect vertebral fracture in the screening of people with risk of osteoporosis and in the follow-up of osteoporotic patients undertaking treatment.

Densitometric vertebral fracture assessment is specified when T-score is lower than -1.0 and when one or more of the above exists[20]:

- Age of Women higher or equal to 70 years or men's age higher or equal to 80 years
- Historical height loss more than 4 cm
- Self-reported but not listed former VF
- Glucocorticoid treatment equal to 5 mg of prednisone or higher or per day equivalent for 3 months or higher

Recommendations of the National and International Osteoporosis Foundation are mostly in accordance with the ISCD, taken a few additions into consideration. For instance the National Osteoporosis Foundation[21] recommends in postmenopausal females and males older than 50 years with low trauma fracture during middle age (>50) or historical height reduction of 4 cm or more and potential height loss of 2 cm or more, or recent or ongoing long term glucocorticoid therapy.

Use of VFA in clinical practice

Vertebral fracture assessment technology has been exclusively designed in order to detect VF's, the diagnosis of which is of great importance in the osteoporosis detection

and treatment. VF's often represent the first osteoporotic fracture, as well as they also validate osteoporosis diagnosis, regardless of each individual's BMD[22].

However, the majority of VF's are not clinically obvious[23]. The undiagnosed fractures are not always asymptomatic but, on the other hand, they are often related to back pain and reduced activity. In addition, they are usually ignored by patients and doctors or attributed to other common diseases such as degenerative joint[24].

Furthermore, vertebral fracture assessment may be proved valuable to people with rheumatic diseases[25], particularly in rheumatoid arthritis and ankylosing spondylitis, in whom the presence of VF and osteoporosis is above average. Exceptional attention should be given to undertake such scans among those with more severe, active or prolonged disease, and those with a history of prolonged high dose glucocorticoid use[26].

A large study[27], showed that VF's identified on bone density vertebral fracture assessment images in clinical practice foresee incident hip, non-vertebral, major osteoporotic, and clinical VF's. The before mentioned study strongly supports the incorporation of targeted vertebral fracture assessment imaging at the time of bone densitometry to increase fracture risk evaluation and identification of post-menopausal females and older males at high risk of fracture.

VFA scans may show other irregularities, such as aortic calcification presence. The degree of calcification may be quantified to deliver an important mark of prevailing cardiovascular disorder, which provides cardiovascular events future prediction[28].

TBS (Trabecular Bone Score)

Definition

The Trabecular Bone Score is a textural index based on assessing the pixel gray-level variations in the lumbar dual-energy X-ray absorptiometry image as an innovative index of bone quality. The Trabecular Bone Score software has been approved for use by FDA in 2012. Applying Trabecular Bone Score measurements to clinical dual-energy X-ray absorptiometry images could be an efficient answer to the typical clinical assessment of TB microarchitecture.

Trabecular Bone Score is determined from the slope of the log-log transform of the 2D experimental variogram, relating gray-level variations in dual-energy X-ray absorptiometry images as a function of distance. A high value of TBS is directly correlated to better bone texture while a reduced value of TBS is related to weaker bone texture.

Trabecular Bone Score approximations normally are robust and independent from the dual-energy X-ray absorptiometry equipment, if the device is appropriately calibrated. The ability to evaluate TBS retrospectively using formerly acquired DXA images was influential in data collection validating with these the use in clinical practice[29-31].

Development of TBS

TBS was developed using two-dimensional projection images derived directly from three dimensional μCT reconstruction of human cadaveric bone specimens. These early results showed substantial associations between Trabecular Bone Score and skeletal volume fraction, trabecular spacing, and trabecular number using cadaveric vertebral, femoral neck, and distal radius samples[31].

Consequently, this method was extended to dual-energy X-ray absorptiometry images obtained ex vivo in cadaveric vertebrae. Various studies have presented noteworthy associations between TBS and various microstructural parameters of bone evaluated by microcomputed tomography.

It is tempting to speculate that TBS provides information on macroscopic parameters which, in turn, correlate with bone microstructure. This remains an area of active investigation. However, TBS has been shown to be a clinically useful tool due to its ability to assess fracture risk[32,33].

