# ORIGINAL PAPER

# The Trabecular Bone Score Predicts Spine Fragility Fractures in Postmenopausal Caucasian Women Without Osteoporosis Independently of Bone Mineral Density

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## ABSTRACT

**Introduction:** The trabecular bone score (TBS) is a gray-level textural metric that can be extracted from the two-dimensional lumbar spine dual-energy X-ray absorptiometry (DXA) image. TBS is related to bone microarchitecture. Several literature data suggest that TBS predicts fracture risk as well as lumbar spine bone mineral density (LS-BMD)  measurements in postmenopausal women. **Objective:** A retrospective case-control study assessing the ability of the TBS to predict spine fragility fractures (SFF) in postmenopausal women with or without osteoporosis (diagnosed by T-score≤-2.5). **Methods:** LS-BMD and the TBS were determined in the L1-L4 vertebrae. Statistical analyses were carried out in the entire group of women (entire-group) (n.699), in women both with osteoporosis (osteoporosis-subgroup) (n.253) and those without osteoporosis (non-osteoporosis-subgroup) (n. 446). **Results:** At the unpaired t-test, both the TBS and the LS-BMD (p≤0.001) were lower in women with SFF (n.62) in the entire-group. In the non-osteoporosis subgroup, the TBS (p≤0.009) was lower in women with SFF (n.29). In the osteoporosis subgroup, the LS-BMD (p≤0.003) was lower in women with SFF (n.33). Considering the TBS and LS-BMD separately in a block logistic regression, the TBS was associated with SFF in the entire-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) whereas LS-BMD was associated with SFF in the entire-group (OR: 1.611, 95% CI: 1.187-2.187) and in the osteoporosis-subgroup (OR: 2.383, 95% CI: 1.135-5.003). According to forward logistic regression, entering the TBS, LS-BMD and confounders as predictors, the LS-BMD in the entire-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 the TBS in the non-osteoporosis subgroup (OR: 1.685, 95% CI: 1.131-2.511) were the only predictors of SFFs. **Conclusions:** In the entire-group, the TBS predicted SFFs almost as well as LS-BMD, but not independently of it. The TBS, but not LS-BMD, predicted SFFs  in the non-osteoporosis subgroup.

**Keywords:**  TBS,  LS-BMD , osteoporosis, osteopenia , spine fragility fractures.

## 1. INTRODUCTION

The measurement of bone mineral density (BMD) using central dual X-ray absorptiometry (DXA) is today the best clinical method for evaluating the risk of osteoporotic fractures in postmenopausal women (1, 2). Nevertheless, for the most part, fragility fractures occur in patients without osteoporosis (1, 3), and several clinical factors other than BMD have been identified in numerous epidemiological studies (4). Evaluation of the clinical risk factors developed by The Fracture Risk Assessment Tool (FRAX) has improved the ability of BMD to evaluate fracture risk in postmenopausal women, leading to new approaches for evaluating fracture risk and as to when drug treatment should begin (5). Nevertheless, evaluation of other fracture risks concerning bone quality, such as macrogeometry of the cortical bone, trabecular bone microarchitecture, bone microdamage, bone mineralization and bone turnover, are considered important in additionally improving the evaluation of fracture risk (2, 6). Although BMD is the main determinant of bone strength and fracture risk, trabecular bone microarchitecture constitutes a major component of bone strength

and is complementary to the BMD (7). The trabecular bone score (TBS), a newly developed tool scoring the DXA scan images using a gray scale analysis, has recently been proposed as a method for evaluating bone structure (7, 8). This new technique has been reported in preliminary studies as being able to predict future fracture risk and also to differentiate women with fragility fractures from those without, having a special sensitivity for women with moderate bone loss, such as those with osteopenia at DXA analysis (7, 9, 14). Moreover, longitudinal and prospective studies have suggested that the TBS is capable of predicting future fracture risk (10, 11, 15, 16). Since the clinical utility of a diagnostic test is that of adding information to that derived from other techniques in order to improve overall diagnostic sensitivity, in this study, the ability of the TBS score was discussed as a marker of bone structure in order to correctly differentiate spine fractures in a sample of women already classified at risk on the basis of clinical risk factors, and to determine whether its discriminant ability was independent of the BMD and could be used to improve upon that of BMD. To achieve this outcome, the association of the TBS with spine fragility fractures (SFF) in women without osteoporosis in which BMD does not detect fragility fractures was particularly studied.

