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Section II: Emerging Uses of Bone Densitometry

Spine Trabecular Bone Score Subsequent to Bone Mineral Density Improves Fracture Discrimination in Women

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Abstract

Bone mineral density (BMD) measured by dual-energy X-ray absorptiometry (DXA) is used to diagnose osteoporosis and assess fracture risk. However, DXA cannot evaluate trabecular microarchitecture. This study used a novel software program (TBS iNsight; Med-Imaps, Geneva, Switzerland) to estimate bone texture (trabecular bone score [TBS]) from standard spine DXA images. We hypothesized that TBS assessment would differentiate women with low trauma fracture from those without. In this study, TBS was performed blinded to fracture status on existing research DXA lumbar spine (LS) images from 429 women. Mean participant age was 71.3 yr, and 158 had prior fractures. The correlation between LS BMD and TBS was low ($r = 0.28$), suggesting these parameters reflect different bone properties. Age- and body mass index–adjusted odds ratios (ORs) ranged from 1.36 to 1.63 for LS or hip BMD in discriminating women with low trauma nonvertebral and vertebral fractures. TBS demonstrated ORs from 2.46 to 2.49 for these respective fractures; these remained significant after lowest BMD T-score adjustment (OR = 2.38 and 2.44). Seventy-three percent of all fractures occurred in women without osteoporosis (BMD T-score > -2.5); 72% of these women had a TBS score below the median, thereby appropriately classified them as being at increased risk. In conclusion, TBS assessment enhances DXA by evaluating trabecular pattern and identifying individuals with vertebral or low trauma fracture. TBS identifies 66–70% of women with fracture who were not classified with osteoporosis by BMD alone.

Key Words: Bone mineral density; fracture risk; microarchitecture; trabecular bone score; vertebral fracture.

Introduction

Osteoporosis is defined as low bone mass and microarchitectural deterioration of bone tissue, with a consequent increase in bone fragility and susceptibility to fracture. This disease is a major health concern *(1)*, with up to 9 million new osteoporotic fractures annually *(2)* causing substantial morbidity and mortality worldwide *(3,4)*. Despite a modest secular decline in fracture rates *(5)*, given population demographics, the number of these fractures is projected to double over the next 40–50 yr *(6)*.

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Major efforts to optimally identify those at risk for osteoporosis-related fractures are ongoing. Bone mineral density (BMD), measured by dual-energy X-ray absorptiometry (DXA), has been the gold standard for osteoporosis diagnosis in the absence of prior fragility fracture *(7)*, but approximately half of the fractures occur in people whose BMD T-score is better than −2.5 *(8,9)*. Other factors influencing bone strength and fracture risk include bone turnover, mineralization, macrogeometry, and, importantly, trabecular bone microarchitecture. Thus, additional information about microarchitecture should enhance identification of individuals at risk for fragility fracture.

Trabecular bone score (TBS) is a novel grey-level texture measurement that is based on the use of experimental variograms of 2-dimensional (2D) projection images *(10)* and is able to differentiate between two 3-dimensional (3D) microarchitectures that exhibit the same bone density but different

trabecular characteristics (11). TBS is obtained by analyzing the DXA acquired image that results from a bone density examination; it measures the mean rate of local grey-level variation in these 2D projection images. TBS is therefore not a physical measurement but rather a texture index of trabecular bone, thus, providing information independent of BMD. This is useful as TBS is highly correlated with microarchitecture as measured by micro computed tomography (CT) (12). TBS and BMD combined may enhance fracture risk assessment because they evaluate 2 components of the same bone. Consistent with this, recent work finds TBS to facilitate identification of prevalent fracture. In the Manitoba study, 956 subjects had fractures with normal bone density or osteopenia by the World Health Organization (WHO) classification of spine BMD T-score (13). TBS identified 30% and 43% of these individuals as having high fracture risk from the normal and osteopenic groups, respectively. Conversely, only 7% of the fracture subjects in the osteoporotic group were identified at low fracture risk by TBS. Overall ~30–40% of the fracture group with normal or osteopenic spine BMD were correctly classified as high risk with TBS. Similar results are found when using the minimum of the hip or spine T-scores for WHO classification instead of the lumbar spine (LS) alone. A similar evaluation of subjects from the Os des Femmes de Lyon (OFELY) population-based study (14), with and without femoral neck fracture, demonstrated TBS, correctly reclassified 25% of fractured subjects at a cost of 13% overdiagnosed control subjects (15,16). Finally, TBS analysis of the Swiss Evaluation of the Methods of Measurement of Osteoporotic Fracture Risk (SEMOF) study demonstrated that combining BMD T-score ≤ -2.5 at any site and high fracture risk by TBS (TBS < 1.200) identified 85% of all women with an osteoporotic fracture (17). In summary, TBS is derived from the texture representation on a DXA image and is related to bone microarchitecture and fracture risk. Specifically, a high TBS reflects strong, fracture-resistant microarchitecture, whereas a low TBS reflects weak, fracture-prone microarchitecture.