Factors that influence TBS values

Reported data[34] indicate that TBS values obtained for all lumbar vertebral combinations reduced with age. There is a linear decrease of 16 percent (~ -2.47 T-score) in the microarchitecture at L1-L4 between 45 &90 years of age versus (-2.34 BMD). The microarchitecture rate of loss rises after the 65 years by 50 percent (from -0.004 up to -0.006).

Even though degenerative diseases of the lumbar spine are expected to affect values of TBS, there are publications[35] which propose that this effect is relatively small. It may be expected that there is vertebral exclusion is not needed for the calculation of TBS. In order to define the appropriate clinical approach, more fracture data studies are needed.

On the other hand, body weight and BMI have a major influence on TBS values. For example, in 82 women 12 to 41 years old, with anorexia nervosa, the values of TBS were reduced in the group with osteoporosis and directly related to parameters such as BMI, body weight and fat mass[36]. Even though soft tissue thickness and BMI are taken into consideration while TBS is derived, the association between TBS and body weight proposes that TBS outcomes should be adjusted for BMI.

In addition, even more technical and clinical studies are essential for the determination of advantages and limitations of the TBS. These, may be proved useful in clinical practice as far as treatment decisions are concerned[37].

Fracture Risk Prediction by TBS

Several studies have displayed that TBS is used for fracture risk prediction in females and males. The Canadian province of Manitoba published a large study assessing TBS[38]. A sum of 29407 women 50 years or older has been identified from a database containing all clinical results, at the time of baseline hip and spine DXA. TBS has been

correlated with many risk factors that predict fractures and considerably reduced spine TBS and BMD were identified in females with major osteoporotic, spine, and hip fractures (all p<0.0001). Spine TBS and BMD predicted osteoporotic fractures equally fine, and the combination was superior to either measurement alone (p<0.001). The TBS prediction on fracture risk has also been studied in 560 postmenopausal white females from the French (OFELY) cohort[39]. Fractured women had, at baseline, reduced LS BMD and TBS than other without incident fractures.

Recent studies[40-43] have shown correlation between LS TBS and vertebral, hip and other types of osteoporotic fractures to postmenopausal females. A more recent study from Leslie and colleagues[44] has shown that TBS is directly correlated to incident fractures in men. In addition, another study in men with limited data[45], has also confirmed the before mentioned statement.

Furthermore, recent studies[46,47] have shown an enhancement in fracture estimation when TBS is used combined with FRAX. Recently published ISCD official reports[48] suggest that "TBS can be used in association with FRAX and BMD to adjust FRAX probability of fracture in postmenopausal women and older men."

Hip Structural Analysis

In the modern era, technological developments of DXA equipment may produce data for the determination of BMD, as well as the bone geometry parameters such as femoral size, shape, and strength. HSA (Hip Structural Analysis) and AHA (Advanced Hip Assessment) have been approved from the FDA in clinical use.

In addition, as far as the scanner is concerned, various parameters such as CSA (cross-sectional area), CSMI (the cross-sectional moment of inertia), BR (the buckling ratio), or SM (section modulus) may be acquired from DXA commercial scans.

Hip Structural Analysis and Advanced Hip Assessment estimate macro-architecture of the hip from the 2D DXA image and obtain parameters that are well known to be related to the fracture risk and the bone strength.

In addition, HAL (the hip axis length) which is defined as the distance from the inner-pelvic brim to the greater trochanter and NSA (the neck shaft angle), which is the angle between femoral neck axis and femoral mid-shaft axis, may be derived from a dual-energy X-ray absorptiometry image manually or automated[49,50].

Faulkner et al[51] studied the Osteoporotic Fractures and presented that a longer hip axis length has been related to an increased risk of hip fracture in postmenopausal females. Following the study results in multiple populations, the hip axis length may predict hip fracture in postmenopausal females only[50].

The risk may not be quantified and as a consequence prior data acquired from the Manitoba database showed that the hip axis length was able to predict hip fractures with adjustments and with a substantial development in total risk reclassification[52].

