Archives of Osteoporosis (2020) 15: 70
https://doi.org/10.1007/s11657-020-00745-0

ORIGINAL ARTICLE

Do patients that fracture with normal DXA-measured BMD have normal bone?

Sindhura Bandaru[1] · Kristyn Hare[2] · Diane Krueger[3] · Neil Binkley[1,3]

Received: 29 November 2019 / Accepted: 30 March 2020 / Published online: 11 May 2020

Abstract

Mini abstract Patients that sustain "osteoporosis-related" fractures may have normal BMD at the hips and spine, but rarely have normal bone when other clinically available studies are considered. Such data often exist and can inform clinical decisions regarding osteoporosis therapy.

Purpose Dual-energy X-ray absorptiometry (DXA) measured bone mineral density (BMD) at the hip and spine is widely used to diagnose osteoporosis. However, patients that sustain "osteoporosis-related" fractures often have normal BMD at these sites. The aim of this study was to explore whether older adults with fracture, but normal reported hip and spine BMD, also have normal bone using additional clinically available assessments.

Methods This retrospective electronic medical record study included 387 patients evaluated by a university-based fracture liaison service with spine and hip DXA; 32 (8.3%) had normal spine/hip BMD reported. In this cohort, clinically available bone data including 0.3 and ultradistal radius T-scores, trochanteric T-scores, lumbar spine trabecular bone score (TBS), L1 opportunistic CT Hounsfield units (HU), and femoral cortical index (FCI) were assessed.

Results One or more of the above noted studies were available in 30/32 patients. UD and 0.3 radius results were available in 21 patients, and 18 (85.7%) had T-scores < -1.0. Trochanteric values were available in 16; T-scores were < -1.0 in 18.8%. TBS data were available in 24; partially degraded or degraded values were present in 41.7%. L1 opportunistic CT was available in 25 patients, 80% were below normal, and < 150 HU. Finally, femoral cortical index (FCI) was measurable in 9 subjects; 66.7% were below < 0.4. When including all additional available data in the skeletal assessment, only 5/387 (1.3%) were identified with normal bone.

Conclusion Patients with normal spine/hip BMD who sustain fracture rarely have normal bone when all available data are considered.

Keywords Fracture · DXA · BMD · TBS · Opportunistic CT

Introduction

Osteoporosis is often defined using bone mineral density (BMD) by dual-energy X-ray absorptiometry (DXA) [1]. With this methodology, osteoporosis is present when the BMD is 2.5 standard deviations or more below the average value for a young healthy reference population (a T-score of ≤ -2.5) [2]. However, most patients that sustain "osteoporosis-related" fractures have T-scores better than -2.5; indeed, 10–20% of these patients are reported to have normal BMD as measured by DXA [3, 4]. Other approaches to diagnosing osteoporosis exist, with some guidelines suggesting that presence of a fragility fracture is diagnostic of osteoporosis [5]. Unfortunately, what constitutes a "fragility" fracture also has challenges; it may be defined as "a fracture resulting from a low-energy trauma that would not damage a normal bone" or "a fracture caused by a fall from a height equal to or less than that of the patient" [6]. However, there is no ideal clinical way to determine when a fracture is "low-energy." Finally, many guidelines recommend pharmacologic therapy with osteoporosis drugs for patients with fracture without need for BMD

✉ Sindhura Bandaru
SBandaru@uwhealth.org

[1] University of Wisconsin School of Medicine and Public Health, UW Health, 2870 University Avenue, Suite 100, Madison, WI 53705, USA

[2] University of Wisconsin Department of Orthopedics, Madison, WI, USA

[3] University of Wisconsin Osteoporosis Clinical Research Program, Madison, WI, USA

measurement, thus implying that these individuals have osteoporosis [7, 8]. However, data documenting that osteoporosis medications reduce fracture risk in those with normal BMD as measured by DXA are very limited [9].