## 2. MATERIAL AND METHODS

This retrospective case-control study enrolled 699 white postmenopausal women who had been selected from a sample of 1087 women who had consecutively undergone bone densitometry of the lumbar spine at the Rizzoli Orthopaedic Institute (IOR Bologna, Italy) at the request of their physician or one of the Rizzoli Institute specialists. In the study, only postmenopausal women presenting with a SFF (n. 62) or having one or more clinical risk factors for osteoporosis but without fractures (n.637) were included. These data were obtained from the requests compiled by physicians in which the motives of the request for DXA (disease, pharmaceuticals, clinical risk factors including previous minimal trauma fractures and radiological findings of a vertebral fracture) were indicated. The same informations were available for patients coming from the specialist clinics of the Rizzoli Institute. Age, age at menopause, height and weight were obtained from the densitometric medical records. Women having secondary osteoporosis, both from iatrogenic causes and from pathologies associated with a risk of osteoporosis, and women with non-vertebral fractures were excluded from the study. Women who had a BMI < 17 Kg/m$^2$ or > 35 Kg/m$^2$, and those who presented evident vertebral morphological anomalies at DXA or had a T-score >1 between contiguous vertebrae were also excluded from the study.

The densitometric examinations were performed using a Hologic densitometer, Discovery QDR (Hologic,Inc., Bedford, MA, USA). The densitometric examinations were performed by an experienced physician. The lumbar spine BMD (LS-BMD) was expressed in g/cm$^2$ and was reported in the study as the average BMD value of the lumbar spine metameres L1-L4. Manufac-

turer reference population data for the European population were used for the T-score calculation. By using the TBS iNsight software (Med-ImapsTBS version 1.9.1), the TBS values were scored in same spinal regions (lumbar spine vertebrae L1-L4) in which the DXA scans were performed in order to measure the lumbar spine BMD. The average TBS scored value of the L1-L4 vertebrae was utilised for the statistical analyses in the study.

Statistical analyses had previously been carried out in the entire sample population and the same sample population was subsequently divided into two subgroups which were obtained by grouping the women according to a T-score value ≤ -2.5 i.e. osteoporotic women or > -2.5 i.e. non-osteoporotic women.

**Statistical analysis:** Elaboration of the data, which were reported as mean and standard deviation (SD) when the variables were continuous, was carried out using SPSS v 11.0 software (SPSS/PC, IL), with the exception of the Hanley-Mc Nail test (17). The comparison between the two groups was carried out using the unpaired Student t-test after verifying that the data of the groups had a normal distribution and homogeneity of variance (Levene test). The ability of LS-BMD and the TBS to differentiate spine fractures from the controls was assessed by entering these parameters as covariates in a logistic regression model having spine fractures as a dependent variable. The fracture detection ability of the LS-BMD and the TBS was estimated by calculating the Odds Ratio (OR), standardised by one SD from the mean value of the population of non-fractured women, together with their 95% confidence intervals (CI). In order to obtain this target, the LS-BMD and the TBS were first considered separately in a block logistic regression model after correcting for the confounders (age, age at menopause, height, weight). The LS-BMD, the TBS and the confounders were then simultaneously included and tested as covariates using the forward stepwise elimination in the logistic regression to select the best fracture predictive model. To compare the two parameters considered (TBS and LS-BMD) in correctly classifying women with and without fractures, receiver operating characteristic (ROC) curves, having LS-BMD or the TBS as test var-