Strong evidence indicates that the neck shaft angle may be able to predict hip fracture in postmenopausal females and males older than 60 years, with inadequate evidence that this risk is not dependent on BMD. On this purpose, no sufficient evidence prove that neck shaft angle may seem useful in clinical practice. Neck shaft angle, also differs by ethnicity and gender with a wider angle in males compared to females, and a higher one in Caucasians compared to Chinese[50].

Limitations

DXA scanners have also limitations concerning bone geometry parameters. Some are due to the irregularity of the proximal end of the femur and the fact that it rotates about the acetabulum, which is not located on its long axis[53]. It has been noted that even minor rotational changes may produce a significant effect on the projected dimensions. The technologist cannot visually identify the femur and rotation of the leg is a matter that may affect the measurement.

Furthermore, another limitation of HSA is that scan images are often blurred so that edge margins can be difficult to locate precisely. Image quality problems tend to be higher with the fastest scan modes and in heavier patients. Also, due to the fact that DXA is two-dimensional, HSA can evaluate CSMI and section modulus only in the image plane. Many bone cross-sections are not axially symmetric, so these properties vary with rotation of the bone[54].

The use of Hip Geometry Parameter for the fracture risk prediction

The risk of hip fracture currently is well estimated by dual energy X-Ray absorptiometry (DXA) which is the most readily quantified skeletal strength measure method. Low BMD DXA has been established as fragility fracture risk factor but, on the other hand, the percentage of fracture risk as explained by bone geometry is considered unclear. For instance, Rotterdam cohort study[55] suggested that the result from the HSA (cortical thickness, section modulus narrow neck width, and buckling ratio) were no better than the ones derived from the predictive capability for hip fracture of BMD because the extreme thinning of cortices in expanded bones plays a key role on local susceptibility to fracture and this do not estimate with DXA yet.

On the contrary, Kaptoge et al[56] study of Osteoporotic Fractures (SOF), showed that proximal femurs of elderly women with hip fracture have lower bending (section modulus) and axial (CSA) strengths, with thinner more asymmetric cortices, and are wider in diameter than those of fracture-free women. These geometrical parameters provided better prediction of hip fracture risk than hip BMD.

The Manitoba study[57] provided data of 30953 woman aged 50 years hip DXA measurements, with 270 hip fractures during 3,7 years of observation. Only HAL and FSI

seemed to give a significant, though small, contribution to hip fracture prediction with no dependence on age and BMD measurement.

The importance of HAL, one of the first geometrical indexes, is still controversial. Although it is proposed as an indicator of proximal femur fracture risk for women, independent on FN BMD measurement[58]. It is not always well considered as an independent risk factor[59]. Recently, Leslie et al[60] demonstrated that HAL was an independent BMD and FRAX risk factor.

The 2015 ISCD guidelines, suggest that the small changes from baseline in hip structural parameters cannot be used for therapy effects monitoring in clinical practice. Neither HAL, nor NSA is expected to change with therapy, although the measurements were precise.

Many studies have shown that hip geometrical parameters are directly associated to the risk of hip fracture (particularly BR, SM, HAL, and NSA), but the risk cannot be quantified. On this purpose these parameters, at this time, cannot be used in order to initiate treatment in clinical practice.

Additional data and studies are needed in order to determine the quantification of the HAL effect for use in clinical practice, not only in postmenopausal women, but also in men, African Americans and more. Moreover studies with newer, better resolution DXAs, may expand the clinical utility of these measurement[50].

Conclusion

DXA can be used not only to measure BMD as well as for other additional tools such as TBS, VFA and HSA for a complete estimation of bone density and fracture risk.

The available scientific data for the use of TBS is promising. Preliminary data has shown that TBS can improve fracture prediction when used in combination with FRAX®. If further studies define TBS limits at age and gender, TBS could become a valuable clinical tool in the fracture risk assessment, helping to take therapeutic decisions especially to those who are at risk for fractures.

Based on the available data, VFA has already been incorporated into a number of clinical guidelines that replace the conventional X-ray to estimate prevalent vertebral fractures and therefore for the risk of fracture. The agreement between morphometric and morphological approaches for vertebral fractures 2 and 3 is high, but there is a felt inequality in mild grade 1 fractures.

