Current Orthopaedics (2008) **22**, 322—327

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journal homepage: www.elsevier.com/locate/cuor

Current ORTHOPAEDICS

MINI-SYMPOSIUM: OSTEOPOROSIS

(ii) Fracture risk assessment

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KEYWORDS
Osteoporosis;
Fragility fractures;
Bone mineral density;
Fracture risk assessment;
FRAX™

Summary
Osteoporotic fractures cause excess mortality, substantial morbidity and health and social service expenditure in older people. The risk of these fractures is determined by skeletal factors, including bone mineral density (BMD), bone turnover, architecture, bone size, and skeletal geometry, together with non-skeletal factors associated with falling. With the advent of treatments which decrease the incidence of fractures and the development of strategies for preventing falls, there is growing interest in identifying people at high risk of fragility fractures, in whom to target therapeutic intervention. The World Health Organization (WHO) has recently developed a Fracture Risk Assessment Tool (FRAX™). This uses clinical risk factors, including prior fracture after age of 50 years, parental hip fracture, current smoking, oral steroid therapy, alcohol intake >2 units/day and chronic conditions such as rheumatoid arthritis, with or without femoral neck BMDt, to estimate the ten year probability of hip and other major osteoporotic fractures.

Introduction

Osteoporosis has been defined as a skeletal disorder characterised by compromised bone strength, predisposing a person to an increased risk of fracture.[1] The incidence of these fragility fractures increases with advancing age, where they are a major cause of excess mortality, substantial morbidity and vast health and social service expenditure in older people. Effective treatments are now available for osteoporosis, which reduce the incidence of fragility fractures. As a result of this, and the development of strategies for preventing falls, there is growing interest in identifying people at high risk of fragility fractures in whom to target therapeutic intervention. This paper reviews the major risk factors for fragility fracture and the approach towards fracture risk assessment, before highlighting the development of the World Health Organization (WHO) Fracture Risk Assessment Tool (FRAX™). It also addresses the use of FRAX™ in clinical practice, including the selection of the most appropriate thresholds for therapeutic intervention.

Epidemiology of fragility fractures

The three major fragility fractures are those of the distal forearm, vertebra and hip, but fractures of the humerus, clavicle, pelvis and ribs are also common in osteoporosis.[2] The incidence of these fracture rises steeply with advancing age, such that that the majority of these fractures occur in people above the age of 65 years. The lifetime risk of fracture for a 50 year old woman in the UK is

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doi:10.1016/j.cuor.2008.10.007

53.2%, compared with 20.7% for a 50 year old man. The risk of individual symptomatic fractures in a 50 year old woman is 16.6% for the forearm, 3.1% for the vertebra and 11.4% for the hip, whereas the corresponding figures for a 50 year old man are 2.9%, 1.2% and 3.1%.[3] The overall risk of fractures is 2.3 fold higher in older people living in residential or nursing homes than in those living in the community, whereas hip fractures are 3.6 fold more common in institutionalised older people,[4] probably due to their lower bone mineral density (BMD) and higher incidence of falls.

The risk of fracture is determined by skeletal and non-skeletal risk factors. The skeletal risk factors include BMD, bone turnover, cortical and trabecular bone architecture, bone size, and skeletal geometry, whereas non-skeletal risk factors include postural instability and a propensity for falling.[2] Prospective studies from the USA, Australia and Europe show that the combination of low BMD and falls-related risk factors confers a greater risk of fracture than either one alone.[5,6,7] The risk of hip fractures is also increased by conditions predisposing to falls, such as strokes, Parkinsonism, dementia, vertigo, alcoholism and visual impairment.

