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Review Article

Osteoporosis: From concepts to T scores and now absolute fracture risk

Sanjeev Patel

Epsom & St. Helier University Hospitals NHS Trust, Wrythe Lane, Carshalton, Surrey, United Kingdom

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ABSTRACT

The definition of osteoporosis has always been challenging. Historically the clinical definition could only be based on the presence or occurrence of an osteoporotic fracture. However waiting for a fracture to occur before making a diagnosis has limitations, not least that high risk individuals cannot be identified for treatment prior to fracture. With the availability of bone density measurements, the definition moved to the use of T-scores. Whilst widely used, this approach has limitations that include low sensitivity and not taking into account other variables that influence bone strength and extra-skeletal risk factors. In view of the limitations of using T scores in isolation, there has been a move towards assessment of individualised risk that incorporates multiple risk factors (with or without bone density measurement) to help predict future fracture risk. This approach potentially allows identification and treatment of individuals at high risk of fracture, the condition that needs to be treated as opposed to treating low bone density. Indeed bone density (where measured) becomes one of the many risk factors without a threshold interpretation for any given value. Numerous tools are available that have varying sensitivity, specificity, utility, applicability to, and that have been validated for any given population. Of the available tools, the World Health Organisation Fracture Risk Assessment Tool (FRAX) calculator has been extensively studied. It is available more widely, with country specific utility with and without bone density measurements, which is important in regions with scarce access to bone densitometry. FRAX is the only tool available that is India specific.

1. Definition of osteoporosis

The definition of osteoporosis has always been challenging.

Historically the clinical definition could only be based on the presence or occurrence of an osteoporotic fracture.[1] This particularly applied to vertebral fractures, if they occurred without a history of trauma, and were most prevalent in post menopausal women as the spinal osteoporosis syndrome. However waiting for a fracture to occur before making a diagnosis has limitations, not least that high risk individuals cannot be identified for treatment prior to fracture. A conceptual definition of osteoporosis was proposed in a consensus statement in 1993[2] that put forward the following:

> *"osteoporosis is a systemic skeletal disease, characterised by low bone mass and microarchitectural deterioration of bone tissue with a consequent increase in bone fragility and susceptibility to fracture"*

E-mail address: sanjeev.patel@esth.nhs.uk.
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This statement recognised that the condition was not focal; bone fragility was secondary to adverse bone parameters and that individuals were at higher fracture risk. These concepts were expanded in 2000 in a report from the National Institutes of Health Consensus Statement,[3] which stated that:

> ''*Osteoporosis is defined as a skeletal disorder characterized by compromised bone strength predisposing to an increased risk of fracture. Bone strength reflects the integration of two main features: bone density and bone quality. Bone density is expressed as grams of mineral per area or volume and in any given individual is determined by peak bone mass and amount of bone loss. Bone quality refers to architecture, turnover, damage accumulation (e.g., microfractures) and mineralization. A fracture occurs when a failure-inducing force (e.g., trauma) is applied to osteoporotic bone. Thus, osteoporosis is a significant risk factor for fracture, and a distinction between risk factors that affect bone metabolism and risk factors for fracture must be made.*''

This broader definition further described the large number of bone parameters that determine bone strength and recognised that non-skeletal risk factors also contribute to fracture risk. At around the time of the first consensus statement on osteoporosis being developed, a study group convened by the World Health Organisation (WHO), defined osteoporosis based purely on bone density.[4] The study group classified bone density according to the standard deviation (SD) difference between the bone density of the tested individual compared to the mean of a young-adult reference population (T-score). A T-score that is 2.5 SD or more below the young-adult mean bone density was defined as osteoporosis. A T-score of 1–2.5 SD below the young-adult mean was termed osteopenia and normal bone density was defined as a T score within 1 SD of young-adult mean.

This approach had a number of issues. As bone density is a normally distributed variable, and there is a gradient of increasing fracture risk with decreasing bone density, these cut-offs were out of necessity arbitrary. There was no agreed recommendation on which skeletal site to use and it was not clear how to apply this diagnostic criterion to men, children, and across ethnic groups.

A further limitation of the T score definition is that bone alone has low sensitivity, so that the majority of osteoporotic (low trauma) fractures in a population will occur in individuals with bone density values above the osteoporosis threshold, typically in the osteopenic range (T-score of less than −1 and greater than −2.5 SD).[5] In part, this is because there are more individuals classified as being osteopenic in the normal population. Also bone density alone does not take into account other bone variables listed in the National Institutes for Health statement that influences bone strength and also does not take into account extra-skeletal risk factors.

Nonetheless for the first time an individual could have a diagnostic definition, which perhaps too quickly became an intervention threshold, even for younger individuals with relatively low fracture risk.

2. Fracture risk calculators

In view of the limitations of using T scores in isolation, there has been a move towards assessment of individualised risk that incorporates multiple risk factors (with or without bone density measurement) to help predict future fracture risk. This approach potentially allows identification and treatment of individuals at high risk of fracture, the condition that needs to be treated as opposed to treating low bone density. Indeed bone density (where measured) becomes one of the many risk factors without a threshold interpretation for any given value.

Numerous tools are available that have varying sensitivity, specificity, utility, applicability to, and that have been validated for any given population.[6] The aim of the tools also differs with some predicting probability of fracture and others designed to predict low bone density as a pre-bone measurement screening tool (although some have subsequently been validated with fracture as an outcome).

3. FRAX

Of the available tools, the WHO Fracture Risk Assessment Tool (FRAX) calculator (Fig. 1 and Table 1) has been extensively studied. It is available more widely, with country specific utility with and without bone density measurements, which is important in regions with scarce access to bone densitometry.[7] FRAX was derived by collating information on risk factors for fracture using the primary individual data from 12 prospectively studied population-based cohorts from Europe, North America, Australia and Japan. Baseline assessment documented clinical risk factors for fracture with approximately 75% having BMD measurements at the hip. Follow-up was approximately 250,000 patient-years in 60,000 men and women during which more than 5000 fractures were recorded. The final FRAX model calculates probability of fracture in men or women from age (40 to 90 years), using independent clinical risk factors and when available bone density (femoral neck preferably as a T-score). Unlike other fracture risk prediction tools, FRAX takes into account the interaction between these clinical risk factors and mortality. The performance of FRAX has been evaluated in independent cohorts from different geographical regions and further validation is ongoing in other studies. FRAX is aimed predominantly for the primary care and non-specialist setting, where clinical experience may be lacking to integrate risk factors for fracture based on clinical experience.

To calculate FRAX, clinicians or patients can freely use the web-based tool or download an app to their smartphones. Demographics are the patient's age, sex, weight (kg) and height (cm). The clinical risk factors are shown in Table 1 and Figure 1. Bone density is not needed, but if available, then the femoral neck measurement as a T score is preferred. This will in most situations improve the prediction accuracy of the results.

Whilst FRAX perhaps has more strengths than other approaches to calculate future fracture risk, it also has significant limitations. These currently include not allowing for a dose response to fracture risk with varying doses of glucocorticoids, alcohol intake and number of prior fractures