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Original Article

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

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Abstract

The trabecular bone score (TBS) is a new parameter that is determined from gray-level analysis of dual-energy X-ray absorptiometry (DXA) images. It relies on the mean thickness and volume fraction of trabecular bone microarchitecture. This was a preliminary case-control study to evaluate the potential diagnostic value of TBS as a complement to bone mineral density (BMD), by comparing postmenopausal women with and without fractures. The sample consisted of 45 women with osteoporotic fractures (5 hip fractures, 20 vertebral fractures, and 20 other types of fracture) and 155 women without a fracture. Stratification was performed, taking into account each type of fracture (except hip), and women with and without fractures were matched for age and spine BMD. BMD and TBS were measured at the total spine. TBS measured at the total spine revealed a significant difference between the fracture and age− and spine BMD−matched nonfracture group, when considering all types of fractures and vertebral fractures. In these cases, the diagnostic value of the combination of BMD and TBS likely will be higher compared with that of BMD alone. TBS, as evaluated from standard DXA scans directly, potentially complements BMD in the detection of osteoporotic fractures. Prospective studies are necessary to fully evaluate the potential role of TBS as a complementary risk factor for fracture.

Key Words: DXA; image analysis; osteoporosis; trabecular bone microarchitecture; trabecular bone score.

Introduction

Osteoporosis is a skeletal disorder characterized by compromised bone strength, which predisposes an affected individual to bone fracture *(1)*. Bone density, a factor affecting bone strength, is evaluated in routine clinical practice by dual-energy X-ray absorptiometry (DXA). A patient's bone mineral density (BMD), measured by DXA, is expressed in g/cm^2; however, by convention, the score then is converted to a T-score, which represents the number of standard deviations (SDs), plus or minus, from a reference value. That reference value, by convention, is the mean BMD of a young, healthy adult. The World Health Organization (WHO) *(2)* has established criteria for the diagnosis of osteoporosis, criteria that rely on a patient's T-score, gleaned from DXA−based BMD measurement at the hip or spine. The classification criteria are as follows: a designation of ''normal'' is assigned to patients whose T-score is above −1.0; a designation of ''low

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bone mass (osteopenia)'' is assigned for T-scores between −1.0 and −2.5; and a diagnosis of ''osteoporosis'' is reserved for T-scores at or below −2.5. This classification scheme commonly is referred to in the literature and in discussions on bone disease. However, in clinical practice, the scheme has certain limitations, and a large degree of overlap exists in BMD values between individuals who develop fractures and those who do not *(3)*.

One of the possible explanations is that BMD does not capture all of the factors that contribute to bone strength *(4)*, factors that encompass several characteristics of bone tissue at different scales of analysis, such as the macrogeometry of cortical bone, trabecular bone microarchitecture, bone microdamage, bone mineralization, and bone turnover *(5,6)*. When referring to ex vivo studies *(7,8)* or to the definition of osteoporosis *(2)*, trabecular bone microarchitecture constitutes an important component of bone strength and is complementary to bone density. Today, establishing an efficient clinical evaluation of trabecular bone microarchitecture remains a crucial challenge.

A 2-dimensional (2D) projection-based evaluation of trabecular bone microarchitecture that could be obtained from standard X-rays, and/or from DXA images, would be a good candidate for efficient clinical use, in that it would be inexpensive and convenient and associated with a low ionizing radiation dose. Transforming a 2D projection into a 3-dimensional (3D) one remains a difficult mathematical problem, however *(9)*. The 3D microarchitecture of tissue or other objects is not directly measurable in 2D projection−based images. However, several kinds of texture analyses have been proposed as indirect measurements of 3D trabecular bone microarchitecture *(9−16)*. Among them, fractal analysis has been widely used. For example, Benhamou et al *(17)* applied fractal analysis to calcaneus plain radiographs. In a square region of measurement, the gray-level profiles are fitted with a mathematical model dedicated to fractal process—the Fractional Brownian Motion model. This modeling, based on 1-dimensional (1D) gray-level profile, is repeated in different directions of the 2D image, leading to the evaluation of a mean Hurst parameter (Hmean). In the case of materials with surface fractal properties, a mathematical relationship can be established between the fractal dimension of the 3D microarchitecture and the fractal dimension evaluated on a 2D-projection image. Unfortunately, this 3D-2D relationship is not adequate for trabecular bone microarchitecture, because it does not satisfy surface fractal properties *(18)*. Other limitations of fractal analysis concern the evaluation of the fractal dimension itself. An accurate estimate of fractal dimension on 2D-projection images necessitates taking into consideration a large surface of projection and, depending on the estimator used, the size of the projection image in the 2-power scale *(17)*. Vokes et al *(16)* adopted a texture measurement based on combined Fourier and multifractal analyses, called the *Minkowski fractal dimension*. This approach was constrained by a square-shaped region of measurement of size in the 2-power scale, for example, a square region equal to 64 × 64 pixels *(16)*. Statistical analyses were performed to compare (1) associating the Minkowski fractal dimension evaluated from heel images on a peripheral densitometer, especially equipped to provide high-resolution heel images and (2) BMD measured at the lumbar spine and proximal hip, using a standard central densitometer.

The *trabecular bone score* (TBS) is a novel gray-level texture measurement that is based on the exploitation of experimental variograms of 2D-projection images *(19,20)*. TBS is not an estimate of fractal dimension. Rather, it measures the mean rate of local variation of gray levels in 2D-projection images. This evaluation is constrained neither by the size nor by the shape of the region measured. Hence, TBS is a good candidate as a texture measurement for small and/or irregular surfaces of analysis, such as the standard region of measurement defined in DXA images. TBS can be compared with BMD because both evaluate the same region. Based on numerical simulations and models of 3D microarchitecture, we have established an empirical 3D-2D relationship expressing TBS as a function of 2 3D bone characteristics: *fs—solid volume fraction*; and *Th—mean solid thickness*. TBS expresses a score for the 3D characteristics of bone microarchitecture and appears to be an indicator of variation in thickness, in cases of bone microarchitecture with the same bone volume (BV).

The aim of this preliminary case-control study has been to evaluate the potential diagnostic value of TBS, as a complement to BMD, in the prediction of osteoporotic fractures overall and vertebral fractures alone.

Materials and Methods

Clinical DXA Population and Subgrouping

Study subjects

A sample of 200 women was selected from the QDR4500A systems database at 2 different Hospitals—*University Hospital of Lausanne* (Switzerland) and *University Hospital of Bordeaux* (France). The subjects were randomly selected from lists of patients who had had their DXA on the same make and model machine, who were within a given age range, and who otherwise met inclusion/exclusion criteria. Subjects with (**cases**) and without (**controls**) fractures were selected at both sites and then merged into a common anonymized study data set after appropriate cross-calibration of DXA−based measurements. At each hospital, the principal investigators reviewed the lists of patients with fractures and selected all otherwise eligible postmenopausal women who had been measured on the same device (QDR4500A, Hologic, Bedford MA, US). Hip fractures were ascertained by X-ray, and cross-referenced with surgical records at the same hospital. A similar approach was used for spine fractures. Only patients who had had an X-ray-confirmed fracture, using the semiquantitative approach developed by Genant et al, were recruited for the study. All the other fractures were also confirmed radiographically. After recruitment of patients with fractures, a sample of age− and spine BMD−matched nonfracture controls was recruited from the pool of 155 eligible