Despite DXA being accepted as the gold standard for clinical osteoporosis diagnosis and treatment monitoring [10], important limitations exist. Notably, spinal degenerative changes elevate BMD with this methodology [11]. Additionally, routine DXA does not allow consideration of bone microarchitecture despite osteoporosis being defined by one consensus conference as "low bone mass and microarchitectural deterioration" [12]. As such, we hypothesized that many patients with fragility fracture and normal BMD measured by DXA at the classic spine and hip sites do not have normal bone. Therefore, the purpose of this study was to explore whether older adults with fracture but normal reported DXA-measured BMD have normal bone when additional clinically available skeletal health assessments are considered. Specifically, we hypothesized that consideration of femoral trochanter and radius 0.3/ultradistal DXA T-scores, lumbar spine trabecular bone score (TBS), lumbar vertebral opportunistic CT, and femoral cortical index would demonstrate that individuals with fracture have abnormal bone mass or quality.

Materials and methods

This is a retrospective electronic medical record review of patients evaluated by a university-based fracture liaison service (FLS). As these data were collected to explore whether patients seen by our FLS with normal BMD should receive osteoporosis medications, this work is IRB exempt. Our FLS evaluation generally includes medical history, physical exam, laboratory assessment, and BMD measurement by DXA. We reviewed 387 patients seen by one FLS provider (KH) who had spine and hip DXA performed either within our health system or elsewhere. Of note, some of these patients had either spine or hip DXA available but not both due to metallic artifacts at one of those sites. In this cohort, 32 (8.3%) were reported to have normal spine/hip BMD in the formal DXA interpretation.

In this subset of 32, a descriptive study involving chart review was performed which consisted of the following:

1. When available, review of the DXA images and testing to:

a. Confirm accuracy of the DXA report, notably assessing if vertebral bodies were excluded when appropriate following ISCD guidelines [10].
b. Obtain T-scores of the femoral trochanter, 0.3, and ultradistal radius. We applied the WHO classification, i.e., T-score ≤ -2.5 as osteoporosis and -2.4 to -1.1 as osteopenia to these sites to identify those with abnormal bone.
c. Obtain lumbar spine TBS. We utilized values from a meta-analysis [13] and defined normal, partially degraded, and degraded bone microarchitecture as TBS values ≥ 1.310, 1.309–1.230, and < 1.230, respectively.

2. Review PACS and perform lumbar spine opportunistic CT Hounsfield unit (HU) measurement at L1 in those patients with prior chest or abdominal images within 10 years prior to fracture [14]. L1 HU was obtained by one person (SB) as previously described [14]. As contrast material increases L1 HU by ~ 11 HU over unenhanced scans [15], we deducted 10 HU for CT images with IV contrast. At L1, CT HU < 100 is suggestive of osteoporosis and > 100 HU to < 150 HU is suggestive of osteopenia [14, 16].
3. Review PACS and calculate the femoral cortical index (FCI) when proximal femur X-rays were available. FCI ≤ 0.40 is highly suggestive of osteoporosis [17]. FCI was calculated by dividing the inner cortical thickness by outer cortical thickness, measured 10 mm below the lesser trochanter [18].
4. Determine the fracture circumstances in those remaining patients with normal BMD by DXA and any other clinically available data as noted above.

Descriptive statistics were performed using Microsoft Excel.

Results

Study cohort

Study group characteristics are shown in Table 1. In this cohort, fractures leading to FLS evaluation included femoral, 20 (of which 10 were periprosthetic fractures); vertebral, 7; tibia, 2; and one each at the wrist, pelvis, and trimalleolar ankle. In these 32 patients, 23 had a history of fracture prior to the one that led to their FLS evaluation. Three of these patients had a diagnosis of rheumatoid arthritis; two of whom had received prednisone therapy. An additional 3 patients had a history of glucocorticoid treatment. Various other clinical risk factors for fracture, e.g., alcohol use, gastric bypass, vitamin D deficiency, prior chemotherapy, were present in 22 of these patients. FRAX scores were calculated; 13/32 had 10-year major fracture risk > 20% and 17/32 had 10-year hip fracture risk > 3%. There was one DXA report error; the L-spine T-score was reported as normal but was actually -1.9 after appropriate vertebral exclusion, and this patient was included in the analysis as the DXA results were originally reported as normal. At least one of the additional bone studies noted above was available in 30/32 of these patients.