Finally, hip structural analysis is an important factor in predicting hip fracture. Therefore, only BMD should not be considered clinically, but it is also important to carefully examine HSA to assess the risk of hip fracture.

References

1. van den Bergh JP, van Geel TA, Geusens PP. Osteoporosis, frailty and fracture: implications for case finding and therapy. Nat Rev Rheumatol 2012;8(3):163-72.
2. Shepherd JA, Schousboe JT, Broy SB, Engelke K, Leslie WD. Executive summary of the 2015 ISCD position development conference on advanced measures from DXA and QCT: fracture prediction beyond BMD. Journal of Clinical Densitometry 2015;18(3):274-86.
3. World Health Organization. Assessment of fracture risk and its application to screening for postmenopausal osteoporosis: report of a WHO study group. Rome: World Health Organization; 1994. p. 8-11.
4. https://www.sheffield.ac.uk/FRAX/, Accessed 15 March 2021.
5. Choksi P, Jepsen KJ, Clines GA. The challenges of diagnosing osteoporosis and the limitations of currently available tools. Clinical diabetes and endocrinology 2018;4(1):1-3.
6. Heilmeier U, Youm J, Torabi S, Link TM. Osteoporosis imaging in the geriatric patient. Current radiology reports 2016;4(4):18.
7. Genant HK, Wu CY, Van Kuijk C, Nevitt MC. Vertebral fracture assessment using a semiquantitative technique. Journal of bone and mineral research 1993;8(9):1137-48.
8. Malgo F, Hamdy NA, Ticheler CH, Smit F, Kroon HM, Rabelink TJ, Dekkers OM, Appelman-Dijkstra NM. Value and potential limitations of vertebral fracture assessment (VFA) compared to conventional spine radiography: experience from a fracture liaison service (FLS) and a meta-analysis. Osteoporosis International 2017;28(10):2955-65.
9. Kanis JA, McCloskey EV, Johansson H, Cooper C, Rizzoli R, Reginster JY. Scientific Advisory Board of the European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis (ESCEO) and the Committee of Scientific Advisors of the International Osteoporosis Foundation (IOF).European guidance for the diagnosis and management of osteoporosis in postmenopausal women. OsteoporosInt 2013;24(1):23-57.
10. Duboeuf F, Bauer DC, Chapurlat RD, Dinten JM, Delmas P. Assessment of vertebral fracture using densitometric morphometry. Journal of Clinical Densitometry 2005;8(3):362-8.
11. Schousboe JT, DeBold CR. Reliability and accuracy of vertebral fracture assessment with densitometry compared to radiography in clinical practice. Osteoporosis international 2006;17(2):281-9.
12. Kaptoge S, Armbrecht G, Felsenberg D, Lunt M, O'Neill TW, Silman AJ, Reeve J, EPOS Study Group. When should the doctor order a spine X-ray? Identifying vertebral fractures for osteoporosis care: results from the European Prospective Osteoporosis Study (EPOS). Journal of Bone and Mineral Research 2004;19(12):1982-93.
13. Ruyssen-Witrand A, Gossec L, Kolta S, Dougados M, Roux C. Vertebral dimensions as risk factor of vertebral fracture in osteoporotic patients: a systematic literature review. Osteoporosis international 2007;18(9):1271-8.
14. Buehring B, Krueger D, Checovich M, Gemar D, Vallarta-Ast N, Genant HK, Binkley N. Vertebral fracture assessment: impact of instrument and reader. Osteoporosis international 2010;21(3):487-94.
15. Hospers IC, van der Laan JG, Zeebregts CJ, Nieboer P, Wolffenbuttel BH, Dierckx RA, Kreeftenberg HG, Jager PL, Slart RH. Vertebral fracture assessment in supine position: comparison by using conventional semiquantitative radiography and visual radiography. Radiology 2009;251(3):822-8.
16. Sun Y, Wang J, Thuring T, Sanchez T. Validation of In Vivo Vertebral Fracture Assessment Using the Norland Illuminatus Software. Journal of Clinical Densitometry 2018;21(1):29-30.
17. Diacinti D, Del Fiacco R, Pisani D, Todde F, Cattaruzza MS, Diacinti D, Arima S, Romagnoli E, Pepe J, Cipriani C, Minisola S. Diagnostic performance of vertebral fracture assessment by the lunar iDXA scanner compared to conventional radiography. Calcified tissue international 2012;91(5):335-42.
18. Lin YC, Huang TS, Wu JS, Cheung YC, Huang YH, Sung CM, Juan YH, Chen FP, Mhuircheartaigh JN. Are bilateral decubitus views

