Osteoporosis Screening and Assessment of Fracture Risk

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Osteoporosis is a skeletal disease characterized by impaired bone strength and an increased risk of fragility fracture. Effective screening should be aimed at evaluating risk factors for osteoporosis with identification of individuals at risk, allowing for intervention prior to fragility fracture. This article presents an overview of the risk factors for fracture in men and women and the integration of these factors in various models, enabling an assessment of the 10-year fracture risk. Through effective screening, early identification, and early intervention with pharmacological therapy of osteoporosis, significant impact can be made on reducing fragility fracture incidence, thereby alleviating the economic and clinical costs to our health care system.

Key words: *osteoporosis, screening, risk factors, diagnosis, FRAX*

Introduction

The National Institutes of Health Consensus Development Panel has defined osteoporosis as "a disorder of the skeletal system characterized by weakened bone strength, which results in an increased risk of fracture."[1] Fragility fractures increase morbidity and mortality and result in a significant health care burden. Osteoporosis is clinically diagnosed by the presence of a fragility fracture. The densitometric diagnosis can be made, however, prior to the onset of the first fragility fracture, enabling early identification of osteoporosis and timely intervention.

Bone quality and bone quantity both impact bone strength.[1] Bone quantity is evaluated by assessment of bone mineral density (BMD). Bone mineral density can be measured by a number of different tools, the most valuable of which is dual energy x-ray absorptiometry (DXA). This technology uses the differential attenuation of high- and low-energy x-ray beams in quantifying calcium content in the region of interest being assessed. The Canadian guidelines that have been published by the Canadian Panel of the International Society of Clinical Densitometry provide recommendations for the appropriate use of DXA technology and identify the limitations as well as the value of this technology.[2]

Bone quality is impacted by multiple factors. These include the rate of bone turnover, the degree of bone mineralization, the quality of the collagen fibres, and the health and function of the osteoblasts, osteoclasts, and osteocytes. The presence of a fragility fracture confirms impaired skeletal strength. Following the diagnosis of osteoporosis either clinically by the presence of a fragility fracture or prior to the onset of a fracture by densitometric criteria, it is necessary to investigate the patient further and exclude secondary causes of osteoporosis. Factors affecting bone quality are also evaluated as well as other risk factors for fracture, enabling risk stratification and selection of the most appropriate management plan.

The relationship between bone density and fracture risk in untreated patients has been evaluated prospectively in a number of well-designed large studies. A meta-analysis of 11 prospective cohort studies has indicated that decreased BMD is associated with increased fracture risk.[3] The predictive power of BMD for hip fracture is actually similar to the predictive power of blood pressure for stroke and better than the predictive power of cholesterol for cardiovascular disease.[2]

The World Health Organization (WHO) has defined the densitometric diagnosis of osteoporosis as a bone density T score ≤–2.5 standard deviations from the healthy, young adult population as measured at the spine, hip, and distal one-third radius in postmenopausal women or men over 50.[4] Other risk factors impact fracture risk independent of BMD. These risk factors also need to be quantified and integrated into the fracture risk assessment in addition to BMD.

Recently, the WHO has developed the Fracture Risk Assessment Tool (FRAX) which, in addition to the clinical assessment and physician judgment, enables the assessment of fracture risk.[5] The FRAX tool has been developed by studying several prospective studies on population-based cohorts from Europe, North America, Asia, and Australia and examining the correlations of various risk factors and fracture events to ensure adequate risk assessment.[5] The FRAX tool includes an assessment of important clinical risk factors for fracture, namely body mass index, prior fracture history, parental hip fracture history, glucocorticoid use (the equivalent of ≥5 mg/d of prednisone for 3 months), rheumatoid arthritis status, smoking status, alcohol use, and other secondary causes of osteoporosis (Table 1).[6] Each factor is computed using a calculation tool (available on

the FRAX website) and enables determination of an individual's 10-year probability of a hip fracture or other osteoporotic fracture.[5]