| Characteristics | Entire population (699 women) | Without fractures (637 women) | With fractures (62 women) |
|---|---|---|---|
| Age (yr) | 68.71 ± 6.92 | 68.65 ± 6.90 | 69.27 ± 7.18 |
| Weight (kg) | 62.94 ± 10.53 | 63.11 ± 10.56 | 61.16 ± 10.07 |
| Height (cm) | 159.43 ± 6.16 | 159.54 ± 6.11 | 158.32 ± 6.59 |
| BMI (kg/m$^2$) | 24.73 ± 3.72 | 24.77 ± 3.73 | 24.37 ± 3.54 |
| Menopause age (years) | 49.42 ± 4.88 | 49.49 ± 4.86 | 48.73 ± 5.03 |
| TBS | 1.211 ± 0.100 | 1.214 ± 0.099 | 1.172 ± 0.099 * |
| LS-BMD (g /cm$^2$) | 0.815 ± 0.118 | 0.821 ± 0.117 | 0.760 ± 0.116 ** |
| T-score | -2.09 ± 1.07 | -2.04 ± 1.06 | -2.59 ± 1.05 ** |

Table 1. Baseline characteristics of the entire study population (699 women) and of the population sub-groups with spine fractures (62 women) or without spine fractures (637 women). Women with spine fractures are compared with those without fractures (unpaired T-test). Note:The data are expressed as mean ± SD- Abbr: SD, standard deviation; LS-BMD , lumbar spine bone mineral density ; TBS, trabecular bone score. unpaired T-test for non fractured Vs fractured women: *p = 0.001, **p = 0.0001

| Logistic regression including LS-BMD | | | Logistic regression including TBS | | |
|---|---|---|---|---|---|
| Parameters | OR (95% CI) | p value | Parameters | OR (95% CI) | p value |
| Age | 1.016 (0.978-1.056) | 0.415 | Age | 1.016 (0.978-1.055) | 0.423 |
| Weight | 1.005 (0.975-1.037) | 0.730 | Weight | 0.980 (0.952-1.008) | 0.163 |
| Height | 0.982 (0.936-1.030) | 0.450 | Height | 0.995 (0.948-1.044) | 0.835 |
| Menopause age | 0.973 (0.925-1.023) | 0.282 | Menopause age | 0.971 (0.923-1.021) | 0.248 |
| LS-BMD | 1.611 (1.187-2.187) | 0.002 | TBS | 1.599 (1.021-2.128) | 0.001 |

Table 2. Block logistic regressions showing the ability of LS-BMD and of TBS, considered separately, to discriminate spine fracture in the entire women's group (adjusted for age, age at menopause, weight, height). Abbr: LS-BMD , lumbar spine bone mineral density ; TBS, Trabecular bone score.

| Characteristics | Women without osteoporosis | | | Women with osteoporosis | | |
|---|---|---|---|---|---|---|
| | All women (n.446) | Without fractures (n.417) | With fractures (n.29) | All women (n.253) | Without fractures (n.220) | With fractures (n.33) |
| | Mean ± SD | Mean ± SD | Mean ± SD | Mean ± SD | Mean ± SD | Mean ± SD |
| Age (years) | 68.53±7.04 | 68.43±6.99 | 69.97±7.72 | 69.02±7.04 | 69.07±6.72 | 68.67±6.73 |
| Weight (kg) | 65.31±10.56× | 65.32±10.64 | 65.17± 9.53 | 58.76 ±9.09 | 58.93±9.07 | 57.64±9.30 |
| Height (cm) | 160.33±6.11× | 160.43±6.01 | 158.76±7.44 | 157.85± 5.93 | 157.84±5.96 | 157.94±5.83 |
| BMI (kg/m$^2$) | 25.39±3.37 × | 25.36±3.78 | 25.84±3.16 | 23.57±3.36 | 23.64±3.36 | 23.08 ±3.39 |
| Menopause age (years) | 49.50±4.73 | 49.57±4.65 | 48.55±5.76 | 49.28± 5.12 | 49.35±5.24 | 48.88±4.36 |
| TBS | 1.239±0.097× | 1.242±0.097 | 1.194±0.087* | 1.160± 0.083 | 1.161± 0.079 | 1.153±0.106 |
| LS-BMD | 0.881±0.090× | 0.883±0.092 | 0.860±0.059 | 0.699±0.056 | 0.704 ±0.052 | 0.673±0.075** |
| T-score | -1.49±0.82× | -1.48± 0.83 | -1.69±0.53 | -3.14±0.51 | -3.10± 0.47 | -3.38±0.69** |

