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Original Article

A study of the value of trabecular bone score in fracture risk assessment of postmenopausal women

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ABSTRACT

Objective: Trabecular Bone Score (TBS) is an index of bone microarchitecture that provides additional skeletal information to areal Bone Mineral Density (aBMD). Recently TBS data has been used to optimize the Fracture Risk Assessment Tool (FRAX) predictive value. The aim of this study was to evaluate the clinical value of TBS on FRAX algorithm.

Materials and Methods: Among total of 358 postmenopausal Iranian women (mean age 61.3 ± 9.5 years) tested for aBMD and TBS, 184 osteopenic women were identified. Thoracolumbar spine X-ray done in all participants revealed twenty-one vertebral fractures. For the osteopenic group, FRAX and TBS adjusted FRAX (FRAX-TBS) were calculated and compared.

Results: Mean TBS of the patients was 1.31 (±0.11). A significant correlation was found between TBS and spine aBMD ($r = 0.50$, $p < 0.001$) and TBS and femoral neck aBMD ($r = 0.37$, $p < 0.0001$). A strong positive correlation was observed between aBMD adjusted FRAX and FRAX-TBS in predicting the risk of major osteoporotic fracture ($r = 0.90$, $p < 0.0001$), and hip fracture ($r = 0.97$, $p < 0.0001$). According to the area under the receiver operating characteristics curve, the predictive value of the three different models using aBMD, TBS, and combination of aBMD and TBS were similar (0.765, 0.776, and 0.781, respectively; $p = 0.19$). The proportion of the women needed treatment remained unchanged using FRAX or FRAX-TBS.

Conclusion: This study showed no clinical benefit for TBS in postmenopausal women. Adding TBS data to aBMD or FRAX neither improved aBMD predictive value for vertebral fracture nor changed the decision on treatment based on FRAX.

Introduction

Osteoporosis as a leading cause of bone fragility fractures, is a major public health problem mostly affecting postmenopausal women and aging individuals of both sexes [1,2]. In 1990, the prevalence of fragility fracture was about 1.5 million worldwide and it is estimated to reach three millions by 2025 [3]. Osteoporotic fragility fractures lead to severe mortality and morbidity, a significant burden on society in general, and a huge economic impact [4]. Osteoporosis is a common health problem among Iranian population, as well [5].

Considering osteoporosis as a skeletal disorder characterized by both low bone density and microarchitectural deterioration, it seems logic that to prevent osteoporotic fracture we need to pay attention to the both surrogates of bone strength [6]. Until recently, areal bone mineral density (aBMD) was the only method used in assessment of osteoporosis and fracture risk. This approach resulted in an important clinical problem: more than half of the fragility fractures occurred in people with aBMD above the diagnostic threshold of osteoporosis [7]. On the other hand, treating everyone with the T-scores between −1 and −2.5 is neither medically nor economically appropriate. Fracture risk assessment tool (FRAX) is a supportive software in the field of osteoporosis management

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initially designed to aid in identifying previously untreated patients with low bone density who are at a higher risk of fragility fracture; in fact it particularly provides a quantitative estimate of absolute fracture risk to decide which osteopenic patient most likely benefits from treatment [8].

Trabecular bone score (TBS) is an indirect indicator of bone microarchitecture. It is a texture measurement that quantifies local variations in gray level distribution from dual-energy X-ray Absorptiometry (DXA) and is significantly correlated with three dimensional parameters of bone microarchitecture, independently of aBMD [9–12]. Given the importance of bone microarchitecture in the evaluation of fragility fractures, TBS has been recently added to FRAX. Considering bone microarchitecture in combination with aBMD and other risk factors, TBS adjusted FRAX (FRAX-TBS) provides its users a 10-year percentage of the risk of hip fracture (HF) and major osteoporotic fracture (MOF) [13].

Here we assessed the bone microarchitecture of postmenopausal Iranian women using TBS. We aimed to compare their FRAX-TBS with the usual aBMD based FRAX in order to find if adding TBS could affect the fracture risk assessment in our population.

Materials and methods

In a cross-sectional study, a number of 358 postmenopausal women indicated for osteoporosis screening were recruited from Rheumatology clinic of Resalat General Hospital, Tehran, Iran. The patients were referred to densitometry ward for aBMD and TBS evaluation. Exclusion criteria included bisphosphonates or any osteoporosis drugs consumption within the past two years, a history of Cushing's syndrome, malabsorption syndrome, liver failure, creatinine clearance <30 mL/min, or any chronic disorders of mineral metabolism. Women with type 2 diabetes were also excluded from the study. Since type 1 diabetes is considered as secondary osteoporosis in FRAX algorithm, we did not consider it in our exclusion criteria. In addition, since TBS can only be computed for patients with Body Mass Index (BMI) in range of 15–37 kg/m^2, only such postmenopausal women were included. Women were considered postmenopausal if they had amenorrhea for more than one year.