Risk Factors for Women

Bone density varies with age. Throughout adolescence, bone accrual occurs with increases in BMD until the achievement of peak bone mass, which occurs in the late teens/early twenties. Bone loss takes place when the rate of bone resorption exceeds that of bone formation. In the case of white women, age-related bone loss begins in the mid-thirties at a rate of 0.5–1.0% per year.[2] After menopause, the rate of bone loss accelerates and may reach rates as high as 5% per year for the following 5 years before returning to the age-related rates of bone loss of approximately 1% per year. Postmenopausal bone loss results in rapid microarchitectural deterioration and increases the risk of fragility fracture as the trabecular structure deteriorates and the horizontal struts are lost. This contributes to placing postmenopausal women at the highest risk of developing osteoporosis.[2]

Race is also an important risk factor to consider for osteoporosis. Blacks achieve a 10% higher peak bone mass than do whites, and this is applicable to both genders.[2] Asians are also at an increased risk of fracture; however, their risk is not as high as whites.

Fragility fracture history is the most important risk factor to consider when screening for osteoporosis, and it is independent of BMD. In a systematic review by Klotzbuecher *et al.*, a prior fracture history at any site is an important risk factor for future fracture.[7] Women with a prior vertebral fracture have a fourfold greater risk of sustaining a subsequent vertebral fracture and a twofold increased risk of sustaining a hip fracture. This risk increases with the number of vertebral fractures sustained.[7] A meta-analysis conducted by Kanis *et al.* in 2004 describes a risk ratio of 1.86 for the development of a future fracture in individuals with prior fracture history in comparison to those without a fracture history.[8]

Table 1: World Health Organization's Factors for Fracture Risk Assessment

Patient age and sex
Body mass index
Prior fracture history
Parental hip fracture history
Glucocorticoid use (equivalent of ≥5 mg/d of prednisone for 3 months)
Rheumatoid arthritis status
Smoking status
Alcohol use
Other secondary causes of osteoporosis (e.g., untreated hypogonadism, inflammatory bowel disease, prolonged immobility, organ transplantation, type 1 diabetes, and thyroid disorders)

Source: Adapted from Kanis, et al., 2008.[6]

Table 2: Osteoporosis Risk Factors for Women

Age	Age-related bone loss begins in the mid-thirties and accelerates after menopause.
Race	White and Asian women are at an increased risk of fracture compared to Black women, who achieve higher peak bone mass.
Fragility fracture history	Women with a prior vertebral fracture have a fourfold greater risk of a subsequent vertebral fracture and a twofold greater risk of sustaining a hip fracture. Risk increases with the number of vertebral fractures sustained.
Secondary risk factors	Untreated hypogonadism, inflammatory bowel disease, diabetes, thyroid disease, and prolonged immobilization

Sources: Khan AA, et al., 2002[2]; Kanis JA, et al., 2008[6]; Klotzbuecher CM, et al., 2000[7]; Kanis JA, et al., 2004.[8]

Table 3: Osteoporosis Risk Factors for Men

Vertebral fracture history	Multiple vertebral fractures in men are associated with risk factors for osteoporosis and increase in age in a pattern similar to that seen in women.
Fragility fracture history	Especially vertebral compression fracture after age 40; men with previous fracture are 2.2 times more likely to have a future fracture.
Hypogonadism	Low estradiol levels have a stronger correlation with low BMD among men than does testosterone.

Sources: Klotzbuecher CM, et al., 2000[7]; Khan AA, et al., 2007[9]; Finkelstein JS, et al., 1989[10]; Amin S, et al., 2000.[11]

Table 4: Laboratory Tests to Exclude Secondary Causes of Osteoporosis

Initial Tests	Further Testing*
Blood count	Parathyroid hormone
Serum calcium	Serum 25-hydroxyvitamin D
Albumin	Serum immunoelectrophoresis
Liver transaminases	Celiac antibody testing (endomysial, tissue transglutaminase)
Serum creatinine and creatinine clearance	24-hour urine calcium
Alkaline phosphatase	24-hour urine-free cortisol
Thyroid-stimulating hormone	
Total testosterone (for men)	
Follicle-stimulating hormone, estradiol†	

