Clinical usefulness of risk factors for osteoporosis

Osteoporosis is a systemic skeletal disease characterised by loss of bone mass and microarchitectural integrity that lead to increased bone fragility and risk of fracture.1 Its natural history is one of slow, progressive bone loss that often remains asymptomatic and undiagnosed for many years. Only when a substantial amount of bone has been lost do the characteristic low trauma fractures occur. Because osteoporotic fractures are associated with considerable morbidity, mortality, and cost,2 there is a need for methods of identifying individuals at risk earlier in the disease process, in whom preventative measures might be effective.

Epidemiological studies have identified a wide range of population risk factors for low bone mass and osteoporotic fracture. These risk factors may relate to low peak bone mass, subsequent bone loss, or determinants of fracture independent of bone mineral density (BMD). Risk factors for low peak bone mass include low body mass index, low dietary calcium intake,2 physical inactivity, and smoking.4 Those associated with increased bone loss include many of those for low peak bone mass (but to varying degrees) with, in addition, corticosteroid drug treatment,5 previous low trauma fracture,5 7 years elapsed since the menopause,8 and tooth loss.9 Risk factors for osteoporotic fracture independent of BMD may relate to poor bone quality or biomechanical determinants, for example a history of previous fracture10 11 or increased hip axis length,12 or to an increased risk of falling, for example poor visual acuity, neuromuscular impairment, lower limb weakness, or long acting psychotropic drug treatment.13

The study of epidemiological risk factors for chronic diseases such as osteoporosis has several uses—first to provide insight into the aetiology, second to point the way towards population based preventative strategies (in this context, measures such as increasing physical activity and dietary calcium intake), and third to guide the clinical management of individual patients. In the case of osteoporosis, this third application remains controversial,14 15 and it is this that we shall discuss in the remainder of this article. The application of risk factors may prove to be of value through their modification in order to reduce subsequent fracture incidence, their incorporation into guidelines for clinical decision making, and their use to select for further investigation those with a high probability of low BMD.

A number of risk factors for osteoporosis are potentially modifiable, and can be used to target specific areas for lifestyle advice.16 These include smoking, high alcohol consumption, physical inactivity, low dietary calcium and vitamin D intake,17 18 the excessive use of drugs known to reduce BMD such as corticosteroids or thyrroxine, and factors associated with an increased risk of falls.19 20 However, it is important to distinguish between those modifications which have been shown only to increase BMD, such as weight bearing exercise,21 and those which reduce fracture risk, such as supplementation of dietary calcium and vitamin D intake, which has been shown to reduce the rate of hip fracture in elderly residents of nursing homes by 23–43%,17 18 and the use of external hip protectors to reduce the effect of falls, which was found to halve the risk of hip fracture in a similar nursing home population.20

There is now evidence that a number of factors are associated with an increased risk of osteoporotic fracture independent of BMD, and that these risks may be additive.13 They might be particularly useful in making decisions as to whether preventative treatment might be indicated in patients who have an intermediate BMD. This is particularly true of factors such as a history of previous low trauma fractures, which is associated with an approximate doubling of fracture risk after correction for BMD.10 11 22 However, the most appropriate method for incorporating these factors into treatment regimens is as yet unclear, and their use remains largely hypothetical.

There is a particular need to identify women during the perimenopausal or early postmenopausal period who are at risk of later osteoporotic fracture so that preventative therapy with hormone replacement or bisphosphonates can be selectively targeted. Currently, the best available predictor is bone mineral densitometry, by dual energy x ray absorptiometry (DXA), which is extremely accurate, precise, and closely related to fracture risk.23 However, this technique is expensive, time consuming, and of limited availability. It is, therefore, necessary to target for further investigation by DXA only those women at greatest risk of osteoporosis. Several attempts have been made to design predictive models based on lifestyle risk factors in order to identify such women,8 24–28 but unfortunately these have all met with only limited success. The proportion of the variation in BMD predicted by lifestyle factors ranges from 17–26%8 24–26 at the femoral neck, to 18–43% at the lumbar spine, and 37–47% at the radius (table). This poor predictive capability would not necessarily present a major problem if, despite a poor correlation with absolute BMD, these models could indicate reliably whether individuals had a lower or higher value than normal. Unfortunately, this has not proved to be the case, and though the presence of multiple risk factors is associated with a substantially greater risk that could justify further investigation, their absence does not exclude osteoporosis.

The weakness of these predictive models may in part reflect that a considerable proportion of an individual’s BMD is genetically determined,29 and studies of heritability have suggested that as much as 70% of the variation in BMD in younger women may be of genetic origin.30 A simple way of incorporating this genetic component into predictive models would be to include a family history of osteoporosis or low trauma fracture. Unfortunately, this simple measure has not been found to correlate well with the presence of a low BMD in perimenopausal women.24–27 Much recent research has been devoted to identifying reliable markers of the genetic predisposition to osteoporosis, but unfortunately the results of these studies have been conflicting.31–34

Which particular risk factors are most useful as predictors of BMD remains the subject of considerable debate as a result of conflicting evidence from different studies. This may be attributable to differences in study design and subject selection. Whilst almost all agree that previous low

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*Predictive value of risk factor models for bone mineral density in early postmenopausal women*

<table>
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<th>Source</th>
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<th>Lumbar spine (%)</th>
<th>Femoral neck (%)</th>
<th>Radius (%)</th>
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trauma fracture, low body mass index, and increasing age are associated with lower BMD, the significance of gynecological risk factors, nutritional deficiency, and family history of osteoporosis or low trauma fracture are more found to be negatively associated with osteoporosis. This protective effect is probably related to the fact that, though osteoporotic vertebral fracture is a cause of back pain, this symptom is more commonly the result of spondylotic change or degenerative disc disease, which coexist frequently with osteoporosis.

Although numerous epidemiological risk factors for osteoporosis have been described, their application to individual patients remains controversial. If appropriate circumstances can be identified, they may yet prove to be useful, but they cannot at present replace bone densitometry as the best method for assessing fracture risk. The bad news is that the use of combinations of risk factors to decide who should be investigated by DXA is currently impractical, though this may improve with further study. In the absence of further data, those risk factors proposed by the Advisory Group on Osteoporosis are the best currently available.

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