Table 1 Study cohort characteristics ($n = 32$)

Parameter	Number (%)
Sex	
Female	25 (78.1)
Male	7 (21.9)
Age (years)	
Mean	71
Range	54–85
BMI (kg/m^2)	
Mean (SD)	32 (7)
Range	22–48
L-spine T-score	
Mean (SD)	0.54 (1.04)
Range	− 1.9–+3.0
Total femur T-score	
Mean (SD)	− 0.14 (0.32)
Range	− 1.0–+0.8
Femur neck T-score	
Mean (SD)	− 0.33 (0.48)
Range	− 1.0–+1.5
FRAX 10-year risk (%)	
Major: mean (SD)	20.7 (12.8)
Range	6.4–44.0
Hip: mean (SD)	7.1 (7.9)
Range	0.2–27.0

All patients were Caucasian

Additional bone status assessments (Fig. 1)

Femoral trochanter

In this cohort, 16/32 had trochanteric T-scores available. The trochanteric T-score was < − 1.0 in 3/16 and normal in the remainder. All of these 3 patients had T-scores in the osteopenic range. Thus, in those in whom trochanteric BMD was available, DXA identified 18.8% with abnormal bone (Fig. 2).

Forearm

In this cohort, 21/32 had forearm DXA available; 8/21 patients (38.1%) had 0.3 radius T-scores in the osteopenic range and 3/21 (14.3%) in the osteoporotic range. In the remaining 10 patients with normal 0.3 radius, the UDR T-score was ≤ − 1.1 in 5. In summary, those with radius DXA had abnormal bone identified at the 0.3 and/or UDR in 85.7% (18/21); in seven, the T-score was ≤ − 2.5 while the others were osteopenic.

TBS

Trabecular bone score (TBS), a bone texture score that serves as a surrogate of bone microarchitecture [19], was available in 24/32 patients. Normal TBS was identified in 14/24 (58%) patients, while 4/24 (16.7%) had TBS between 1.309 and 1.230 demonstrating partially degraded scores, and the remaining 6/24 patients (25%) had scores < 1.230 signifying degraded TBS. Thus, in those with TBS, 10/24 (41.7%) were identified as abnormal.

Opportunistic CT

Chest or abdominal CT scans performed within 10 years prior to fracture were available in 25/32 patients. L1 HU was < 100 in 13/25 (52%) and < 150 but > 100 in 7/25 patients (28%). Thus, L1 HU was low in 20/25 (80%) of this cohort.

FCI

Proximal femur X-rays were available in 9/32 patients, thus allowing calculation of FCI. In these 9 patients, only 2 had both right and left femur radiographs; the remaining 7 had either right or left FCI. FCI identified 6 patients with abnormal bone (FCI < 0.4).

Fractures in those with normal spine/hip DXA plus other normal studies

In this cohort, only 2 patients had no additional bone-relevant imaging available in the EMR. In those with one or more available studies ($n = 30$), the additional available bone data were normal in only 3 (10%). Thus, only 5 of these 32 patients with fracture and normal spine and hip BMD could not be classified as having abnormal bone. The patients with normal spine/hip BMD and all additional bone studies being normal had the following fracture history: One with a normal trochanteric T-score sustained right elbow and left wrist fracture following fall on outstretched hand, a second with normal TBS and trochanteric T-score sustained a spontaneous T7 compression fracture, and a third with normal 0.3 and UD radius T-scores sustained a left femur periprosthetic fracture after tripping and falling on the stairs. In summary, in this review of 387 fracture patients seen by a FLS provider, only 5 (1.3%) could not be identified as having abnormal bone using data available in the EMR.