Certainly, other methodologies such as high-resolution CT and magnetic resonance imaging are capable of microarchitectural assessment. However, it seems unlikely that these methodologies will see routine clinical use due to a variety of factors including expense, radiation exposure, and availability of appropriate instrumentation. Additionally, with these methodologies, there are no established quantitative cut-points to discriminate patients into high or low fracture risk groups. In contrast, TBS uses existing DXA images, thus generating no additional radiation exposure and little expense. Moreover, one could anticipate that TBS could use existing data from large studies to establish quantitative values to stratify patients into risk categories.

A limitation of existing TBS studies is lack of spine fracture status. As vertebral fracture is often unappreciated, without spine imaging fracture subjects may be inappropriately grouped with the nonfracture subjects (18). The aim of this study was to evaluate the ability of TBS measurement to discriminate between older women with prior fragility fracture, including unappreciated vertebral fracture, from those without fracture, independent of their BMD. Additionally, we investigate whether the combination of TBS and BMD enhances fracture detection compared with either measurement alone.

Materials and Methods

Study Subjects

We conducted a retrospective, nonrandom case-control study at the University of Wisconsin Osteoporosis Clinical Research Program (Madison, WI). Postmenopausal Caucasian women, between the ages of 50 and 96 yr, with a body mass index (BMI) between 15 and 37 kg/m^2 who had DXA-acquired spine bone density scans from prior research study participation were potentially eligible for this evaluation. DXA scans were obtained between 2005 and 2011 on either a Lunar Prodigy or Lunar iDXA densitometer (GE Healthcare, Madison, WI). The sample was limited to participants with DXA vertebral fracture assessment (VFA) performed at the time of BMD to allow evaluation of vertebral fracture status. Densitometric VFA, a well-accepted method of identifying vertebral fracture, was performed in routine clinical manner following manufacturer guidelines (19–21). Specifically, when using a GE Healthcare Lunar densitometer, VFA is acquired by positioning the patient in the lateral decubitus position. An experienced clinician (N.B.) evaluated VFAs.

Women were classified by age and fracture status (fracture, no fracture). Those classified with fracture either reported a low-energy nonvertebral fracture or had a prevalent vertebral fracture identified on VFA using the Genant semi-quantitative classification (22). Conversely, nonfracture controls could not have any evidence of a low-energy fracture of any bone except skull, hands, feet, fingers, and toes as determined both by clinical history and by VFA. Individuals in either group were excluded if they (1) had undergone any spinal surgery evident on DXA or (2) they had 3 or more non-evaluable lumbar vertebra. Ultimately, 158 women with self-reported low trauma fracture or prevalent vertebral fracture were included in the fracture group and 271 age-matched controls were also identified.

This study was deemed exempt by the University of Wisconsin Human Subjects Committee and was conducted in accordance with the Declaration of Helsinki. Subject anonymity was maintained by using unique numeric identification codes rather than subject names on all records.

BMD and TBS

All DXA scans were performed by The International Society for Clinical Densitometry–certified technologists in accordance with manufacturer recommendations following standard operating procedures in place at the UW Osteoporosis Clinical Research Program. BMD measurements were obtained at LS (L1–L4) and proximal femur using