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

Yong Jun Choi

Department of Endocrinology and Metabolism, Ajou University School of Medicine, Suwon, Korea

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].
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 of 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 (VF) 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-
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 bioimpedance 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.

ORCID

Yong Jun Choi  http://orcid.org/0000-0003-3960-8470

REFERENCES

1. Briot K. DXA parameters: beyond bone mineral density. Joint Bone Spine 2013;80:265-9.
2. NIH Consensus Development Panel on Osteoporosis Prevention, Diagnosis, and Therapy. Osteoporosis prevention, diagnosis, and therapy. JAMA 2001;285:785-95.
3. Gonzalez Rodriguez E, Favre L, Lamy O, Pralong F, Hans D. DXA imaging: the multifunction Swiss army knife? Rev Med Suisse 2015;11:645-50.
4. Faulkner KG, Wacker WK, Barden HS, Simonelli C, Burke PK, Ragi S, et al. Femur strength index predicts hip fracture independent of bone density and hip axis length. Osteoporos Int 2006;17:593-9.
5. Bonnick SL. HSA: beyond BMD with DXA. Bone 2007;41(1 Suppl 1):S9-12.
6. Roark RJ, Young WC. Roark’s formulas for stress and strain. 6th ed. New York: McGraw-Hill; 1989. p. 688.
7. Szulc P, Duboeuf F, Schott AM, Dargent-Molina P, Meunier PJ, Delmas PD. Structural determinants of hip fracture in elderly women: re-analysis of the data from the EPIDOS study. Osteoporos Int 2006;17:231-6.
8. Martin RB, Burr DB. Non-invasive measurement of long bone cross-sectional moment of inertia by photon absorptiometry. J Biomech 1984;17:195-201.
9. Consensus development conference: diagnosis, prophylaxis, and treatment of osteoporosis. Am J Med 1993;94:646-50.
10. Harvey NC, Gluer CC, Binkley N, McCloskey EV, Brandi ML, Cooper C, et al. Trabecular bone score (TBS) as a new complementary approach for osteoporosis evaluation in clinical practice. Bone 2015;78:216-24.
11. Silva BC, Leslie WD, Resch H, Lamy O, Lesnyak O, Binkley N, et al. Trabecular bone score: a noninvasive analytical method based upon the DXA image. J Bone Miner Res 2014;29:518-30.
12. Hans D, Goertzen AL, Krieg MA, Leslie WD. Bone microarchitecture assessed by TBS predicts osteoporotic fractures independent of bone density: the Manitoba study. J Bone Miner Res 2011;26:2762-9.
13. Winzenrieth R, Michelet F, Hans D. Three-dimensional (3D) microarchitectural correlations with 2D projection image gray-level variations assessed by trabecular bone score using high-resolution computed tomographic acquisitions: effects of resolution and noise. J Clin Densitom 2013;16:287-96.
14. Nassar K, Paternotte S, Kolta S, Fechtenbaum J, Roux C, Briot K. Added value of trabecular bone score over bone mineral density for identification of vertebral fractures in patients with areal bone mineral density in the non-osteoporotic range. Osteoporos Int 2014;25:243-9.
15. Iki M, Tamaki J, Kadowaki E, Sato Y, Dongmei N, Win-
Trabecular bone score (TBS) predicts vertebral fractures in Japanese women over 10 years independently of bone density and prevalent vertebral deformity: the Japanese Population-Based Osteoporosis (JPOS) cohort study. J Bone Miner Res 2014;29:399-407.

16. McCloskey EV, Oden A, Harvey NC, Leslie WD, Hans D, Johansson H, et al. A meta-analysis of trabecular bone score in fracture risk prediction and its relationship to FRAX. J Bone Miner Res 2015 Oct 24 [Epub]. http://dx.doi.org/10.1002/jbmr.2734.

17. Leslie WD, Johansson H, Kanis JA, Lamy O, Oden A, McCloskey EV, et al. Adjusting fracture probability by trabecular bone score. Calcif Tissue Int 2015;96:500-9.

18. Eller-Vainicher C, Morelli V, Ulivieri FM, Palmieri S, Zhukouskaya VV, Cairoli E, et al. Bone quality, as measured by trabecular bone score in patients with adrenal incidentalomas with and without subclinical hypercortisolism. J Bone Miner Res 2012;27:2223-30.

19. Black DM, Arden NK, Palermo L, Pearson J, Cummings SR. Prevalent vertebral deformities predict hip fractures and new vertebral deformities but not wrist fractures. Study of Osteoporotic Fractures Research Group. J Bone Miner Res 1999;14:821-8.

20. Link TM, Guglielmi G, van Kuijk C, Cairoli C, Palmieri S, Zhukouskaya VV, et al. Lumbar spine texture enhances 10-year fracture probability assessment. Osteoporo Int 2014;25:2271-7.

21. Link TM, Guglielmi G, van Kuijk C, Cairoli E, et al. Bone quality, as measured by trabecular bone score in patients with adrenal incidentalomas with and without subclinical hypercortisolism. J Bone Miner Res 2012;27:2223-30.

22. Link TM, Guglielmi G, van Kuijk C, Cairoli E, et al. Bone quality, as measured by trabecular bone score in patients with adrenal incidentalomas with and without subclinical hypercortisolism. J Bone Miner Res 2012;27:2223-30.