Discussion

In this cohort of fracture patients but normal reported spine/hip BMD, additional readily available clinical bone data were available in over 90%. When including these data in the

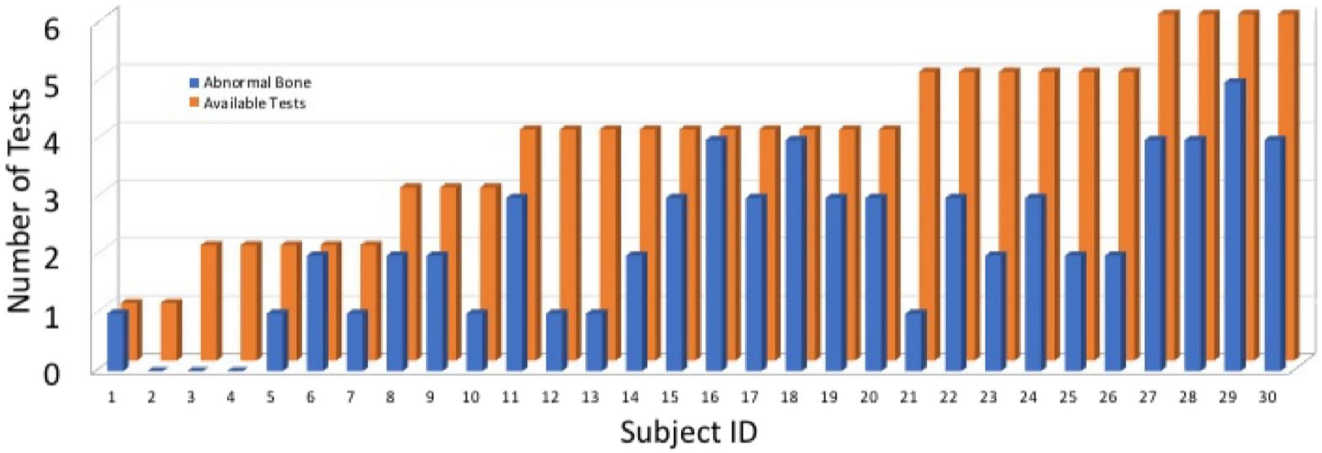

Fig. 1 Number of additional bone studies available and number abnormal in this cohort. In this group of 32 patients with a normal spine/hip DXA report, multiple other relevant bone studies were available in the electronic medical record. These additional studies identified abnormal bone with a frequency ranging from 16% (trochanter) to 80–86% (opportunistic CT and radius DXA respectively). Only two subjects had no additional imaging

clinical skeletal assessment, very few (1.3% of the entire cohort) were identified as having normal bone. Moreover, it is plausible that even some of these few might have had abnormal bone if additional imaging studies were available. In those where radius DXA or lumbar opportunistic CT was available, over 80% of patients were identified as having abnormal bone. Thus, clinicians who are reluctant to utilize osteoporosis medications in fracture patients with normal spine and hip DXA are advised to seek additional data or testing evaluating bone status in such individuals. Such data is often readily available in the EMR with no additional cost or radiation exposure. Moreover, while the focus of this report is to identify abnormal bone in fracture patients, estimated fracture risk is often used to guide use of pharmacologic therapy. In this regard, approximately half of this cohort met FRAX thresholds for therapy whether 10-year major or hip fracture risk were considered. As such, the results of this FLS-based cohort study could be utilized to support pharmacologic agent use for patients with fracture and normal hip and spine BMD.

Our data demonstrating that ~ 8% of fracture patients overall have normal DXA-measured BMD are generally comparable to prior reports. For example, Schuit et al. reported that 12.6% of women with non-vertebral fractures and 5.2% with hip fractures had normal BMD and in men 17.9% with non-vertebral fractures and 2.8% with hip fractures were reported to have normal BMD [4]. Cranney et al. concluded that most of postmenopausal women with osteoporotic fractures had non-osteoporotic BMD values with an estimated 17% and 13% of women with fracture having normal BMD at the spine and hip, respectively [20]. It is plausible that the numerically

