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Dual-Energy X-Ray Absorptiometry: Beyond Bone Mineral Density Determination

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Significant improvements in dual-energy X-ray absorptiometry (DXA) concerning quality, image resolution and image acquisition time have allowed the development of various functions. DXA can evaluate bone quality by indirect analysis of micro- and macro-architecture of the bone, which and improve the prediction of fracture risk. DXA can also detect existing fractures, such as vertebral fractures or atypical femur fractures, without additional radiologic imaging and radiation exposure. Moreover, it can assess the metabolic status by the measurement of body composition parameters like muscle mass and visceral fat. Although more studies are required to validate and clinically use these parameters, it is clear that DXA is not just for bone mineral densitometry.

Keywords: Absorptiometry, photon; Bone quality; Trabecular bone score; Hip structural analysis; Vertebral fracture assessment; Sarcopenia; Intra-abdominal fat

INTRODUCTION

Dual-energy X-ray absorptiometry (DXA) is indispensable for clinical practice in osteoporosis. DXA is the reference method for measuring bone mineral density (BMD) at the lumbar spine and proximal femur [1]. However, bone strength mostly reflects the integration of bone density and bone quality. BMD accounts for only 70% of bone strength [2]. Refinements in image quality, resolution and acquisition time, combined with more advanced computation power, have extended the utility of DXA from BMD to other functions [3]. It can evaluate bone quality by indirect analysis of micro- and macro-architecture of the bone, which improves the prediction of fracture risk. DXA can also detect existing fractures, such as vertebral and atypical femur fractures (AFFs), without additional radiologic imaging and radiation exposure. As a third example, it can assess the metabolic status by the measurement of body composition [1,3]. This paper adds to the list, by detailing another application of DXA.

EVALUATION OF BONE QUALITY

Hip structural analysis

DXA allows the measurement of geometric contributions to bone strength in the proximal femur, which is termed hip structural or hip strength analysis (HSA). HSA programs are commercially available can automatically assess structural variables including femoral neck cross-sectional moment of inertia (CSMI), cross-sectional area (CSA), femoral neck shaft angle, and hip axis length (HAL). In addition, models that combine these structural parameters with age, height, and weight allow the calculation of the femur strength index (FSI), which is a measure of the ability of a hip to withstand a fall on the greater trochanter [4].

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The proximal femur remodels itself with age by redistributing bone mass; this mechanically compensates for the declining mass to preserve strength in bending [5]. CSMI reflects the distribution of the mass about a neutral or centroidal axis. The section modulus (Z) is a strength parameter based on the CSMI. Z is a physical property of a section that is inversely related to the maximum bending stress in the section, making it an index of the strength of the section. Z is equal to the CSMI divided by the centroidal distance or distance from the neutral axis to the outermost edge of the section, which in the case of bone, is the subperiosteal surface. Cortical instability may result when excessive cortical thinning is present. This can occur even with redistribution of the remaining mass toward the periphery of the cross-section. This is reflected in the final strength parameter, the buckling ratio (BR; the ratio of the outer radius to the cortical thickness). A ratio >10 indicates the heightened chance of a precipitous loss of strength with local buckling [6]. HSA with DXA enables the *in vivo* measurement of the CSA, CSMI, Z, and BR [7].

HAL is another geometric measure proposed as an indicator of hip fracture risk for females independent of BMD at the femoral neck. An increase in HAL equivalent to one standard deviation (SD) was associated with a 1.8-fold increase in the risk of hip fracture in women enrolled in the Study of Osteoporotic Fractures [8]. The proprietary FSI was statistically significantly lower in the fractured women compared to the controls. This was true even after adjustment of the FSI for BMD and HAL [4].

HSA with DXA has provided unique insights into the mechanisms of the pathophysiology of osteoporotic fracture. However, the HAS structural parameters are highly correlated with BMD and while predictive of fracture risk, are not currently better predictors of fracture risk. The major limitations of HSA with DXA primarily reflect limitations imposed by the two-dimensional (2D) nature of DXA [5].