Table 3. Baseline characteristics of the two sub-groups of women without osteoporosis (446 women) or with osteoporosis (253 women). Within each sub-group of women those with spine fractures and without fractures are shown and compared by unpaired T-test. Abbr: LS-BMD, lumbar spine bone mineral density; TBS, trabecular bone score. Unpaired T-test *p≤0.009 (women without osteoporosis: subjects with fractures Vs those without fractures) Unpaired T-test **p≤0.003 ( osteoporotic women with fractures Vs those without fractures) Unpaired T-test ×p< 0.001 (all women without osteroporosis Vs all women with osteoporosis)

iables, and fracture as a state variable, were generated. Their areas under the ROC curves (AUROCs) were compared using the Hanley-Mc Nail test (17). P-values lower than 0.05 were considered to be significant.

## 3. RESULTS

The biological characteristics of the entire sample of women (age range 50-90 years) are reported in Table 1. At the unpaired T-test, the women with SFF (n.62) had a significantly lower LS-BMD and TBS (p ≤ 0.001) as compared with the women with clinical risk factors but without reported and/or diagnosed fractures (n.637). No statistically significant differences were found for age, age at menopause, height and weight between the two groups.

In the entire population sample, both the LS-BMD and the TBS, considered separately in the block logistic regression with adjusting for confounders (age, age at menopause, height and weight) (Table 2), had a statistically significant association with SFF. None of the other confounders entered into the logistic model were significantly associated with SFF. In the forward logistic model, simultaneously entering both the fracture predictors (LS-BMD and TBS) and the confounders previously considered (Table 2) only LS-BMD (OR: 1.620, 95% CI: 1.229 - 2.135) provided the best predictive model for spine fracture prediction in the entire sample of women.

The characteristics of the women subdivided into two subgroups according to their T-score value (253 osteoporotic women and 446 non-osteoporotic women) are shown in Table 3. The non-osteoporotic women had, as expected, a significantly higher LS-BMD; they also had a higher TBS, (unpaired T-test p ≤ 0.001), and were also

taller and heavier as compared with the osteoporotic women (unpaired T-test p ≤ 0.001). In the subgroup of non-osteoporotic women, the lower TBS of those with fractures was the only parameter significantly differentiating the women with fractures (n.29) from those without fractures (n.417) (unpaired T-test: p = 0.009). On the contrary, in the subgroup of osteoporotic women, only the values of LS-BMD and of the LS-T-score were significantly lower in fractured women (n.33) compared with non-fractured women (n.220) (unpaired T-test p =0.003). In the subgroup of non-osteoporotic women, at block logistic regression (after adjusting for confounders) including LS-BMD and TBS separately as covariates, the TBS significantly predicted SFF (p = 0.014) while the LS-BMD did not (Table 4). In the subgroup of osteoporotic women, LS-BMD was significantly associated with fracture (p=0.022) while TBS failed to reach statistical significance (Table 5). When LS-BMD and the TBS were simultaneously included in the forward logistic regression after adjusting for confounders, in the subgroup of osteoporotic women only LS-BMD (OR: 2.344, 95% CI: 1.194 – 4.600) was significantly associated with SFF while, in the subgroup of non-osteoporotic women, only the TBS (OR: 1.685, 95% CI: 1.131 – 2.511) was a significant predictor of fracture. Observing the ROC curve analysis in the entire population sample, the LS-BMD (AUROC: 0.627, 95% CI: 0.552-0.702) and the TBS (AUROC: 0.616, 95% CI: 0.542-0.689) significantly divided the women with and without fractures (p ≤ 0.001). However, according to the Hanley-McNail test, the two curves were not significantly different. In the subgroup of non-osteoporotic women, only the TBS (AUROC:

| Logistic regression including LS-BMD | | | Logistic regression including TBS | | |
|---|---|---|---|---|---|
| Parameters | OR (95% CI) | P value | Parameters | OR (95% CI) | P value |
| Age | 1.033 (0.980-1.090) | 0.222 | Age | 1.035 (0.981-1.092) | 0.207 |
| Weight | 1.014 (0.974-1.056) | 0.497 | Weight | 0.992(0.950-1.035) | 0.698 |
| Height | 0.952 (0.890-1.018) | 0.148 | Height | 0.971 (0.907-1.039) | 0.394 |
| Menopause age | 0.957 (0.888-1.030) | 0.241 | Menopause age | 0.954 (0.884-1.028) | 0.219 |
| LS-BMD | 1.283 (0.749-2.197) | 0.364 | TBS | 1.725 (1.118-2.660) | 0.014 |

