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Original Article

Trabecular Bone Score (TBS) and TBS-Adjusted Fracture Risk Assessment Tool are Potential Supplementary Tools for the Discrimination of Morphometric Vertebral Fractures in Postmenopausal Women With Type 2 Diabetes

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Abstract

Type 2 diabetes mellitus (T2DM) is associated with fracture risk but, paradoxically, greater bone mineral density (BMD). The trabecular bone score (TBS) has been proposed as an index of bone microarchitecture associated with bone quality. This study compared the performance of TBS, BMD, and original and TBS-adjusted Fracture Risk Assessment Tool (FRAX®) scores in the discrimination of vertebral fractures (VFs) in T2DM patients. This retrospective study enrolled 169 Korean postmenopausal women with T2DM. Lateral plain radiographs of the thoracolumbar spine were taken. Lumbar spine and femur neck BMDs were obtained using dual-energy X-ray absorptiometry (DXA). TBS was obtained using the TBS iNsight software program (Med-Imaps, Pessac, France) with BMD DXA images (L1–L4). VFs were diagnosed when at least 1 of the 3 height measurements was decreased by >25% compared to the nearest uncompressed vertebral body. Among the subjects, 34 women (20.1%) had VFs. Significantly lower TBS ($p = 0.008$) and higher TBS-adjusted FRAX scores were shown ($p = 0.019$) in the group with VFs compared to the group without VFs. In contrast, there were no significant differences in BMD and original FRAX scores between the 2 groups. Odds ratios (ORs) per standard deviation decrease in BMD or TBS and per standard deviation increase in the FRAX score were estimated with adjustment for age. TBS (OR = 1.8, 95% confidence interval [CI]: 1.1–2.7, $p = 0.011$) and TBS-adjusted FRAX score (OR = 2.0, 95% confidence interval: 1.1–3.5, $p = 0.020$) showed statistically significant ORs but the others did not. TBS and TBS-adjusted FRAX could be supplementary tools to discriminate osteoporotic fractures in T2DM.

Key Words: FRAX; trabecular bone score; type 2 diabetes mellitus; vertebral fracture.

Introduction

Bone strength mostly reflects the integration of bone density and bone quality. Bone mineral density (BMD) accounts for approximately 70% of bone strength and is frequently used as a representative measure *(1)*. Occasionally, overall fracture risk cannot be predicted by utilizing only BMD measurement. A good example of this is osteoporotic fracture in type 2 diabetes mellitus (T2DM). Subjects with T2DM have higher osteoporotic fracture risk despite having higher BMDs than nondiabetic individuals *(2,3)*. Therefore, it is possible that bone quality may be contributing more to the increased risk of fractures in individuals with T2DM than BMD. However, the problem is that bone quality is difficult to measure. Novel imaging techniques, such as quantitative computed tomography and high-resolution (peripheral) quantitative computed tomography *(4,5)*, and invasive approaches for probing bone

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material properties (6) have been tried to evaluate bone quality. None of these techniques appears to show better performance than BMD in the prediction of the osteoporotic fractures, and their general weakness of availability and validation in the clinical setting means that an additional role of BMD is unlikely to be possible in the near future (7).

The trabecular bone score (TBS) is a new texture parameter from analysis of dual-energy X-ray absorptiometry (DXA) images. TBS evaluates pixel gray-level variations in the spine DXA image and is related to bone microarchitecture and fracture risk, providing information independent of BMD (8–10). Trabecular microarchitecture is an important component of bone quality that had not been measured by conventional DXA. Although it is unclear to what extent TBS reflects in vivo 3-dimensional characteristics of bone microarchitecture in the spine, TBS could evaluate ex vivo 3-dimensional characteristics of bone microarchitecture in the spine and might be an indicator of variation in trabecular bone volume fraction and mean trabecular bone thickness (8–10). Low lumbar spine TBS is associated with both history of fracture and incidence of new fracture. The effect is independent of BMD and enhances the risk stratification with BMD (4). In terms of measuring bone quality, TBS could be an appropriate technique to predict the fracture risk, especially in T2DM patients. In a large cohort study, lumbar spine TBS predicts osteoporotic fractures in those with T2DM and captures a larger portion of the diabetes-associated fracture risk than BMD (11). However, there have been only a few studies to validate the effectiveness of TBS on the prediction of fracture risk in T2DM patients.