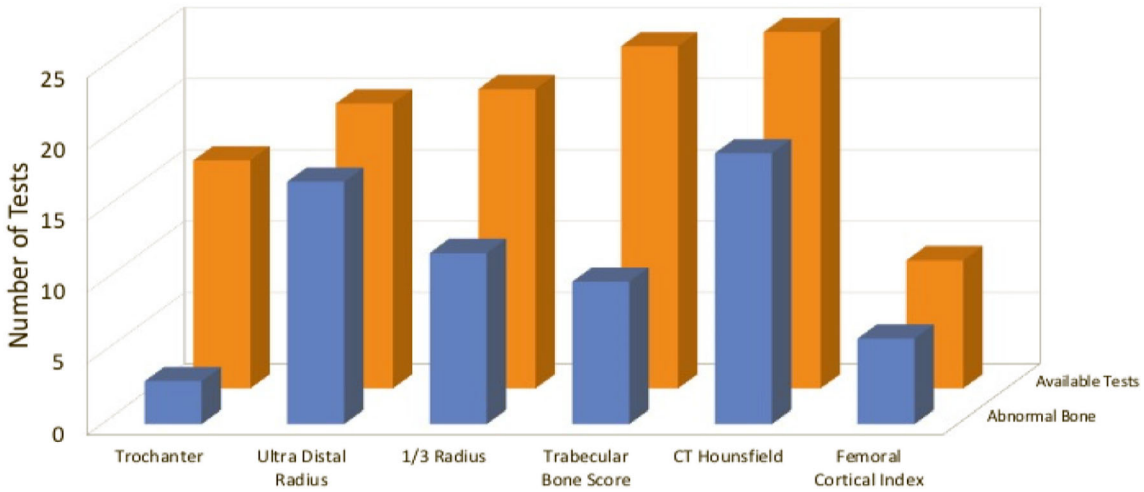

Fig. 2 Prevalence of Abnormal Bone with Multiple Tests. Individual patient data demonstrating the number of additional bone studies available (orange bars) and the number abnormal (blue bars) is depicted. In those with two or more additional bone study available ($n = 28$) abnormal results were present at two or more sites in 20 (78.6%)

lower number with normal BMD reported here reflects patients seen by a university hospital based FLS that might include those with more severe bone disease.

In patients who sustain fracture with a fall and are reported to have normal BMD based on standard hips/spine DXA, it is important to first assess for DXA errors [21] and subsequently further evaluate to see if the bone is truly normal as such knowledge may be important in treatment decisions, especially whether to utilize pharmacotherapy to decrease the subsequent fracture risk. Forearm BMD, lumbar spine TBS, opportunistic CT HU, and femoral cortical index calculated from proximal femur X-rays are often clinically available to add insight into the patients' bone status.

We recognize that T-scores of the ultradistal radius were not included in the WHO technical document used to develop the T-score-based classification [2]. Nonetheless, we believe this reasonable as low forearm BMD is a strong predictor of fracture risk [22]. Similarly, trochanteric T-scores are not included in current definition of osteoporosis. However, we believe this reasonable as the trochanter was previously considered a diagnostic site and predicts fracture risk [23]. Low TBS to define abnormal bone is reasonable as it is a surrogate marker for trabecular bone microarchitecture and its fracture predictive ability is independent of FRAX clinical risk factors and femoral neck BMD [24]. The cut-points selected to define abnormal bone were evidence based [24] and are being advocated by the TBS manufacturer. Moderate to severe compression fractures identified at CT are frequently associated with non-osteoporotic T-scores by DXA but have abnormally low vertebral attenuation values in majority of the cases [14]. Osteoporosis screening can be performed concomitantly with chest or abdominal CT regardless of original study indication; such studies are often available in the EMR. This opportunistic approach allows bone assessment with no additional radiation exposure or cost. The overall performance for predicting osteoporosis is similar between enhanced and unenhanced CT scans, thus either can be employed for initial opportunistic screening. CT HU < 100 is suggestive of osteoporosis and > 100 HU while HU < 150 is suggestive of osteopenia [14, 16]. Finally, femoral cortical thinning and porosity are important in bone fragility making FCI a reasonable assessment of bone status [18].

It is worthy of emphasis that not all available tests were abnormal. We believe this is to be expected, given that these methods assess skeletal sites with differing proportions of cortical and trabecular bone and that trabecular bone is lost more rapidly after menopause is widely recognized resulting in diagnostic discordance when multiple skeletal sites are measured [25]. Additionally, it is possible/likely that the various tests available clinically have differential sensitivity and precision to define abnormal reproducibility. As such, we believe it appropriate that clinicians characterize their fracture patients' bones as abnormal if any of these tests are low.

