The diagnosis of osteoporosis

Osteoporosis is defined by the World Health Organization (WHO) as a systemic skeletal disease that is characterised by low bone mass and microarchitectural deterioration of bone tissue, with a consequent increase in bone fragility and susceptibility to fracture which usually involves the wrist, spine, hip, ribs, pelvis or humerus. In 1994, the WHO proposed a stratified definition of osteoporosis, which was updated in 2008, that encompassed the concepts of both low bone mass and fracture. According to this classification, there are four general categories: normal, low bone mass (osteopenia), osteoporosis and severe osteoporosis.

Currently, a diagnosis of osteoporosis is established based on evidence of (i) a fragility fracture or (ii) low bone mineral density (BMD) measured with central dual-energy X-ray absorptiometry (DXA). In its recently published guidelines on the diagnosis and management of osteoporosis, the National Osteoporosis Foundation of South Africa (NOFSA) made recommendations for the diagnosis of osteoporosis in postmenopausal females and males over the age of 50 years (based on the T-score), in premenopausal women and younger males (based on Z-scores), and in children (based on Z-scores and fracture profiles). In this edition of JEMDSA, Kruger et al propose cut-off values of peripheral BMD for the diagnosis of central osteoporosis in black postmenopausal South African women.

Whereas the WHO criteria have been useful in identifying postmenopausal women at risk of fracture, and also carry an acceptable specificity (±85%), we need to take cognisance of their limitations. The single most important limitation of the WHO criteria is lack of sensitivity. In fact, less than 50% of patients with a known osteoporotic fracture have a BMD value that is in the so-called osteoporosis range (T-score below -2.5). Furthermore, the WHO criteria are based on epidemiological data that are obtained from healthy Caucasian postmenopausal women, employing DXA of the axial (spine and hips) skeleton. Extrapolation of these criteria to other populations (younger individuals, males, black patients and children) assessed with different techniques (QUS and QCT) at different skeletal sites is scientifically unacceptable in confirming a diagnosis of osteoporosis. Therefore, this author cannot agree with Kruger et al that osteoporosis can be confirmed by employing peripheral DXA in black subjects. This does not imply that peripheral BMD measurements cannot be used to evaluate fracture risk in populations. This is particularly important in areas where no central DXA facilities are available (vide infra). The exclusively BMD-based diagnostic approach of the WHO classification also does not include extraskeletal risk factors, e.g. fall propensity, nor does it assess bone quality. Moreover, a low BMD may result from metabolic bone diseases other than osteoporosis, e.g. osteomalacia and primary hyperparathyroidism, which are treated differently to osteoporosis.

Treatment of osteoporosis with specific bone-active drugs should be initiated in those with confirmed osteoporosis, i.e. subjects with a typical osteoporosis fracture, or those with a BMD T-score ≤ -2.5. However, the difference between diagnostic criteria and interventional thresholds should be emphasised. Since most patients with osteoporotic fractures have BMD values which are not in the osteoporosis range, but in the low bone mass or osteopenia category of the WHO classification, it stands to reason that further methods to increase the sensitivity of fracture risk assessment need to be sought. One possible way to accomplish this would be to promote wider screening of individuals by employing BMD measurements. This is also endorsed in the article by Kruger et al who propose that peripheral DXA can be used to safely and economically exclude osteoporosis and therefore reduce the need for unnecessary, expensive DXA densitometry. However, screening, even using central DXA, has never been shown to be cost-effective. Similar to the guidelines that were published by the International Osteoporosis Foundation (IOF)/WHO and the American Society for Bone and Mineral Research/National Osteoporosis Foundation, NOFSA also recommends that BMD measurements should only be performed if a clinical indication exists. In this regard, it is important to note that age per se, > 65 years in women and > 70 years in men, constitutes an indication.

Alternatively, to improve sensitivity, the BMD threshold could be lowered to -2.0, for example. However, this would significantly decrease the specificity of the test. A better alternative to improve the gradient of risk would be to combine the BMD measurement with other risk factors. These could include the use of clinical risk factors, assessment of bone turnover (a BMD independent risk factor), other methods to measure bone strength (QUS) or the use of genetic markers. Whereas QUS holds much promise and the selective use of biomarkers of bone turnover, e.g. osteocalcin and deoxypyridinoline, has been shown to be helpful in problem cases, it is the use of clinical risk factors in combination with BMD that has revolutionised the management of osteoporosis in recent years.

Employing meta-analyses from 12 large prospective population studies (> 60 000 subjects), John Kanis and his team at the WHO have recently identified a number
of robust clinical risk factors that appear to predispose to fracture in most populations. These include an advanced age, previous fragility fracture, a family history of osteoporotic hip fracture, bone-toxic drugs like glucocorticoids, lifestyle factors, e.g., alcohol and smoking, excessive leaness [BMI < 19 kg/m²] and secondary osteoporoses.

Having identified the major clinical risk factors for the development of osteoporosis, the WHO team then proceeded to assess their relative clinical importance (weight and interactions) and, with and without the use of femoral BMD, compiled the FRAX® assessment model. The model output is the estimated 10-year probability of either a hip fracture alone or the major osteoporotic fractures (spine, hip, wrist and humerus) combined. This WHO assessment tool has been widely published® and is also freely available online (www.shef.ac.uk/FRAX) to all clinicians and healthcare professionals. The model does not signify an intervention threshold, but merely indicates a fracture probability. In order to determine an intervention threshold, a local cost-effective analysis, to estimate the level of fracture risk above which it is reasonable to consider treatment, must be performed.

However, the model is entirely calibrated to the population of interest, based on the incidence of osteoporosis, as well as mortality rates across a range of ages for men and women in that specific population. Given the outdated and incomplete local epidemiological data on hip fracture incidence and death rates in all populations in this country, the need for further study is clear before scientific use of the FRAX® tool will be possible. Currently, NOFSA is involved in a multicentre study to address this important issue. Furthermore, the need to establish normal reference data, especially for BMD in the different local ethnic populations, is as important. In this regard, the study by Kruger et al. is to be commended. The currently recommended central DXA T-score criteria of the WHO to define osteoporosis cannot be universally applied to BMD measurements of the peripheral skeleton. Moreover, these criteria are based on data obtained in Caucasian women and cannot be extrapolated to other populations, including those of black women. Whereas osteoporosis is generally regarded as being rare in black people, Kruger et al. documented a high prevalence of this disease by employing central DXA. Previous studies by Daniels et al.® Conradie et al.® and Chantler et al.® have emphasised the fact that while the incidence of osteoporosis in our white, Asian (from the Indian sub-continent) and mixed-race populations appears to be similar to that of developed countries (although no robust fracture data exist), its incidence in our black populations remains unclear. Like the USA, hip osteoporosis is less prevalent in blacks, although vertebral bone mass and possibly also vertebral fracture prevalence in black and white South Africans appear to be similar. As emphasised in the recent Middle East and Africa regional audit of the IOF, the need to assess the incidence of osteoporotic fractures in different South African populations has now become a priority. Only then, a sensible health economic strategy can be formulated to treat osteoporosis in this country.

Stephen Hough
Editor-in-chief: JEMDSA
Chairman: NOFSA

References