The World Health Organization Fracture Risk Assessment Tool (FRAX®) estimates the 10-yr probability of hip and major osteoporotic fracture based on an individual's risk factor profile (12). FRAX has become the leading risk assessment tool used worldwide (13). However, BMD is a dominant factor in the risk factor profile in FRAX estimates. Therefore, the current FRAX algorithm may be inappropriate in T2DM. A TBS-adjusted FRAX algorithm was recently derived from the Manitoba cohort (14). This modified FRAX algorithm could be a better tool than the original FRAX algorithm, especially in T2DM, but requires validation in different settings including T2DM.

The present study compared the performance of TBS, BMD, and FRAX scores in the prediction of vertebral fractures (VFs) in postmenopausal Korean patients with T2DM. In addition, the performances of the TBS-adjusted FRAX algorithm and the original FRAX algorithm were also compared in T2DM patients.

Materials and Methods

Subjects

Study subjects volunteered to participate. Study participants were recruited through a diabetes clinic in a medical center and recruitment posters placed at the hospital from October 2008 to March 2009 in South Korea. Inclusion criteria were postmenopausal women who were ≥50 yr of age and could stand without help, had diabetes onset at >30 yr of age, had medical history/records consistent with T2DM, and had available BMD data reviewed by trained data abstractors. Exclusion criteria were a history of cancer and a serum creatinine level greater than 2.0 mg/dL. Any subjects with other metabolic disorders and/or secondary causes of osteoporosis were also not included. All 169 enrolled subjects had lateral radiographs of the thoracic and lumbar spine taken and morphometric assessments were performed to identify prevalent VFs. The time lag between the radiographs and BMD measurements was <6 mo.

The participants completed questionnaires during a face-to-face interview that included information on demographics; previous medical history including previous fragility fractures (spine, hip, humerus, wrist, and ankle) diagnosed by a doctor; presence of menopausal status; alcohol intake; diabetic complications; smoking; parental history of fractures; and medications such as glucocorticoids, oral contraceptives, estrogen, drugs for diabetes, and drugs for osteoporosis such as bisphosphonates, estrogens, and selective estrogen receptor modulators. Anthropometric parameters were measured by standard methods. Body mass index was calculated as weight in kilogram divided by the square of the height in meter. The present study was approved by the ethical review board of the Ajou University Hospital and was in compliance with the Helsinki Declaration. All subjects agreed to participate in the study and provided written informed consent.

Biochemical and BMD Measurements

Fasting blood was obtained and the concentrations of fasting plasma glucose, hemoglobin A1c, and serum creatinine were measured by automated techniques at the laboratory of the institution. The densitometric examinations were performed with a Lunar Prodigy apparatus (GE Lunar, Madison, WI). For lumbar spine (L-spine) BMD, when the specific vertebrae were not suitable for analysis due to compression fracture or degenerative changes or any other reasons, BMD was calculated excluding the affected vertebrae. The coefficients of variation for BMD were 0.339% (L1–L4) and 0.679% (femur neck).

Radiography and Definitions of VF

Lateral radiographs of the thoracic and lumbar spine were obtained in the upright position for better detection of VFs (15). To limit exposure to radiation, a single radiography of the thoracolumbar column was obtained. All radiographs were obtained using a tube-to-film distance of 105 cm, with the tube positioned over T11. All radiographs from the Digital Imaging and Communications in Medicine files were transferred to another center and evaluated for the presence of VFs. Two musculoskeletal radiologists blinded to all data concerning the patients performed the manual 6-point vertebral quantitative morphometry evaluation of the radiographs. The overall