Table 4. Block logistic regressions showing the ability of LS-BMD and of TBS, considered separately, to discriminate spine fracture in women without osteoporosis (adjusted for age, age at menopause, weight, height).

| Logistic regression including LS-BMD | | | Logistic regression including TBS | | |
|---|---|---|---|---|---|
| Parameters | OR (95% CI) | P value | Parameters | OR (95% CI) | P value |
| Age | 0.997 (0.942-1.055) | 0.908 | Age | 0.993 (0.939-1.050) | 0.798 |
| Weight | 0.999 (0.952-1.049) | 0.976 | Weight | 0.976 (0.932-1.023) | 0.314 |
| Height | 1.017 (0.949-1.089) | 0.635 | Height | 1.022  (0.954-1.096) | 0.533 |
| Menopause age | 0.985 (0.918-1.058) | 0.681 | Menopause age | 0.985 (0.919-1.056) | 0.666 |
| LS-BMD | 2.383 (1.135-5.003) | 0.022 | TBS | 1.229 (0.783-1.927) | 0.370 |

Table 5. Block logistic regressions showing the ability of LS-BMD and of TBS, considered separately, to discriminate spine fracture in women with osteoporosis (adjusted for age, age at menopause, weight, height). Abbr : LS-BMD, Lumbar spine bone mineral density; TBS, trabecular bone score

0.649, 95% CI: 0.554-0.743) reached asymptotic statistical significance (p=0.007) in correctly classifying the fractured and non-fractured women while the LS-BMD (AUROC: 0.546, 95% CI: 0.447-0.646) did not reach statistical significance (p= 0.403). In the subgroup of osteoporotic women, only the LS-BMD (AUROC: 0.606, 95% CI: 0.488-0.725) reached borderline asymptotic statistical significance (p=0.049) while the TBS (AUROC: 0.53, 95% CI: 0.416-0.656; p=0.507) did not.

## 4. DISCUSSION

In this study, the ability of the TBS, which has been proposed as a novel method of evaluating bone structure in differentiating patients with SFF as compared to those without fractures, in a population of postmenopausal women with clinical risk factors for osteoporosis was evaluated. Considering our entire study population in which women with and without osteoporosis, diagnosed at DXA according to the WHO densitometric criteria (1), were well represented, it was found that the TBS was lower in women with SFF and was able to significantly predict fragility fractures as well as LS-BMD. These findings are in agreement with the data in the literature which point out the lower score of the TBS in women with fractures in both cross-sectional (7, 9, 14, 15) and prospective studies (10, 11, 15, 16); these studies also showed that the TBS was a significant predictor of SFF.