Skeletal risk factors for fracture

A prospective study of older women in the USA showed that for each standard deviation decrease in femoral neck BMD, there was a 2.6 fold increase in age-adjusted risk of hip fracture.[8] Nevertheless, even after adjustment for BMD, fracture risk doubled for each decade increase in age, highlighting the importance of other risk factors for fracture. A meta-analysis of studies examining the relationship between BMD and fracture risk demonstrated a two to three-fold increase in fracture incidence for each standard deviation reduction in BMD, but the best estimate of fracture risk at any location was provided by BMD measurements at that site.[9] There is a similar relationship between BMD and fracture risk in men and women, but as men have higher BMD values, their absolute risk of facture is generally lower than women of the same age.[10]

There are a number of other skeletal factors which increase fracture independently of BMD. Prospective studies show that biochemical markers of bone turnover predict fracture risk, even after adjustment for BMD. When bone turnover is increased, the imbalance between bone resorption and new bone formation that occurs with advancing age is amplified, leading to increased bone loss. Furthermore, the accompanying increase in resorption cavities makes it more likely that perforation of individual trabeculae may occur, leading to disruption of the trabecular structure. The increase in bone resorption also leads to greater porosity of cortical bone. These changes in trabecular and cortical bone structure adversely affect the mechanical properties of bone, increasing the risk of fracture. Fracture risk is also influenced by skeletal size and geometry. Individuals with a larger skeleton are at lower risk of fracture, which accounts in part for the gender differences in fracture incidence. Femoral neck length is another determinant of fracture risk, with an increase in risk associated with a longer femoral neck. The degree of mineralization is also important, as vitamin D deficiency osteomalacia is associated with accumulation of unmineralised osteoid, which leads to skeletal weakness and increased fracture risk. Hypermineralisation of the skeleton is also associated with increased risk of fracture, as the bone becomes more brittle.

Non-skeletal risk factors for fracture

Postural instability increases the risk of falls and fractures in older people. There is an increase in postural sway with advancing age, which is generally greater in women than men. This may account in part for the gender differences in falls and fractures. A large prospective study from France showed an association between increased postural instability and the risk of hip fracture in older women. In individuals with increased body sway, any associated impairment in neuromuscular function may restrict the ability to correct for the wider excursions of postural change, leading to an increased risk of falls and fractures. Epidemiological studies also show a relationship between physical and mental frailty and an increased risk of fractures. Low body mass index (BMI) is associated with an increase in the risk of fracture. This may be due in part to lower BMD because of reduced mechanical loading of the skeleton. It may also increase the risk of hip fracture, because the lower soft tissue and muscle mass is less able to absorb the energy associated with a fall on to the greater trochanter.

Bone density throughout life

Bone density at any age and therefore the risk of fracture is determined by the peak bone mass, the age at which bone loss starts and the rate at which it proceeds. Genetic factors account for as much as 80% of the variance in peak bone mass. Other potential determinants of peak bone mass include exercise, dietary calcium, smoking, alcohol consumption and hormonal factors. Bone loss starts between the ages of 35 and 40 in both sexes, possibly related to impaired new bone formation, due to declining osteoblast function. The onset of bone loss is likely to be genetically determined, and the subsequent rate of bone loss may also be influenced by genetic factors. Recent studies suggest that a number of gene polymorphisms influence BMD and fracture risk.[11,12] The genes involved include those regulating RANKL, OPG and the oestrogen receptor gene. Although the individual effect of variation in these genes is relatively small, the combined impact of these is similar to other major risk factors for fracture.[11,12] Bone loss increases in the decade following the menopause in women, due to the increased bone resorption associated with the marked reduction in the circulating oestradiol concentration. Other causes of age-related bone loss include low body weight, smoking, excess alcohol consumption, physical inactivity, declining vitamin D concentration and secondary hyperparathyroidism. In addition to the factors influencing the attainment of peak bone mass and subsequent involutional bone loss, there are a number of conditions which may accelerate the development of osteoporosis. The most frequently encountered are oral steroid therapy, male hypogonadism, hyperthyroidism, myeloma, skeletal metastases and the use of anti-epileptic drugs.[2]