*Based on initial results.
†To assess gonadal status in peri- and premenopausal women.
Source: Adapted from Khan AA et al., 2007.[9]

FRAX also takes into account several other secondary risk factors, including untreated hypogonadism, inflammatory bowel disease, diabetes, thyroid disease, and prolonged immobilization (Table 2).[6]

Risk Factors for Men

On average, men reach a peak bone mass that is approximately 10% higher than that of women. Rates of bone loss are lower among men, and men are spared the dramatic increases in bone turnover that accompany menopause. Additionally, with age men have enhanced periosteal bone formation and greater cross-sectional bone diameter, providing them a biomechanical advantage with respect to fracture risk in comparison to women.[9] However, osteoporosis does affect men. Fractures occur less often, however, and occur approximately 10 years later than in women. Cross-sectional studies have shown that vertebral deformities occur at similar rates in men and women.[9] It has been seen that multiple vertebral fractures in men are associated with risk factors for osteoporosis and increase in age in a pattern similar to that seen in women.[9] Multiple vertebral fractures in men are therefore likely to be caused by underlying osteoporosis, while single vertebral deformities are more likely to be associated with trauma. While the majority of hip fractures occur in women (around 73%), mortality and disability rates are much higher among men.[9]

As with women, the most important risk factor to consider for men is fragility fracture history, especially a vertebral compression fracture after age 40. The review by Klotzbuecher *et al.* notes that men who have sustained a previous fracture are 2.2 times more likely to experience a future fracture.[7]

Hypogonadism is associated with an increased risk of osteoporosis and fragility results.[10] Physicians often overlook the importance of estradiol levels in men, but low estradiol levels have a stronger correlation with low BMD than does testosterone.[11]

In evaluating fracture risk in men, it is important to also include other secondary risk factors and existing diseases associated with bone loss, as outlined in a recent review (Table 3).[9]

Key Points

- Risk stratification enables identification of the patient at high risk of fracture, enabling early intervention.
- Bone densitometry allows diagnosis of osteoporosis prior to the development of the first fragility fracture.
- Fragility fractures are a sign of impaired bone strength and are also a marker of increased fracture risk independent of BMD.
- Integration of clinical risk factors for fracture with the BMD results allows an accurate assessment of fracture risk. Osteoporosis Canada has developed guidelines for the assessment of absolute fracture risk based on BMD, age, previous fracture, and previous steroid use. Such guidelines are of greater value in assessing fracture risk than focusing on BMD alone as it is now recognized that fracture risk is determined by multiple factors in addition to BMD.
- Absolute fracture risk is also a useful patient education tool and should be incorporated in the assessment of skeletal health.

Case Example

The following case example illustrates the application of FRAX in assessing fracture risk.

Mrs. Smith is a 55-year-old Caucasian woman who experienced a fracture of the wrist at age 45 after falling on ice. Her mother had a hip fracture at the age of 70. Mrs. Smith also has rheumatoid arthritis and has been taking 5 mg/d of prednisone for the past 5 years. She is a smoker and has an average of two drinks of alcohol per day. Her physical examination is unremarkable. Her

weight is 50 kg and she has a height of 150 cm. Her T score at the femoral neck is –2.5.

Entering Mrs. Smith's risk factors into the FRAX calculation tool allows us to quantify her 10-year risk of a major osteoporotic fracture at 59% and her 10-year risk of hip fracture at 22%.[5] Clearly, this woman is at a greatly increased risk of future fracture, and aggressive management is warranted.

Following the confirmation of osteoporosis, a complete history and physical examination are necessary, with appropriate laboratory assessment with exclusion of secondary causes of osteoporosis (Table 4). Clinical judgment guides the degree of evaluation necessary for individual patients.

Conclusion

Osteoporotic fractures can be prevented. The key is to screen those at an increased risk of fracture and identify the presence of bone loss early. Then one can implement strategies focused on lifestyle changes and appropriate pharmacological intervention. Such strategies are of great value in preventing fracture and the associated morbidity and mortality. Advances in risk stratification have enabled us to target therapy to those with the greatest risk of fracture.

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