In our study, however, the TBS was not superior to LS-BMD in predicting SFF in a population which included both women with and without osteoporosis when they were simultaneously tested using logistic regression; this was in agreement with the findings of other Authors (18, 11). However, other studies were in contrast with our results (10, 14, 16) as they showed that, when combining the TBS and BMD, the spine fracture prediction of LS-BMD improved (10, 14, 16). Differences in the characteristics of the populations examined, such as LS-BMD value, age, BMI and study sample size, may explain, at least in part, the contrast between our results and those of the above-mentioned authors. Our findings regarding the failure of the TBS to improve the capability of LS-BMD in predicting SFF does not speak in favor of the TBS as a source of information derived from the bone structure, i.e. independent of bone density. However, when the women without osteoporosis were statistically analyzed separately from those with osteoporosis, a significant difference was found between the TBS and LS-BMD in differentiating women with SFF from those without fractures. In fact, among women without osteoporosis, the TBS significantly predicted women with SFF independently of LS-BMD, as has already been reported by Winzenrieth et al. (9) and Rabier et al. (14) in osteopenic women and by Krueger et al. (15) who showed that the TBS improved the classification of women with fractures by correctly classifying fractures in non-osteoporotic women. On the contrary, in women with osteoporosis, it was found that the TBS was not associated with SFF while LS-BMD was, regardless of the TBS value. In women with and without osteoporosis, there are differences which affect structure and bone density; the different relationships which exist between the TBS and LS-BMD as indicators of the risk of SFF in postmenopausal women with or without osteoporosis suggests that the TBS and LS-BMD are related to these fractures in different ways, namely by bone structure and bone density, respectively. The combined results of the studies of Nassar et al. (12) and Genant et al. (19) support our arguments. In fact, Nassar K. et al. (12) reported that the TBS is correlated with the number and severity of the spine fractures evaluated using the Spinal Deformity Index (SDI) which, in turn, according to the data of Genant et al. (19), is related to progressive impairment of the cancellous and cortical bone microarchitecture, regardless of the lumbar spine density. Therefore, the TBS and the bone microarchitecture, due to their common relationship with the SDI, should be related to each other, regardless of bone density.

The results of our study and those of the above mentioned reports in the literature seem to therefore indicate that, in non-osteoporotic women, a worse bone structure is crucial in favoring the appearance of fragility fractures while changes in the LS-BMD do not significantly influence the occurrence of fragility fractures. These considerations are in agreement with the data in the literature suggesting a better link of spinal fractures with the TBS value as compared with the LS-BMD value in subjects with type II diabetes, in whom there is an increased incidence of fractures despite normal bone density (20-22).

These findings are central to proposing the clinical use of the TBS subsequent to LS-BMD in order to improve the ability of DXA to classify people at risk for fragility fractures using a triage approach, as has already been reported by other AA (15). Since the women enrolled all had clinical risk factors for fragility fractures, the results of our study also showed that the TBS, by significantly differentiating spine fractures in these women, could improve the fracture risk evaluation assessed not only by BMD but also by clinical risk factors.

Our study has some limitations. The major limitations are related to its being a retrospective study and to having enrolled women who all had been classified at risk for osteoporosis based only on the evaluation of the clinical risk factors for osteoporosis. This last selection criterion may have led us to enroll women with a lower LS-BMD as compared with that of the general population thus negatively influencing the overall ability of the two techniques to predict spine fragility fractures. Moreover, the fact that women without radiological diagnosis of osteoporotic fractures, were not investigated with spine X-rays may represent an additional limitation of our study due to the possible presence of undetected spine fractures in these women. This may have led to underestimating the real ability of the two techniques to predict fragility fractures without, however, affecting the validity of the statistical analysis in the case of a significant statistical association regarding the risk of fracture between the two techniques. However, this enrollment bias should not be relevant in comparing the ability of these two techniques to differentiate fractures due to the fact that they were compared using the same population. Finally, our study did not consider secondary osteoporosis in which the validity of the TBS in predicting osteoporotic fractures has already been demonstrated, as it has been for patients with diabetes.

## 5. CONCLUSION

Despite these limitations, our study showed that the TBS predicted SFF as well as LS-BMD in a population sample including women with and without osteoporosis. It also showed that the TBS fracture predicting ability was much better than that of LS-BMD when only non osteoporotic women were investigated, and that the TBS was able to predict fractures in women already classified at risk based on a clinical examination. The combined use of TBS, LS-BMD and clinical risk factors is recommended in order to improve fracture risk evaluation in postmenopausal women. Larger prospective studies on this topic are nevertheless necessary to confirm the results currently emerging in this field.