Trabecular bone score

Trabecular bone score (TBS) is one the most recently developed diagnostic tools using DXA that could be important in osteoporosis. Micro-architectural deterioration of bone tissue contributes to bone fragility and susceptibility to fracture as low bone mass [9]. Several novel imaging techniques that include quantitative computed tomography (QCT) and high resolution (peripheral) QCT, and minimally invasive approaches for probing bone material properties have been tried to evaluate micro-architectural properties of bone tissue. However, none of these modalities shows better performance than BMD in the prediction of the various types of osteoporotic fractures, and their lack of availability and validation in the clinical setting means that an adjunctive role alongside DXA-measured BMD is unlikely to be feasible in the near future [10]. However, TBS is a novel imaging technique, based on standard DXA images that could prove to be a useful index of bone texture to provide skeletal information in addition to the standard BMD results [11]. TBS uses experimental variograms of 2D projection images, quantifying variation in grey-level texture from pixel to the adjacent pixels. TBS is not a direct measurement of bone microarchitecture but it is related to bone characteristics that include trabecular number, trabecular separation and the connectivity density [12,13]. An elevated TBS indicates a strong and fracture-resistant microarchitecture. A low TBS reflects weak, fracture-prone microarchitecture [10]. Another advantage of TBS is that it can be obtained by re-analysis of past lumbar spine DXA images without taking another scans, which allows prior data to be used. The usefulness of TBS in osteoporosis is becoming increasingly clear. Low TBS is associated with both a history of fracture and incidence of new fracture [10,12,14-16]. The effect is independent of BMD and is of sufficient magnitude to enhance risk stratification with BMD. The effect is also partly independent of the World Health Organization fracture risk assessment tool (FRAX), with likely greatest utility for those individuals who lie close to an intervention threshold [10,17]. TBS adjusted FRAX probabilities were developed using the Manitoba data [18]. A recent meta-analysis validated this tool and suggested that TBS would have clinical utility, for example in the reclassification of those close to intervention thresholds [16]. A number of smaller investigations have suggested a role for TBS in specific causes of increased fracture risk, such as glucocorticoid excess and type 2 diabetes [10,19,20]. The TBS program is commercially available as TBS iNsight software (Medimap, Geneva, Switzerland) and can be used after installation as an add-on program to the current DXA-operating program.

DETECTION OF PREEXISTING FRACTURES

Vertebral fracture assessment

The presence of vertebral fractures (VFs) suggests that the patient is at increased risk for subsequent osteoporotic fractures. Patients with VFs have a 5-fold increased risk for additional VFs and about 3-fold increased risk for proximal femoral frac-

tures [21]. However, only 30% of VFs are clinically recognized [22]. Standard radiography of the thoracic and lumbar spine is the reference method for detecting VFs, but it cannot be used routinely because of cost and radiation exposure considerations [1]. Vertebral fracture assessment (VFA) is potentially a clinically useful alternative to standard spine radiography for VF identification. Radiation exposure is low, about 3 to 8 micro Sieverts (mSv), compared to 700 to 800 mSv for a lateral radiograph of the lumbar and thoracic spine. Additionally, VFA has the convenience of being done at the same time and location as measurement of BMD by DXA, allowing integration of the two major risk factors for fracture (BMD and prior fracture) in clinical decisions. The digital images can be easily stored and compared as patients are followed-up over time [23].

The fracture-grading method devised by Genant et al. [24] is the most widely used for VFA as standard radiography. The anterior, middle and posterior height of each vertebral body (T7 to L4) are visually estimated on the lateral films. Deformities are graded according to their severity: grade 0 (<20% deformity); grade 1, mild deformities (20% to 25% deformity); grade 2, moderate deformities (25% to 40% deformity); and grade 3, severe deformities (≥40% deformity) [24]. Vertebral height is measured on VFA images manually or automatically using software, but these measurements should be used only for research purposes and not for clinical practice, as vertebral height does not differentiate between VFs and vertebral deformities due to other causes [1]. VFA sensitivity and specificity have been compared to radiographs in studies of postmenopausal women. VFA is an accurate imaging technique to identify grade 2 and 3 fractures in postmenopausal women being evaluated for osteoporosis including those with osteopenia [23,25-30]. Standard spine radiographs possess similar limitations in the accurate identification of grade 1 fractures, patients with scoliosis [23,27] and at vertebrae above the level of T7 [23,26,27]. Therefore, VFA is a reliable alternative to spine radiographs for the identification of VFs in postmenopausal women [23].

