Published in final edited form as:

Curr Opin Rheumatol. 2018 July ; 30(4): 410–411. doi:10.1097/BOR.0000000000000518.

Fracture Prediction and Prevention: Will Newer Technologies Help?

Gregory Chang^a, Stephen Honig^b

^(a)Department of Radiology, Center for Biomedical Imaging, NYU Langone Medical Center

^(b)Division of Rheumatology, The Osteoporosis Center, NYU Langone Orthopedic Hospital, NYU Langone Medical Center

An often quoted statistic is that at age 50, a white woman has a about a 50% likelihood of sustaining a fracture during her lifetime including a 40% chance of experiencing a hip, spine or wrist fracture (1). Identifying patients at risk for such fractures remains challenging and has traditionally relied on the use of bone density testing to identify patients with a low bone mass. It was estimated that in 2010 almost 7% of women age 50–59 had a bone density diagnosis of osteoporosis (T score -2.5) and that the prevalence of osteoporosis reached 35% of the population aged 80 and above. Additionally, about 50% of all U.S. female residents have some degree of low bone mass (osteopenia) at age 50 and above (2). The risk of osteoporotic related fracture increases with age and with progressively lower T scores among individuals with osteoporosis. However many fractures occur among postmenopausal women with non-osteoporotic T scores. We and other groups have been evaluating new imaging techniques in the hope of identifying patients who are at increased fracture risk before they sustain the first fragility fracture.

Osteoporosis is defined as a disease of increased fracture risk due to low bone mass and microarchitectural deterioration of bone tissue (3). Dual-energy x-ray absorptiometry (DXA) measurement of areal bone mineral density (BMD) has high specificity in terms of detecting individuals with osteoporosis at increased risk for fracture (T-score < -2.5) (3). However, the majority of individuals who fracture do not meet DXA criterion for an osteoporosis diagnosis and therefore go undetected and untreated (4,5). The low sensitivity of DXA has motivated the development of other fracture risk assessment tools, such as FRAX (6), which computes a 10 year probability of hip or major osteoporotic fracture based on 11 clinical variables that are easily measured in an office visit. Femoral neck areal BMD can be included as a 12th variable. Among the criticisms of the FRAX algorithm is the lack of weighting for the number of prior fractures (and when they occurred relative to the present time) as well as not having an input variable for a history of fall(s).

While FRAX remains a critical tool for fracture prediction, there has been great interest in other approaches that may provide further insight into increased fracture risk by focusing on identifying differences in bone strength and bone microarchitecture among at risk subjects. These novel imaging methods noninvasively assess bone health in vivo while DXA only

provides an estimate of BMD in 2-dimensions and does not assess other metrics of bone health, such as its microarchitecture or mechanical properties. Many imaging approaches have been pursued, including advanced image analysis of DXA data (e.g., hip structural analysis), lumbar spine trabecular bone score (TBS), ultrasound (US), quantitative computed tomography (QCT), high-resolution peripheral quantitative computed tomography (HR-pQCT), and magnetic resonance imaging (MRI) (7–10).

Each novel imaging method has advantages and disadvantages. MRI can offer 3-D, high-resolution imaging without the administration of ionizing radiation, albeit at a higher cost than DXA. Images of bone microarchitecture in the distal extremities (wrist, ankle) and even the proximal femur can be obtained, and cross-sectional MRI studies of microarchitecture have shown the ability to discriminate fracture cases from controls and the ability to monitor longitudinal changes (11, 12). For example, two recent studies in the hip applied finite element analysis (FEA, to estimate bone mechanical properties) or volumetric topological analysis (VTA, to measure microarchitectural parameters) to high-resolution MR images of the proximal femur and demonstrated the ability of MRI to discriminate fracture cases from controls even when BMD could not (13, 14). The results suggest that MRI-based FEA or VTA deserve further study as potential methods to identify high risk fracture patients who currently go undetected by DXA.