necessary in assessing for vertebral compression fractures using DXA vertebral fracture assessment? Osteoporosis International 2017;28(8):2377-82.
19. Lee JH, Lee YK, Oh SH, Ahn J, Lee YE, Pyo JH, Choi Y, Kim D, Bae SC, Sung YK, Kim DY. A systematic review of diagnostic accuracy of vertebral fracture assessment (VFA) in postmenopausal women and elderly men. Osteoporosis International 2016;27(5):1691-9.
20. https://www.iscd.org 2019 ISCD Official Positions – Adult, Accessed 15 March 2021.
21. Cosman F, de Beur SJ, LeBoff MS, Lewiecki EM, Tanner B, Randall S, Lindsay R. Clinician's guide to prevention and treatment of osteoporosis. Osteoporosis international 2014;25(10):2359-81.
22. Zeytinoglu M, Jain RK, Vokes TJ. Vertebral fracture assessment: Enhancing the diagnosis, prevention, and treatment of osteoporosis. Bone 2017;104:54-65.
23. Cosman F, Krege JH, Looker AC, Schousboe JT, Fan B, Isfahani NS, Shepherd JA, Krohn KD, Steiger P, Wilson KE, Genant HK. Spine fracture prevalence in a nationally representative sample of US women and men aged ≥40 years: results from the National Health and Nutrition Examination Survey (NHANES) 2013-2014. Osteoporosis international 2017;28(6):1857-66.
24. Nevitt MC, Thompson DE, Black DM, Rubin SR, Ensrud K, Yates AJ, Cummings SR. Effect of alendronate on limited-activity days and bed-disability days caused by back pain in postmenopausal women with existing vertebral fractures. Archives of Internal Medicine 2000;160(1):77-85.
25. Lee JH, Cho SK, Han M, Lee S, Kim JY, Ryu JA, Choi YY, Bae SC, Sung YK. Validity and role of vertebral fracture assessment in detecting prevalent vertebral fracture in patients with rheumatoid arthritis. Joint Bone Spine 2014;81(2):149-53.
26. Carey JJ, Buehring B. Current imaging techniques in osteoporosis. ClinExpRheumatol 2018;36(Suppl 114):115-26.
27. Schousboe JT, Lix LM, Morin SN, Derkatch S, Bryanton M, Alhrbi M, Leslie WD. Prevalent vertebral fracture on bone density lateral spine (VFA) images in routine clinical practice predict incident fractures. Bone 2019;121:72-9.
28. Mohammad A, Lohan D, Bergin D, Mooney S, Newell J, O'Donnell M, Amin S, Coughlan RJ, Carey JJ. Vertebral fracture assessment-detected abdominal aortic calcification and cardiovascular disease in rheumatoid arthritis.In Seminars in arthritis and rheumatism 2014; 632-637.
29. Ulivieri FM, Silva BC, Sardanelli F, Hans D, Bilezikian JP, Caudarella R. Utility of the trabecular bone score (TBS) in secondary osteoporosis. Endocrine. 2014;47(2):435-48.
30. Martineau P, Silva BC, Leslie WD. Utility of trabecular bone score in the evaluation of osteoporosis. Current Opinion in Endocrinology & Diabetes and Obesity 2017;24(6):402-10.
31. Hans D, Barthe N, Boutroy S, Pothuaud L, Winzenrieth R, Krieg MA. Correlations between trabecular bone score, measured using anteroposterior dual-energy X-ray absorptiometry acquisition, and 3-dimensional parameters of bone microarchitecture: an experimental study on human cadaver vertebrae. Journal of Clinical Densitometry 2011;14(3):302-12.
32. Roux JP, Wegrzyn J, Boutroy S, Bouxsein ML, Hans D, Chapurlat R. The predictive value of trabecular bone score (TBS) on whole lumbar vertebrae mechanics: an ex vivo study. Osteoporosis International 2013;24(9):2455-60.
33. Muschitz C, Kocijan R, Haschka J, Pahr D, Kaider A, Pietschmann P, Hans D, Muschitz GK, Fahrleitner-Pammer A, Resch H. TBS reflects trabecular microarchitecture in premenopausal women and men with idiopathic osteoporosis and low-traumatic fractures. Bone 2015;79:259-66.