## REFERENCES

1. Assessment of fracture risk and its application to screening for postmenopausal osteoporosis. Report of a WHO Study Group. WHO Technical report series. 1994; 843: 1-129.
2. Marshall D, Johnell O, Wedel H. Meta-analysis of how well measures of bone mineral density predict occurrence of osteoporotic fractures. BMJ. 1996; 312: 1254-9.
3. Pasco JA, Seeman E, Henry MJ, Merriman EN, Nicholson GC, Kotowicz MA. The population burden of fractures originates in women with osteopenia, not osteoporosis. Osteoporos Int. 2006; 17: 1404-9.
4. Kanis JA, Oden A, Johnell O, Johansson H, De Laet C, Brown J, et al. The use of clinical risk factors enhances the performance of BMD in the prediction of hip and osteoporotic fractures in men and women. Osteoporos Int. 2007; 18: 1033-46.
5. Hans DB, Kanis JA, Baim S, Bilezikian JP, Binkley N, Cauley JA. et al. Joint Official Positions of the International Society for Clinical Densitometry and International Osteoporosis Foundation on FRAX(®). Executive Summary of the 2010 Position Development Conference on Interpretation and use of FRAX(®) in clinical practice. J Clin Densitom. 2011; 14: 171-80.
6. Bouxsein ML. Determinants of skeletal fragility. Best Pract Res Clin Rheumatol. 2005; 19: 897-911.
7. Pothuaud L, Barthe N, Krieg MA, Mehsen N, Carceller P, Hans D. Evaluation of the potential Use of Trabecular Bone Score to Complement Bone Mineral Density in the Diagnosis of Osteoporosis: A Preliminary Spine BMD-Matched, Case-Control Study. J Clin Densitom. 2009; 2: 170-6.
8. Silva BC, Leslie WD, Resch H, Lamy O, Lesnyak O, et al. Trabecular bone score: a non invasive analytical method based upon the DXA image. J Bone Miner Res. 201; 29: 518-30.
9. 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. Calcif Tissue Int. 2010; 86: 104-9.
10. Hans D, Goertzen AL, Krieg MA, Leslie WD. Bone micro-architecture assessed by TBS predicts osteoporotic fractures independent of bone density: The Manitoba study. J Bone Miner Res. 2011; 26: 2762-9.
11. 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. Osteoporos Int. 2013; 24: 77-85.
12. Nassar K, Paternotte S, Kolta S, Fechtenbaum J, Roux C, Briot K. Added value of trabecular bone score over bone mineral density for identification of vertebral fractures in patients with areal bone mineral density in the non-osteoporotic range. Osteoporos Int. 2014; 25: 243-9.
13. 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. J Clin Densitom. 2015; 18: 309-30.
14. Rabier B, Heraud 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: 176-81.
15. Krueger D, Fidler E, Libber J, Aubry-Rozier B, Hans D. Binkley N. Spine trabecular bone score subsequent to bone mineral density improves fracture discrimination in women. J Clin Densitom. 2014; 201: 60-5.
16. Briot K, PaternotteS, Kolta S, Eastell R, Reid DM, Felsenberg D. et al. Added value of trabecular bone score to bone mineral density for prediction of osteoporotic fractures in postmenopausal women: the OPUS study. Bone. 2013; 57: 232-6.
17. Hanley JA, McNail BJ. A method of comparing the areas under receiver operating characteristic curves derived from the same cases. Radiology. 1983; 148: 839-43.
18. 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. Osteoporos Int. 2013; 24: 2455-60.
19. Genant HK, Delmas PD, Chen , Jiang Y, Eriksen EF, Dalsky GP. et al. Severity of vertebral fracture reflects deterioration of bone microarchitecture. Osteoporos Int. 2007; 18: 69-76.
20. Leslie WD, Aubry-Rozier B, Lamy O, Hans D. Manitoba Bone Density Program. TBS (trabecular bone score) and diabetes-related fracture risk. J Clin Endocrinol Metab. 2013; 98: 602-9.
21. Pritchard JM, Giangregorio LM, Atkinson SA, Beattie KA, Inglis D, et al. Association of larger holes in the trabecular bone at the distal radius in postmenopausal women with type 2 diabetes mellitus compared to controls. Arthritis Care Res (Hoboken). 2012; 64: 83-91.
22. Leslie WD, Rubin MR, Schwartz AV, Kanis JA. Type 2 diabetes and bone. J Clin Endocrinol Metab. 2013; 98: 602-9.