Whether such advanced imaging methods provide added value to the existing well-established, low-cost methods of FRAX and DXA remains to be determined. Longitudinal fracture incidence studies and cost-effectiveness analyses are needed, especially given the higher price of CT and MRI compared to DXA. One recent cost-effectiveness analysis provided some evidence that the combination of 3-D virtual bone strength testing via FEA (even across a broad price range, up to \$1,000) and BMD testing was the most cost-effective societal osteoporosis screening strategy (as opposed to BMD or virtual bone strength testing alone) (15). For the workup of the risk of ischemic heart disease, there is a multi-tiered risk stratification approach using more basic testing (EKG, blood tests) initially followed by advanced testing (exercise treadmill, nuclear medicine, US, or even CT and MRI) that is specifically tailored to the patient. Perhaps one day the workup delineating the risk for fragility fractures and fracture prevention strategies will be similarly multi-faceted. In the interim, however, we are reminded that the need for initiating bone strengthening treatments is greatest among those with a recent fragility fracture who are at increased risk for subsequent fractures. Despite the imperative of this need, most patients with the greatest need for treatment are not receiving such it (16). While the focus on identifying patients at increased fracture risk is vital and the use of new technologies to facilitate such identification is important, we should not lose sight of the critical need to initiate treatment among those already identified as being at high fracture risk.

Acknowledgments

Financial support and sponsorship: GC is supported by the National Institute of Arthritis and Musculoskeletal and Skin Diseases (R01 AR066008, R01 AR070131)

References:

1. Cooper C, Melton LJ 3rd. Epidemiology of osteoporosis. *Trends Endocrinol Metab.* 1992; 3: 224–229 [PubMed: 18407104]
2. Wright NC, Looker AC, Saag KG, Delzell ES, Randall S et al. the recent prevalence of osteoporosis and low bone mass in the United States based on bone mineral density at the femoral neck or lumbar spine. *J Bone Miner Res* 2014; 29: 2520–2526 [PubMed: 24771492]
3. Kanis JA. Diagnosis of osteoporosis and assessment of fracture risk. *Lancet.* 2002;359(9321):1929–36. [PubMed: 12057569]
4. Wainwright SA, Marshall LM, Ensrud KE, Cauley JA, Black DM, Hillier TA, et al. Hip fracture in women without osteoporosis. *J Clin Endocrinol Metab.* 2005;90(5):2787–93. [PubMed: 15728213]
5. Siris ES, Chen YT, Abbott TA, Barrett-Connor E, Miller PD, Wehren LE, et al. Bone mineral density thresholds for pharmacological intervention to prevent fractures. *Arch Intern Med.* 2004;164(10):1108–12. [PubMed: 15159268]
6. Kanis JA, Johnell O, Oden A, Johansson H, McCloskey E. FRAX and the assessment of fracture probability in men and women from the UK. *Osteoporos Int.* 2008;19(4):385–97. [PubMed: 18292978]
7. Link TM. Osteoporosis imaging: state of the art and advanced imaging. *Radiology.* 2012;263(1):3–17. [PubMed: 22438439]
8. 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(3):518–30. [PubMed: 24443324]
9. Bonnick SL. HSA: beyond BMD with DXA. *Bone.* 2007;41(1 Suppl 1):S9–12. [PubMed: 17459802]
10. Cheung AM, Adachi JD, Hanley DA, Kendler DL, Davison KS, Josse R, et al. High-resolution peripheral quantitative computed tomography for the assessment of bone strength and structure: a review by the Canadian Bone Strength Working Group. *Curr Osteoporos Rep.* 2013;11(2):136–46. [PubMed: 23525967]
11. Chang G, Boone S, Martel D, Rajapakse CS, Hallyburton RS, Valko M, et al. MRI assessment of bone structure and microarchitecture. *J Magn Reson Imaging.* 2017;46(2):323–37. [PubMed: 28165650]
12. Wehrli FW. Structural and functional assessment of trabecular and cortical bone by micro magnetic resonance imaging. *J Magn Reson Imaging.* 2007;25(2):390–409. [PubMed: 17260403]
13. Chang G, Honig S, Brown R, Deniz CM, Egol KA, Babb JS, et al. Finite Element Analysis Applied to 3-T MR Imaging of Proximal Femur Microarchitecture: Lower Bone Strength in Patients with Fragility Fractures Compared with Control Subjects. *Radiology.* 2014;272(2):464–74. [PubMed: 24689884]
14. Chang G, Rajapakse CS, Chen C, Welbeck A, Egol K, Regatte RR, et al. 3T MRI of proximal femur microarchitecture can discriminate between subjects without and with fragility fracture who do not have osteoporotic proximal femur bone mineral density. *Radiology* In press.
15. Agten CA, Ramme AJ, Kang S, Honig S, Chang G. Cost-effectiveness of Virtual Bone Strength Testing in Osteoporosis Screening Programs for Postmenopausal Women in the United States. *Radiology.* 2017;285(2):506–17. [PubMed: 28613988]
16. Khosla S, Shane E. A crisis in the treatment of osteoporosis. *J Bone Miner Res* 2016;8: 1485–1487