Historically, periprosthetic fractures may not have been considered "osteoporosis-related." This perception is changing, we believe appropriately, as osteoporosis is increasingly recognized as a risk factor for these fractures [26]. Moreover, similar to classic osteoporotic fractures, the majority of periprosthetic fractures result from low trauma [27]. Finally, the morbidity and mortality of periprosthetic femur fractures is virtually identical to that of the classic hip fracture [28].

A clear limitation of our study is small sample size; larger studies evaluating other measures of bone in patients with fracture but normal DXA-measured BMD are clearly called for. Additionally, as noted above, it is possible that this cohort has more severe bone disease given that they were evaluated by a university-based FLS; thus generalizability may be limited. Another important limitation is that none of these measures directly assess bone quality. It has long been known that osteoporosis is loss not only of mass but also quality [29]. Indeed, changes in quality likely contribute to bones becoming more brittle with age [30]. Clinical tools evaluating bone quality are sorely needed. Nonetheless, these data highlight not only the availability of additional tests but also the importance of assessing other parameters in patients who sustain fracture following minimal trauma but have normal BMD based on T-scores at hips/spine.

In conclusion, patients with normal spine and hip BMD who sustain fracture rarely have normal bone when all available data are considered. These data indirectly support recommendations that postmenopausal women and men age 50 and older with a hip or vertebral fracture should receive osteoporosis medication as their bone is rarely normal.

References

1. Kanis JA (2002) Diagnosis of osteoporosis and assessment of fracture risk. Lancet (London, England) 359:1929–1936
2. Organization WH (1994) Assessment of fracture risk and its application to screening for postmenopausal osteoporosis. WHO technical report series 843. World Health Organization
3. Siris ES, Miller PD, Barrett-Connor E, Faulkner KG, Wehren LE, Abbott TA, Berger ML, Santora AC, Sherwood LM (2001) Identification and fracture outcomes of undiagnosed low bone mineral density in postmenopausal women: results from the National Osteoporosis Risk Assessment. J Am Med Assoc 286:2815–2822
4. Schuit SCE, van der Klift M, Weel AEAM, de Laet CEDH, Burger H, Seeman E, Hofman A, Uitterlinden AG, van Leeuwen JPTM, Pols HAP (2004) Fracture incidence and association with bone mineral density in elderly men and women: the Rotterdam study. Bone 34:195–202
5. NOF (2014) Clinician's guide to prevention and treatment of osteoporosis. National Osteoporosis Foundation, Washington DC
6. Reginster JY, Burlet N (2006) Osteoporosis: a still increasing prevalence. Bone 38:S4–S9
7. Cosman F, de Beur SJ, LeBoff MS, Lewiecki EM, Tanner B, Randall S, Lindsay R (2014) Clinician's guide to prevention and treatment of osteoporosis. Osteoporos Int 25:2359–2381