23. Link TM, Guglielmi G, van Kuijk C, Cairoli E, et al. Bone quality, as measured by trabecular bone score in patients with adrenal incidentalomas with and without subclinical hypercortisolism. J Bone Miner Res 2012;27:2223-30.

24. Link TM, Guglielmi G, van Kuijk C, Cairoli E, et al. Bone quality, as measured by trabecular bone score in patients with adrenal incidentalomas with and without subclinical hypercortisolism. J Bone Miner Res 2012;27:2223-30.

25. Gehlbach SH, Bigelow C, Heimisdottir M, May S, Walker M, Kirkwood JR. Recognition of vertebral fracture in a clinical setting. Osteoporos Int 2000;11:577-82.

26. Ferrar L, Jiang G, Eastell R, Peel NF. Visual identification of vertebral fractures in osteoporosis using morphometric X-ray absorptiometry. J Bone Miner Res 2003;18:933-8.

27. Schousboe JT, Debold CR. Reliability and accuracy of vertebral fracture assessment with densitometry compared to radiography in clinical practice. Osteoporos Int 2006;17:281-9.

28. Rea JA, Li J, Blake GM, Steiger P, Genant HK, Fogelman I. Visual assessment of vertebral deformity by X-ray absorptiometry: a highly predictive method to exclude vertebral deformity. Osteoporos Int 2000;11:660-8.

29. Binkley N, Krueger D, Gangnon R, Genant HK, Dreznz MK. Lateral vertebral assessment: a valuable technique to detect clinically significant vertebral fractures. Osteoporos Int 2005;16:1513-8.

30. Wu C, Genant HK, von Ingersleben G, Chen Y, Johnston C, Econs M, et al. Validation of lateral DXA imaging for assessment of vertebral fractures. J Bone Miner Res 2004;19(Suppl 1):S295.

31. Shane E, Burr D, Abrahamsen B, Adler RA, Brown TD, Cheung AM, et al. Atypical subtrochanteric and diaphyseal femoral fractures: second report of a task force of the American Society for Bone and Mineral Research. J Bone Miner Res 2014;29:1-23.

32. Shkolnikova J, Flynn J, Choong P. Burden of bisphosphonate-associated femoral fractures. ANZ J Surg 2013;83:175-81.

33. Ahlman MA, Rissing MS, Gordon L. Evolution of bisphosphonate-related atypical fracture retrospectively observed with DXA scanning. J Bone Miner Res 2012;27:496-8.

34. Miki S, Yang KH, Lim H, Lee YK, Yoon HK, Oh CW, et al. Detection of prefracture hip lesions in atypical subtrochanteric fracture with dual-energy X-ray absorptiometry images. Radiology 2014;270:487-95.

35. Cooper C, Dere W, Evans W, Kanis JA, Rizzoli R, Sayer AA, et al. Frailty and sarcopenia: definitions and outcome parameters. Osteoporos Int 2012;23:1839-48.

36. Baumgartner RN, Koehler KM, Gallagher D, Romero L, Heymsfield SB, Ross RR, et al. Epidemiology of sarcopenia among the elderly in New Mexico. Am J Epidemiol 1998;147:755-63.

37. Okusun IS, Liao Y, Rotimi CN, Prewitt TE, Cooper RS. Abdominal adiposity and clustering of multiple metabolic syndrome in White, Black and Hispanic americans. Ann Epidemiol 2000;10:263-70.

38. You T, Ryan AS, Nicklas BJ. The metabolic syndrome in...
obese postmenopausal women: relationship to body composition, visceral fat, and inflammation. J Clin Endocrinol Metab 2004;89:5517-22.

40. Ding J, Visser M, Kritchevsky SB, Nevitt M, Newman A, Sutton-Tyrrell K, et al. The association of regional fat depots with hypertension in older persons of white and African American ethnicity. Am J Hypertens 2004;17:971-6.

41. Albu JB, Murphy L, Frager DH, Johnson JA, Pi-Sunyer FX. Visceral fat and race-dependent health risks in obese nondiabetic premenopausal women. Diabetes 1997;46:456-62.

42. Ross R, Aru J, Freeman J, Hudson R, Janssen I. Abdominal adiposity and insulin resistance in obese men. Am J Physiol Endocrinol Metab 2002;282:E657-63.

43. Ross R, Fortier L, Hudson R. Separate associations between visceral and subcutaneous adipose tissue distribution, insulin and glucose levels in obese women. Diabetes Care 1996;19:1404-11.

44. Kaul S, Rothney MP, Peters DM, Wacker WK, Davis CE, Shapiro MD, et al. Dual-energy X-ray absorptiometry for quantification of visceral fat. Obesity (Silver Spring) 2012;20:1313-8.

45. Lin H, Yan H, Rao S, Xia M, Zhou Q, Xu H, et al. Quantification of visceral adipose tissue using lunar dual-energy X-ray absorptiometry in Asian Chinese. Obesity (Silver Spring) 2013;21:2112-7.

46. Choi YJ, Seo YK, Lee EJ, Chung YS. Quantification of visceral fat using dual-energy X-ray absorptiometry and its reliability according to the amount of visceral fat in Korean adults. J Clin Densitom 2015;18:192-7.