34. Simonelli C, Leib E, McClung M, Winzenrieth R, Hans D. Creation of the age-related TBS curve at lumbar spine in US Caucasian women derived from DXA. Journal of Clinical Densitometry 2013;3(16):272-3.
35. White R, Binkley N, Krueger D. Effect of vertebral exclusion on TBS and FRAX calculations. Archives of osteoporosis2018;13(1):1-5.
36. Maury E, Guignat L, Winzenrieth R. BMD and relationship between 3D microarchitecture and 2D with anorexia nervosa. J Bone Miner Res. 2009;24:M00017.
37. Briot K. DXA parameters: beyond bone mineral density. Joint Bone Spine 2013;80(3):265-9.
38. Hans D, Goertzen AL, Krieg MA, Leslie WD. Bone microarchitecture assessed by TBS predicts osteoporotic fractures independent of bone density: the Manitoba study. Journal of Bone and Mineral Research 2011;26(11):2762-9.
39. Boutroy S, Hans D, Sornay-Rendu E, Vilayphiou N, Winzenrieth R, Chapurlat R. Trabecular bone score improves fracture risk prediction in non-osteoporotic women: the OFELY study. Osteoporosis International 2013;24(1):77-85.
40. Iki M, Tamaki J, Kadowaki E, Sato Y, Dongmei N, Winzenrieth R, Kagamimori S, Kagawa Y, Yoneshima H. Trabecular bone score (TBS) predicts vertebral fractures in Japanese women over 10 years independently of bone density and prevalent vertebral deformity: the Japanese Population-Based Osteoporosis (JPOS) cohort study. Journal of Bone and Mineral Research 2014;29(2):399-407.
41. Winzenrieth R, Dufour R, Pothuaud L, Hans D. A retrospective case–control study assessing the role of trabecular bone score in postmenopausal Caucasian women with osteopenia: analyzing the odds of vertebral fracture. Calcified tissue international 2010;86(2):104-9.
42. Rabier B, Héraud A, Grand-Lenoir C, Winzenrieth R, Hans D. A multicentre, retrospective case–control study assessing the role of trabecular bone score (TBS) in menopausal Caucasian women with low areal bone mineral density (BMDa): analysing the odds of vertebral fracture. Bone 2010;46(1):176-81.
43. Del Rio LM, Winzenrieth R, Cormier C, Di Gregorio S. Is bone microarchitecture status of the lumbar spine assessed by TBS related to femoral neck fracture? A Spanish case–control study. Osteoporosis International 2013;24(3):991-8.
44. Leslie WD, Aubry-Rozier B, Lix LM, Morin SN, Majumdar SR, Hans D. Spine bone texture assessed by trabecular bone score (TBS) predicts osteoporotic fractures in men: the Manitoba Bone Density Program. Bone 2014;67:10-4.
45. Leib E, Winzenrieth R, Aubry-Rozier B, Hans D. Vertebral microarchitecture and fragility fracture in men: a TBS study. Bone 2014;62:51-5.
46. McCloskey EV, Odén A, Harvey NC, Leslie WD, Hans D, Johansson H, Barkmann R, Boutroy S, Brown J, Chapurlat R, Elders PJ. A meta-analysis of trabecular bone score in fracture risk prediction and its relationship to FRAX. Journal of bone and mineral research 2016;31(5):940-8.
47. Tamaki J, Iki M, Sato Y, Winzenrieth R, Kajita E, Kagamimori S. Does Trabecular Bone Score (TBS) improve the predictive ability of FRAX® for major osteoporotic fractures according to the Japanese Population-Based Osteoporosis (JPOS) cohort study?. Journal of bone and mineral metabolism 2019;37(1):161-70.
48. Silva BC, Broy SB, Boutroy S, Schousboe JT, Shepherd JA, Leslie WD. Fracture risk prediction by non-BMD DXA measures: the 2015 ISCD official positions part 2: trabecular bone score. Journal of Clinical Densitometry 2015;18(3):309-30.
49. Iolascon G, Moretti A, Cannaviello G, Resmini G, Gimigliano F. Proximal femur geometry assessed by hip structural analysis in