Detection of atypical femur fracture

Atypical subtrochanteric and diaphyseal fracture (AFF) is a serious complication in patients with osteoporosis, especially for those on prolonged bisphosphonate (BP) therapy. The absolute risk of AFFs in patients on BP therapy is low, ranging from 3.2 to 50 cases per 100,000 person-years. However, long-term use may be associated with higher risk (~100 per 100,000 person-years) [31]. The burden of BP-associated fractures is significant. In-patient hospital stay is lengthy and the injury and its treatment are associated with significant complications [32]. Therefore, early detection of prefracture lesions is important for the prevention of impending subtrochanteric fracture [33,34]. Recently, a Korean study reported that assessment of hip DXA images combined with conventional assessment of prodromal symptoms enables detection of more AFFs earlier than assessment based on prodromal symptoms alone [35]. In 2013, the United States Food and Drug Administration (USFDA) approved using the latest generation of Hologic densitometers for detection of radiological changes of AFF. Clinical routine application will require additional studies [3].

MEASUREMENT OF BODY COMPOSITION

Application in sarcopenia

Significant progress in the acquisition time of DXA (5 to 10 minutes) has enabled the rapid assessment of whole body composition or of a region of the body based on whole-body imaging. The measurement of body composition by DXA is a particularly attractive feature because of its noninvasive nature, low cost and very low irradiation (2.6 to 75 mSV) compared to other techniques including computed tomography (CT) and magnetic resonance imaging [1,3]. One of the applications of body composition assessment is the diagnosis of sarcopenia, an age-related muscle mass decline for which several definitions have been suggested. The European Working Group on Sarcopenia in Older People developed a definition based on three criteria: low muscle mass as measured using DXA or bioimpedence analysis, low muscle strength and low physical performance [1,36]. Skeletal muscle index (SMI) is usually used for muscle mass computed as the ratio of appendicular skeletal muscle mass over height squared [37]. SMI values more than SDs below values in young individuals generally indicate low muscle mass [1]. Measurements of body composition by DXA are expanding in many fields, such as for evaluation of lipodystrophy in human immunodeficiency virus patients and changes in lean mass in athletes. At present, body composition assessment is reserved for research and is not in routine clinical use [1,3].

Visceral fat measurement

Abdominal fat (AF) is associated with increased morbidity, independent of age, race, and sex [38]. Increase in visceral AF is particularly important, since it significantly contributes to many metabolic abnormalities associated with body weight

gain [39-43]. Anthropometric measurements such as body mass index, waist circumference and waist-to-hip ratio are commonly used in large epidemiologic studies. However, these measurements actually assess total AF, and therefore cannot differentiate between visceral AF and subcutaneous AF. A newly developed fully automated method for segmenting AF into subcutaneous AF and visceral AF within the android region using DXA has been approved for clinical use by the USFDA [44]. Additional commercial software (CoreScan or Hologic's InnerCore, GE Healthcare, Chicago, IL, USA) is required to measure VF. Technical performance of DXA VF has been demonstrated in both American and Chinese populations. These studies showed a high correlation and small average difference between DXA and CT [44,45]. Recently, a Korean study showed that VF measured by DXA is highly correlated with the VF measured by CT and could be a reliable estimate of VF in Korean population [46]. However, additional studies are required for its clinical routine application.

CONCLUSIONS

The significant improvements in DXA on the quality, resolution of the images and acquisition time have allowed the development of variable functions. With the evaluation of bone quality by indirect analysis of micro- and macro-architecture, such as HSA and TBS, may improve the prediction of fracture risk. It may also replace or gradually replace conventional radiology with VFA or detection of AF. Moreover, it can assess the metabolic status by the measurement of the whole body composition, such as muscle mass and VF.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

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