Assessment of Fracture Risk in Osteoporosis

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Abstract: *The study of risk factors for any disease help in understanding the pathogenesis and mechanisms of disease occurrence. Risk factors may also be used to predict individual who are risk with a view to targeting intervention or preventive measures, specially in patients of osteoporosis.*

PREDICTORS OF FRACTURE RISK

Osteoporosis is a common and disabling disorder; its incidence is increasing in most developing countries. The major **predictors** of **osteoporotic fracture risk** are bone mineral density (BMD), biochemical markers of bone turnover, quantitative ultrasound (QUS) and clinical risk factors.

BONE MINERAL DENSITY

Reduction in bone mass assessed using bone mineral densitometry, is an important determinant of future fracture risk. Site specific measurement show stronger gradients of risk for fracture than measurement made elsewhere. In a large meta-analysis looking at prediction of various fracture type using measurement made at the hip, wrist and spine being for hip BMD predicting hip fracture (table)[1].

Table: *Relative risk of fracture in women for every1 SD decrease in bone mineral density below the age adjusted mean.*

Site of measurement	Forearm Fractures	Hip fractures	Vertebral fractures	All fractures
Diatal	1.7(1.4-2.2)	1.8 (1.4-2.2)	1.7 (1.4-2.1)	1.4 (1.3-
Hip	1.4 (1.4-1.6)	2.6 (2.0-3.5)	1.8 (1.1-2.7)	1.6 (1.4-1.8)
Lumbar spine	1.5 (1.3-1.8)	2.3 (1.9-2.8)	2.3 (1.9-2.8)	1.5 (1.4-1.7)

Source:*Marshall et al 1996*

A normal BMD does not necessarily mean that a fracture will not occur and conversely a low BMD not necessarily mean a fracture will occur. In the Rotterdam study, for example, mole 44% of all non-vertebral fracture occurred in women with a T- score below -2.5[2,3].

BIOCHEMICAL MARKERS

Markers of bone formation include total alkaline phosphates, bone alkaline phosphates, osteocalcin and the procollagen properties of type 1 collagen. Markers of bone resumption include hydroxyproline, pyridine cross links and their associate peptides. Prospective studies have shown a fairly clear association between increased bone and fracture risk, an effect in independent of BMD[4,5,6].

ULTRASOUND MEASUREMENT

Skeletal status can be assessed using QUS method. The heel is the most widely used site and broadband ultrasound attenuation and of sound the most commonly assessed parameters. Data from several prospective that the unit change in these measures in linked with an increase fracture risk. In he EPIDOS study, the risk of hip fracture increase by a factor of 2.1 for each SD decrease in speed of sound in speed of sound[7].

CLINICAL RISK FACTORS

Age: Some of the age-related changes in fracture risk are related to a reduction in BMD; however, both age and decreasing BMD add independently to fracture risk. In the Rotterdam study, when comparing an 80- year old women with average bone density with a 60 year old women the RR for hip fracture was 13.6; age contributed only 7.1 to risk while the age-related decline in bone density contributed only 1.9 for men the result were broadly similar[8]. For given BMD level (female neck) the absolute 10 year risk of sustaining any osteoporosis. Fracture increase by a factor of two threefold between those in the younger in the oldest age groups[9].

Fracture history: The result from a large meta-analysis of published studies are presented in table 2[10] among women, for both wrist spine fracture the risk of future hip fracture is increase by a factor of approximately twofold. The strength of prediction is most marked for a prior and subsequent vertebral fracture. A pre-existing vertebral fracture in linked with number a fourfold increase risk of sustaining a future vertebral fracture, with the risk increase with number of baseline spine fracture[11,12].

In a meta-analysis of prospective population-based studies a previous fracture, osteoporosis fracture and hip fracture (RRs 1.85-1.86) in men and women[13]. Skeletal factors such as changes in micro-architecture with rapid bones loss following fracture/immobilization may also play a part.

Family history: In a meta-analysis of prospective population surveys a parental history of any fracture was associated with a modest but significantly risk of any fracture (RR 1.18) and hip fracture RR 1.49) in men and women[12].

Smoking: In meta-analysis of prospective population surveys current smoking was associated with an increase risk any fracture (RR1.84). Past cigarette smoking was linked with an increase risk of fracture, through the RRs were lower than for current smoking.

Low body mass index: Low weight or body mass index (BMI) is a well document risk factor for future hip and spine fracture white a high BMI appears protective[15,16]. Increasing BMI was associated with a lower risk of any fracture (RR 0.98)[17].