8. Kanis JA, Cooper C, Rizzoli R, Reginster JY (2019) European guidance for the diagnosis and management of osteoporosis in postmenopausal women. Osteoporos Int 30:3–44
9. Gnant M, Pfeiler G, Dubsky PC, Hubalek M, Greil R, Jakesz R, Wette V, Balic M, Haslbauer F, Melbinger E, Bjelic-Radisic V, Artner-Matuschek S, Fitzal F, Marth C, Sevelda P, Mlineritsch B, Steger GG, Manfreda D, Exner R, Egle D, Bergh J, Kainberger F, Talbot S, Warner D, Fesl C, Singer CF, Austrian Breast and Colorectal Cancer Study Group (2015) Adjuvant denosumab in breast cancer (ABCSG-18): a multicentre, randomised, double-blind, placebo-controlled trial. Lancet 386:433–443
10. Baim S, Binkley N, Bilezikian JP, Kendler DL, Hans D, Lewiecki EM, Silverman SL (2008) Official positions of the International Society for Clinical Densitometry and Executive summary of the 2007 ISCD position development conference. J Clin Densitom 11:75–91
11. Belmonte-Serrano MA, Bloch DA, Lane NE, Michel BE, Fries JF (1993) The relationship between spinal and peripheral osteoarthritis and bone density measurements. J Rheumatol 20:1005–1013
12. Anonymous (2001) Osteoporosis prevention, diagnosis and therapy NIH consensus development panel on osteoporosis prevention, diagnosis and therapy. J Am Med Assoc 285:785–795
13. McCloskey EV, Oden A, Harvey NC et al (2016) A meta-analysis of trabecular bone score in fracture risk prediction and its relationship to FRAX. J Bone Miner Res 31:940–948
14. Pickhardt PJ, Pooler BD, Lauder T, del Rio AM, Bruce RJ, Binkley N (2013) Opportunistic screening for osteoporosis using abdominal computed tomography scans obtained for other indications. Ann Intern Med 158:588–595
15. Pickhardt PJ, Lauder T, Pooler BD, Munoz Del Rio A, Rosas H, Bruce RJ, Binkley N (2016) Effect of IV contrast on lumbar trabecular attenuation at routine abdominal CT: correlation with DXA and implications for opportunistic osteoporosis screening. Osteoporos Int 27:147–152
16. Gausden EB, Nwachukwu BU, Schreiber JJ, Lorich DG, Lane JM (2017) Opportunistic use of CT imaging for osteoporosis screening and bone density assessment: a qualitative systematic review. J Bone Joint Surg Am 99:1580–1590
17. Sah AP, Thornhill TS, LeBoff MS, Glowacki J (2007) Correlation of plain radiographic indices of the hip with quantitative bone mineral density. Osteoporos Int 18:1119–1126
18. Tarantino U, Rao C, Tempesta V, Gasbarra E, Feola M (2016) Hip fractures in the elderly: the role of cortical bone. Injury 47(Suppl 4): S107–S111
19. Leslie WD, Johansson H, Oden A, McCloskey E, Hans D, Kanis JA (2015) Improved risk assessment using lumbar spine trabecular bone score (TBS) to adjust fracture probability: the Manitoba BMD cohort. J Bone Miner Res. American Soceity for Bone and Mineral Research, pp http://www.asbmr.org/education/AbstractDetail?aid=26762bba-26762c26718-24287-b26077-e26768bcaf26118bf26766
20. Cranney A, Jamal SA, Tsang JF, Josse RG, Leslie WD (2007) Low bone mineral density and fracture burden in postmenopausal women. Can Med Assoc J 177:575–580
21. Krueger D, Shives E, Siglinsky E, Libber J, Buehring B, Hansen KE, Binkley N (2019) DXA errors are common and reduced by use of a reporting template. J Clin Densitom 22:115–124
22. Holmberg A, Johnell O, Akesson K, Nilsson P, Nilsson JA, Berglund G (2004) Forearm bone mineral density in 1294 middle-aged women: a strong predictor of fragility fractures. J Clin Densitom 7:419–423
23. Lewiecki EM, Watts NB, McClung MR, Petak SM, Bachrach LK, Shepherd JA, Downs RW Jr (2004) Official positions of the international society for clinical densitometry. J Clin Endocrinol Metab 89:3651–3655
24. McCloskey EV, Oden A, Harvey NC, Leslie WD, Hans D, Johansson H, Kanis JA (2015) Adjusting fracture probability by trabecular bone score. Calcif Tissue Int 96:500–509
25. Nilas L, Christiansen C (1988) Rates of bone loss in normal women: evidence of accelerated trabecular bone loss after the menopause. Eur J Clin Investig 18:529–534
26. Marsland D, Mears SC (2012) A review of periprosthetic femoral fractures associated with total hip arthroplasty. Geriatr Orthop Surg Rehab 3:107–120
27. Della Rocca GJ, Leung KS, Pape HC (2011) Periprosthetic fractures: epidemiology and future projections. J Orthop Trauma 25(Suppl 2):S66–S70
28. Hoellwarth JS, Fourman MS, Crossett L, Goodman M, Siska P, Moloney GB, Tarkin IS (2018) Equivalent mortality and complication rates following periprosthetic distal femur fractures managed with either lateral locked plating or a distal femoral replacement. Injury 49:392–397
29. (1993) Consensus development conference: diagnosis, prophylaxis, and treatment of osteoporosis. Am J Med 94:646–650
30. Zioupos P, Kirchner HOK, Peterlik H (2020) Ageing bone fractures: the case of a ductile to brittle transition that shifts with age. Bone 131:115176