hip fracture in women. Aging clinical and experimental research 2015;27(1):17-21.
50. Broy SB, Cauley JA, Lewiecki ME, Schousboe JT, Shepherd JA, Leslie WD. Fracture risk prediction by non-BMD DXA measures: the 2015 ISCD official positions part 1: hip geometry. Journal of Clinical Densitometry 2015;18(3):287-308.
51. Faulkner KG, Cummings SR, Black D, Palermo L, Glüer CC, Genant HK. Simple measurement of femoral geometry predicts hip fracture: the study of osteoporotic fractures. Journal of bone and mineral research 1993;8(10):1211-7.
52. Leslie WD, Lix LM, Morin SN, Johansson H, Odén A, McCloskey EV, Kanis JA. Hip axis length is a FRAX-and bone density-independent risk factor for hip fracture in women. The Journal of Clinical Endocrinology & Metabolism 2015;100(5):2063-70.
53. Hillier TA, Beck TJ, Oreskovic T, Rizzo JH, Pedula KL, Black D, Stone KL, Cauley JA, Bauer DC, Taylor BC, Cummings SR. Predicting long term hip fracture risk with bone mineral density and hip structure in post-menopausal women: the Study of Osteoporotic Fractures (SOF). Washington: Journal of Bone and Mineral Research;2003. p. S21-S21.
54. Beck TJ. Extending DXA beyond bone mineral density: understanding hip structure analysis. Current osteoporosis reports 2007;5(2):49-55.
55. Rivadeneira F, Zillikens MC, De Laet CE, Hofman A, Uitterlinden AG, Beck TJ, Pols HA. Femoral neck BMD is a strong predictor of hip fracture susceptibility in elderly men and women because it detects cortical bone instability: the Rotterdam Study. Journal of Bone and Mineral Research 2007;22(11):1781-90.
56. Kaptoge S, Beck TJ, Reeve J, Stone KL, Hillier TA, Cauley JA, Cummings SR. Prediction of incident hip fracture risk by femur geometry variables measured by hip structural analysis in the study of osteoporotic fractures. Journal of Bone and Mineral Research 2008;23(12):1892-904.
57. Leslie WD,Pahlavan PS, Tsang JF, Lix LM. Prediction of hip and other osteoporotic fractures from hip geometry in a large clinical cohort. Osteoporosis international 2009;20(10):1767-74.
58. Gao G, Zhang ZL, Zhang H, Hu WW, Huang QR, Lu JH, Hu YQ, Li M, Liu YJ, He JW, Gu JM. Hip axis length changes in 10,554 males and females and the association with femoral neck fracture. Journal of Clinical Densitometry 2008;11(3):360-6.
59. Yu N, Liu YJ, Pei Y, Zhang L, Lei S, Kothari NR, Li DY, Papasian CJ, Hamilton J, Cai JQ, Deng HW. Evaluation of compressive strength index of the femoral neck in Caucasians and Chinese. Calcified tissue international 2010;87(4):324-32.
60. Leslie WD, Lix LM, Morin SN, Johansson H, Odén A, McCloskey EV, Kanis JA. Hip axis length is a FRAX-and bone density-independent risk factor for hip fracture in women. TheJournal of ClinicalEndocrinology&Metabolism 2015;100(5):2063-70.