Steroid use: Glucocorticoids are an important determinant of bone loss and fracture[18]. The risk of fracture increase rapidly following the start of corticosteroid therapy (within 3-6 month) and decreases after therapy is stopped. Risk increase with the dose of steroids used[18,19]. There is evidence that for a given level of bone mass the risk of fracture is greater among those taking corticosteroids suggesting an effect that is independent of BMD[20].

Other clinical risk factors : Other clinical risk factors for osteoporosis have been identified including amenorrhea hypogonadism (men), poor visual, neuromuscular disorder, excessive alcohol consumption, immobilization, low dietary calcium intake and vitamin deficiency. Various disease states are linked also with an increase risk of osteoporosis, including rheumatoid arthritis. Inflammatory bowel disease, malabsorption syndrome, rimary hyperparathyroidism, hyperthyroidism and anorexia nervosa. Facture linked with an increase risk of falls are linked with an increase fracture risk

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particularly in the elderly these include impaired mobility, visual impairment and various drugs sedatives.

FRAX SCORE

The National Osteoporosis Foundation has released a 2008 a update to the NOF guidance published in 1999. The guideline, which are evidence based, provide recommendation for screening counseling and treatment of osteoporosis. The fracture risk assessment tool developed and evaluated by Prof. John A. Kanis and colleagues from the WHO Collaborating Centre for Metabolic Bone Disease at the University of Sheffield Medical School in the UK and is underpinned by the WHO Technical Report entitled. Assessment of Osteoporosis at Primary Health Care Level.

The World Health Organization has developed a new risk assessment tool - FRAX SCORE to identify individual at high risk of osteoporosis fracture. The current standard which bases treatment decisions largely on bone mineral density measurement and has proven to be specific, but not sensitive for the identification of patients at high risk of fracture. Because nearly 50% of postmenopausal women in the community over the age of 50 years who an osteoporosis fracture do not have osteoporotic defined by a BMD test, and because of the limited availability of BMD in many countries, clinical risk fracture factors were added to BMD to identify patients at high risk for osteoporotic fracture.

FRAX integrates the future osteoporotic fracture risk associated with clinical risk factors with that associated with femoral neck BMD, BMI may be used when BMD is unavailable. BMI and BMD would not be in the same individual. The incident rates of fracture are country specific and provide the clinical the 10 year probability of hip fracture and 10 year probability of major osteoporotic fracture (clinical vertebral, forearm, hip and shoulder). FRAX is currently being validated in additional longitudinal cohort databases. It is anticipated that in the latter half of 2009, the FRAX will be available as a software update for DXA equipment. The FRAX provides an estimated fracture risk in given individual but does not identify the level of fracture risk at which treatment should be stared (intervention). The intervention threshold decision is based on the willingness of a given country or region to pay for the treatments recommended.

LIMITATIONS

Like any other initial evaluation, limitation abound which includes:

1) The FRAX model is a model in progress. It does not include spinal BMD data or bone turnover markers, as bone marker data is not available from of the countries that contribution longitudinal cohorts to generate to the FRAX
2) FRAX does not include data on BMD measured at the peripheral skeletal sites.
3) Most patients were women. And data on ethnic groups are limited
4) The FRAX cannot be used in patients who have been treatment with osteoporosis medications since the probability of fracture may be overestimated.
5) Patients being assessed osteoporotic fracture risk may not be to make a treatment decision based on a 10 year probability of a fracture, although the one-year probability would be 10% of a ten-year probability.
6) The main limitation is that no large studies have been done on the Indian population till date to evaluate the bone mineral density and as such we are still dependable on the data generated by evaluation of the Caucasian race. BMD measurement alone fails to identify a high number of subjects who subsequently develop fracture. The addition of clinical risk factors may indeed be an improvement in risk factor assessment. While FRAX provide a method to evaluate fracture risk with and without BMD to use for global health, understanding exactly what level of fracture risk is appropriate for therapeutic intervention probably requires additional research.

The tool, previously available for China. France, Italy, Japan, Spain, Sweden, Turkey, UK, and the USA in now extended for use in Austria, Germany and Switzerland. It is expected that FRAX will be available for several other countries before the end of the year. In their most sophisticated form, the FRAX tool is computer-driven and is available on website http//www.shef.ac,uk/FRAX/

CONCLUSION

The diagnosis of osteoporosis is currently based on assessments of BMD. These are however, additional factors that influence fragility and fracture risk that are not captured by BMD. The development and application of such assessment tools in clinical practice should help reduce the morbidity linked with the disease.

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