



Osteoporosis Diagnosis and Assessment: What is in the Future?

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Osteoporosis is a chronic condition that causes bone fragility fractures and is a major public health issue worldwide [1]. According to the Scorecard for Osteoporosis in Europe (SCORE), the prevalence and burden of osteoporosis are expected to rise over the next 10 years, primarily as a result of population aging. According to the estimates, more than 30 million people in Europe and a comparable number of individuals in the United States suffer with osteoporosis [2]. The availability of the standard dual-energy X-ray absorptiometry (DXA), which has been adopted in the majority of western countries but is still underutilized in many other developing countries is strictly correlated with the prevalence of osteoporosis [3]. Osteoporosis is a societal burden brought on by both individual and environmental factors.

The World Health Organization (WHO) defined osteoporosis for epidemiological purposes as 'BMD less than -2.5 SD below the peak bone mass of young healthy adults [4]. Although the WHO definition is frequently used in routine clinical practice to make an osteoporosis diagnosis, it should be noted that it has number of drawbacks. The biggest drawback of basing diagnosis of osteoporosis only on BMD levels is the possibility of overlooking people who fracture with T-score above -2.5. Indeed, patients with osteopenia or even with normal T-score experience almost half of all fragility fractures [5]. In an order to avoid this mistake, we frequently incorporate clinical characteristics to BMD when determining an individual's fracture risk. A common approach, such as Fracture Risk Assessment Tool (FRAX) utilizes several clinical risk factors in an estimation of the absolute fracture risk over the time of the patient but do not capture all the determinants of fractures [6]. In 2001, the NIH further expanded the definition of osteoporosis by adding the 'bone strength' concept, which is mostly, but not entirely, dependent on BMD [7]. This is crucial in conditions like diabetes and glucocorticoid induced osteoporosis (GIOP), which decrease bone quality without decreasing bone quantity. There are some potential new imaging techniques that can aid in diagnosis and evaluation of the risk of fracture in those who have osteoporosis.

The trabecular bone score (TBS) is one of the most promising method for determining bone strength. It is calculated by using an analytical tool that processes the gray-level texture of normal DXA scans to estimate trabecular microarchitecture [8]. TBS can be easily implemented in most of the DXA instruments. Independent of clinical risk factors and femoral neck BMD, Leslie and colleagues revealed that the TBS was inversely correlated with fracture risk. It was also found to be significant predictor of fracture independently from FRAX [9]. The availability and price of software is a drawback.

Hip-axis length (HAL), hip-strength analysis (HSA), and finite element analysis (FEA) are other methodologies that, similarly to TBS that can be obtained from DXA analysis.

The hip-axis length (HAL) Which is defined as the length from the great trochanter and the pelvic brim, has been positively correlated with the risk of hip fracture [10]. Independent of other clinical and densitometric risk variables, the longer the HAL the greater the risk of fracture. The greater trochanter protrusion, which increases impact susceptibility in lateral falls, is most likely the mechanism underlying this increased risk. The benefit is that HAL can be easily determined from DXA images but the drawback is that it cannot be modified by therapy and is not endorsed by international society for fracture risk assessment.

The hip strength analysis (HSA) is an imaging post-processing software that was first developed in 1990 by Beck, *et al.* [11]. The HSA is derived from the analysis of the femoral neck cross-sectional area (CSA) and cross-sectional moments of inertia (CSMI). It estimates the cortical stability in buckling and represents an index of structural rigidity. Few small clinical studies have evaluated the HSA's prowess in assessing fracture risk. HSA can help in improving the prediction of hip fractures when combined with conventional BMD measurements [12]. It should be noted that HSA parameters are not significantly affected by anti-osteoporotic treatments and should be regarded as a nonmodifiable risk factor for fractures.

The finite element analysis (FEA) is another computerized method that estimates the microarchitectural geometry of the hip. FEA can be used to study the behavior of bone in relation to mechanical loading. Although FEA has mostly been used in computer tomography, it now available in DXA too, making this method more widely used. However, the International Society for Clinical Densitometry (ISCD) did not endorse their use in routine clinical practice as recent as 2015 despite the enthusiasm around these techniques. Large conclusive clinical trials are still lacking despite the recent advent of new imaging processing technologies and improved FEA simulation model prediction capabilities [13].

Radiofrequency echo graphic multi spectrometry (REMS) is a novel approach that uses ultrasound to analyze BMD [14]. A software program analyzes unprocessed, raw ultrasound pictures of the lumbar spine and femoral neck to produce BMD value that is DXA comparable. In one study, the correlation between the DXA and REMS T-score values and the ability to predict fractures was similar for both vertebral, hip and nonvertebral, non-hip fractures [15]. Additionally, REMS can calculate bone strength (fragility index), which is independent from BMD and has been proved to be an accurate fracture risk predictor. The European Society for Clinical and Economic Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal Diseases (ESCEO) has just approved REMS for use in clinical settings [16]. The benefit of this technology is that there is no risk of radiation exposure, it is a transportable apparatus with comparable sensitivity and specificity to DXA, however it is operator dependent.

High-resolution peripheral quantitative computed tomography (HRpQCT) is an alternative imaging technique that can provide both quantitative and qualitative information regarding the skeleton. Cortical thickness and FEA, two HRpQCT characteristics, have demonstrated their ability to accurately predict the fracture risk without the need of the FRAX score or a real BMD value as determined by DXA alone [17]. Additionally, significant developments in CT technology have decreased the exposure to ionizing radiation, making this method appealing for routinely evaluating both the quantity and quality of bone in individuals with osteoporosis. However, because HRpQCT is an expensive technology its usage in clinical practice might be limited.

Conclusion

Osteoporosis is a worldwide health problem and an economic burden to the society. It's a silent progressive disease affecting largely the women and goes unnoticed until they develop a fragility

fracture. The WHO recommended diagnostic tool of BMD measurement by DXA has its own limitations. The novel diagnostic imaging tools are very promising and can be useful in identifying at risk individuals suffering from osteoporosis with poor quality bones.

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