Journal of Clinical Densitometry: Assessment & Management of Musculoskeletal Health, vol. 18, no. 3, 309–330, 2015

1094-6950/18:309–330/$36.00
http://dx.doi.org/10.1016/j.jocd.2015.06.008

2015 ISCD Position Development Conference

Fracture Risk Prediction by Non-BMD DXA Measures: the 2015 ISCD Official Positions Part 2: Trabecular Bone Score

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Abstract

Bone mineral density (BMD) as measured by dual-energy X-ray absorptiometry (DXA) is the gold standard for the diagnosis and management of osteoporosis. However, BMD explains only 60%–80% of bone strength, and a number of skeletal features other than BMD contribute to bone strength and fracture risk. Advanced imaging modalities can assess some of these skeletal features, but compared to standard DXA, these techniques have higher costs and limited accessibility. A major challenge, therefore, has been to incorporate in clinical practice a readily available, noninvasive technology that permits improvement in fracture-risk prediction beyond that provided by the combination of standard DXA measurements and clinical risk factors. To this end, trabecular bone score (TBS), a gray-level textural index derived from the lumbar spine DXA image, has been investigated. The purpose of this International Society for Clinical Densitometry task force was to review the evidence and develop recommendations on how to incorporate TBS in clinical practice. Clinical applications of TBS for fracture risk assessment, treatment initiation, monitoring of treatment, and use of TBS in special conditions related to greater fracture risk, were addressed. We present the official positions approved by an expert panel following careful review of the recommendations and evidence presented by the TBS task force.

Key Words: Dual energy X-ray absorptiometry; fracture risk; FRAX; official positions; trabecular bone score.

Introduction

Bone mineral density (BMD) as measured by dual-energy X-ray absorptiometry (DXA) is a major determinant of bone strength and fracture risk *(1)*. Currently, a BMD T-score from DXA of −2.5 or less at the lumbar spine (LS), total hip (TH), femoral neck (FN), or one-third radius, allows the diagnosis of osteoporosis in postmenopausal women and in men >50 years old *(2)*. However, although DXA BMD is considered the gold standard for the diagnosis of osteoporosis, most individuals with a fragility fracture will have BMD values in the low bone mass (osteopenic) or even normal range *(3–5)*. This observation implies that the risk of fracture depends on factors other than BMD.

A number of skeletal features other than BMD, such as bone geometry, microarchitecture, mineralization, bone remodeling, and microdamage contribute to bone strength and overall fracture risk. These features and characteristics of the skeleton that influence a bone's ability to resist fracture are known as bone quality *(6)*. Important aspects of bone quality, namely, bone microarchitecture and bone remodeling, can be assessed in bone biopsies by histomorphometry and

Received 06/20/15; Accepted 06/22/15.
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micro−computed tomography (7). However, iliac crest bone biopsy is an invasive, not widely available procedure, now used primarily as a research tool. Alternatively, a number of noninvasive imaging modalities, including quantitative computed tomography (QCT), high-resolution peripheral QCT (HRpQCT), and high-resolution magnetic resonance imaging, can measure bone geometry, microarchitecture, and bone strength and distinguish among individuals with and without fragility fracture (8−10). However, compared to standard DXA, these technologies have higher cost, greater ionizing radiation dose (QCT), and limited accessibility.

In addition to these aspects of bone quality, clinical risk factors for fracture, such as older age, lower body mass index (BMI), family or personal history of osteoporotic fractures, and prolonged glucocorticoid use, increase fracture risk independent of DXA BMD. More important, the combination of clinical risk factors with BMD improves the prediction of fragility fractures compared to BMD alone (11). Based on these findings, a fracture risk assessment tool (FRAX) that assesses clinical risk factors with and without FN BMD, was developed for the prediction of fracture risk and can be used in clinical practice to determine treatment recommendations (12,13).

A major challenge, therefore, has been to incorporate in clinical practice a readily available, noninvasive technology that permits improvement in fracture-risk prediction beyond that provided by the combination of standard DXA measurements and clinical risk factors. This would allow for a more accurate identification of individuals with greater risk of fracture, improving the cost-effectiveness of treatment. To this end, trabecular bone score (TBS) has been investigated. TBS is a gray-level textural index derived from the LS DXA image that has been previously reported to be associated with fracture risk, partially independent of clinical risk factors and DXA BMD. TBS is measured by dedicated software in the same region of interest as the LS BMD measurement. Although the Food and Drug Administration and the European agency have approved the use of TBS as an adjunct to standard DXA testing, there is no guidance on how to use it in clinical practice. The purpose of this International Society for Clinical Densitometry (ISCD) TBS task force was to review the evidence and develop official positions on how to incorporate TBS in clinical practice.

Background

TBS is a textural index that evaluates pixel gray-level variations in the LS DXA image, providing an indirect index of trabecular architecture (14). TBS is evaluated by determining the variogram of the projected image of the region of interest, calculated as the sum of the squared gray-level differences between pixels at a specific distance. TBS is then calculated as the slope of the log-log transform of this variogram. A dense trabecular structure produces a 2D image with a large number of pixel-value variations of small amplitude and consequently, a steep variogram slope and a high TBS value. Conversely, a 2D projection of deteriorated bone architecture produces an image with a low number of pixel-value variations of high amplitude and therefore, a mild slope at the origin of the variogram and a low TBS (14,15).

TBS is measured in the same region of interest as the LS BMD measurement by dedicated software (TBS iNsight; Medimaps, Plan-les-Ouates, Switzerland). TBS can be obtained from LS DXA images acquired using the latest generations of GE Lunar, Madison, WI or Hologic, Bedford, MA densitometers, such as Prodigy and iDXA or Delphi, Horizon, QDR 4500, and Discovery. The TBS result (unitless) is given for each vertebra and for the total spine (L1−L4). Abnormal vertebrae, including fractured vertebrae and vertebrae with osteoarthritic changes, can be excluded from the TBS analysis, as is done for the BMD measurement.

In its first description, TBS was derived from simulated 2D-projection micro−computed tomography images of human cadaveric bones (16). TBS is not a direct measure of trabecular microarchitecture but is postulated to improve fracture prediction in part based on its correlations in a few small ex vivo studies with trabecular microarchitecture measures, including connectivity density, trabecular number, and trabecular separation (17−19).

Three small studies have examined, in vivo, the association between LS TBS and parameters of bone geometry, volumetric density, and bone microarchitecture as assessed by HRpQCT of the distal radius and tibia (20−22). In these studies, the correlations between TBS and HRpQCT parameters of microarchitecture were weak to moderate and were insignificant after multivariable adjustment (21). Larger cadaver studies evaluating the level of agreement between TBS from *in situ* spine DXA, and direct measures of vertebral microarchitectural parameters are needed to firmly establish the hypothesis that TBS predicts fractures independent of BMD largely through its correlations with trabecular microarchitecture.

Methodology

The ISCD TBS task force reviewed all English language literature available on PubMed. The search term used was ''Trabecular Bone Score'', and the search was completed on November 26, 2014. In total, 62 articles were identified and reviewed by the TBS task force. Articles were added as required to enable review of proposed topics. In addition, unpublished or in press articles were reviewed when considered essential to respond to specific questions. The expert panel rated proposed official positions using a modification of the RAND-UCLA method, fully described in the PDC executive summary article that accompanies this report (23).

Question: Can TBS be Used to Assess Fracture Risk in a Clinical Practice?

ISCD Official Position

- TBS is associated with vertebral, hip, and major osteoporotic fracture risk in postmenopausal women

  Grade: Good-B-W