Thoracolumbar spine X-ray was obtained to evaluate the vertebrate fracture using the semi quantitative approach developed by Genant et al. [14].

Dual-energy X-ray absorptiometry (DXA) and TBS

aBMD of the spine (L1-L4) and femoral neck were evaluated using a DXA machine (Hologic Discovery). Bone mineral density was expressed in mg/cm^2 and T-score. T-score > −1, −1 to −2.5 and <−2.5 was considered as normal, osteopenic and osteoporotic, respectively.

TBS evaluation was performed along with aBMD evaluation. Anteroposterior (AP) spine acquisitions were implemented to evaluate TBS for L1–L4. TBS calculation was performed by TBS iNsight software (version 2.2; Medimaps, Geneva, Switzerland). TBS was assessed by determining the variogram of the trabecular bone projected image, calculated as the sum of the squared gray-level differences between pixels at a specific distance and angle. Subsequently, TBS was computed as the slope of the log–log transform of this variogram [12]. The average value of the individual measurements for L1–L4 represents the lumbar spine TBS (unit less). TBS results were classified as Degraded (<1.2), Partial degraded (1.2–1.35), and Normal (>1.35).

FRAX

Calculations of MOF and HF risk were performed using recently released Iranian aBMD adjusted FRAX (FRAX-BMD) online software (www.shefac.uk/FRAX). The clinical risk factors included were sex, age, weight, previous fracture, parental hip fracture, smoking, glucocorticoids consumption, alcohol consumption, rheumatoid arthritis and secondary osteoporosis. National Osteoporosis Foundation (NOF) cutoff values of 20% for MOF risk and 3% for HF risk were considered as high absolute 10 years risk of fracture [15].

TBS adjusted FRAX (FRAX-TBS)

In order to evaluate the effect of TBS on vertebral fragility fracture risk and to decide who may mostly benefit from pharmaceutical treatment, FRAX algorithm was calculated for osteopenic women before and after adjustment on TBS. Since osteoporotic patients are indicated for pharmaceutical treatment regardless of their fragility fracture risk, FRAX was not calculated for that group. In addition, normal individual are not indicated for pharmaceutical treatment. As a result, FRAX was not assessed for this group either.

Statistical analysis

IBM SPSS statistics version 21.0.1 (SPSS Inc., Chicago, IL, USA) and Stata software were used for data analysis. The sample size was estimated using sample size calculator for multiple regression models (http://www.danielsoper.com/statcalc/calculator.aspx?id=1). With a statistical power of 0.80, probability level of 0.05, and 10 predictors, the sample size was estimated almost 350. During the study period, we recruited 358 subjects. Pearson's/Spearman's correlation coefficients were calculated to assess association between numeric variables. Independent sample T-test or Mann–Whitney U and chi-square tests were used to assess differentiation of means and percentages across groups respectively. In order to assess means across more than two groups, Analysis of Variance (ANOVA) was used. Comparison of the proportion of patients needing a therapeutic intervention before and after TBS adjustment of FRAX was performed using McNemar's test. In order to evaluate the predictive effect of aBMD and TBS adjusted with age and BMI on vertebral fracture, binary multiple logistic regressions was used. Finally, in order to show the fracture predictive validity of spine aBMD (Model 1), spine TBS (Model 2) and their combination (Model 3), adjusted for age and BMI, Receiver Operating Characteristic Curve (ROC) was used. Area under the curve (AUC) was tested using chi-square test in Stata software. Significance level was considered as 0.05.

Results

From a total of 358 postmenopausal Iranian women, mean age of 61.3 ± 9.5 years, ninety-nine osteoporotic, 184 osteopenic and 75 normal women were identified. The mean spine and femoral neck aBMD were 882 ± 134 mg/cm^2, and 692 ± 114 mg/cm^2, respectively. Their corresponding mean T-scores were −1.51 ± 1.21 at lumbar spine, and −1.48 ± 0.98 at femoral neck region.

FRAX-BMD and FRAX-TBS have also been computed and the data have been shown in Table 1.

The mean TBS was 1.31 ± 0.11, ranging from 0.95 to 1.6. TBS value was significantly different across a BMD status ($p < 0.0001$). Post Hoc tests demonstrated that TBS value was also significantly different between all possible pairs of aBMD status ($p < 0.0001$).

According to TBS status, the bone microarchitecture was degraded in 45 (12.6%), partially degraded in 176 (49.1%), and normal in 137 (38.3%) postmenopausal women.