

Principles of Bone and Joint Disease Control Programs — Osteoporosis

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ABSTRACT. During the past decade osteoporosis has emerged as a major public health problem. In societies with aging populations, an increasing number of persons are at risk of fracture, the most detrimental outcome of osteoporosis. Osteoporosis was initially identified as a problem of westernized countries, but a rising number of fractures are occurring in Asia and South America, and the global estimates show steep increases in these regions. Over the age of 70 years, only 31–36% of people are estimated to have normal bone mass. The lifetime risk for hip fracture for 50-year-old women is 18 to 25% and the risk for men 6 to 7%. Hip fractures affect the most aged, and are a contributing factor to death, with up to 20% of patients having died within the first year. Rehabilitation is needed, but only 30% regain pre-fracture function. The lifetime risk of vertebral fracture has been estimated to be 15.4% after age 45 years, but this most likely largely underestimates the true risk. The demand on the health care system is therefore increasing, as are costs for society. Prevention of osteoporosis and fracture must be considered particularly for the elderly at highest risk. Awareness is needed at all levels, including decision making bodies, in order to raise the priority of, and effectively implement, strategies to reduce the number of persons suffering. Interventions for prevention of fractures must be cost-effective; therefore strategies are needed to identify those who will benefit most from more costly secondary measures. (J Rheumatol 2003;30 Suppl 67:21–25)

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OSTEOPOROSIS

FRACTURE

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OSTEOPOROSIS — A PUBLIC HEALTH PROBLEM

Osteoporosis has become a major public health concern, not only in Western Europe and North America, but globally. A rising number of fractures are occurring in Asia and South America, and the global estimate shows a steep increase in these regions, not only related to the demographic shift towards elderly populations. Osteoporosis, i.e., low bone mass, is a silent condition with microarchitectural deterioration of the bone structure leading to decreased bone strength. The clinical consequence of osteoporosis is fracture; hip fracture, forearm fracture, and vertebral fractures are the most common. The risk of osteoporosis and fracture increases with age. Within the European population the number of persons above age 65 years is expected to increase to above 20% within the next 15 years. An even greater relative percentage of elderly is expected in Japan, and a similar increase will occur in many other Asian countries, while in developing countries, particularly in Africa where life expectancy is low, other problems are of greater concern.

Fracture

Fracture is the clinical endpoint of osteoporosis. Fragility

fractures are related to low bone density but also to numerous other risk factors, one of the most important of which is a tendency to fall. It is estimated that 1 in 3 women and 1 in 6 men will have a fracture at some point during their lifetime¹. The lifetime risk for specific fractures such as shoulder, forearm, and spine in women from the age of 45 years is estimated at 13.3%, 21.5%, and 15.4%, while the estimated lifetime risk for men at the age of 45 years is 4.4%, 5.2%, and 8.6%². This study includes only vertebral fractures that are clinically significant, and the number of vertebral fractures not coming to medical attention has been estimated at an equal number. Fractures of the appendicular skeleton such as the forearm fracture, proximal humeral fracture, hip fracture, or ankle fracture also require orthopedic consultation and surgery, and therefore incur larger costs. The estimated one-year cost for a hip fracture is US\$ 15,000³. Vertebral fractures and pelvic fractures are most often conservatively treated and therefore less costly to society, but nevertheless inflict significant pain and descending impaired functioning on the individual. In general, the disability and pain resulting from osteoporotic fractures have detrimental effects on the health status of the elderly and often require extended hospitalization, rehabilitation, and nursing home care. Osteoporotic fractures also inflict an enormous burden on society in terms of costs.

Diagnosis

Osteoporosis is a multifactorial condition and a number of risk factors have been identified, of which bone mineral

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density (BMD) or bone mass is the strongest predictor of fracture. With the availability of high precision bone densitometers, the World Health Organization has established criteria for diagnosing osteoporosis. The diagnostic score (T-score) is related to bone mass in young healthy women. Bone mass above -1 SD (standard deviation) is normal, BMD between -1 and -2.5 SD is assigned to osteopenia, while below -2 SD is the diagnostic criterion for osteoporosis (T-score).

BMD is preferably measured by dual energy X-ray absorptiometry (DXA). It is estimated that BMD accounts for 75–90% of the variance of bone strength⁴. For each decrease of 1 SD in BMD at the proximal femur or lumbar spine there is a 2- to 3-fold increase in fracture risk at the measured site⁵. BMD assessed by DXA technique can be measured at the following sites: hip, spine, forearm, and heel. Measurement of the total hip is regarded as most reliable since degenerative changes of the lumbar spine may affect spine measurement, especially with advancing age. The precision of the measurement is between 0.5 and 2%. DXA measurement of the heel is not validated in fracture studies.

Bone mass measured by ultrasound uses a different technique and is also estimated to provide a measure of bone quality. Heel ultrasound is most commonly used and is of predictive value for hip fracture. Ultrasound has, however, not been evaluated for monitoring treatment. Ultrasound of the finger may not be a useful tool in the elderly because of low discriminative ability⁶.

Several serum and urine biochemical markers of bone turnover have been developed. Bone markers, in particular high levels of resorption markers, may indicate progress of bone loss and add an independent predictive value to fracture risk⁷.

Before the age of 50, less than 8% have osteoporosis, while from the age of 70 only between 16 and 28% have normal BMD (Figure 1).

Risk Factors for Osteoporosis and Fracture

The pathogenesis of most osteoporotic fractures depends on factors related to the risk of falling, the impact of the fall, and bone strength.

Bone strength is related to bone mass, bone structure, and bone quality; at present only bone mass can be accurately determined. Through population studies risk factors for development of low bone mass have been identified. In addition to ageing and female sex they include: low body weight, weight loss, physical inactivity, glucocorticoid steroid therapy, reduced lifetime estrogen exposure, and low calcium intake⁸. Osteoporosis may also develop as a secondary condition to, e.g., hypoparathyroidism, hyperthyroidism, anorexia nervosa, gastrectomy, pernicious anemia, and rheumatoid arthritis. The risk factors for osteoporosis may also be divided into nonmodifiable risk factors or potential modifiable risk factors and some of these are listed in Table 1.

Osteoporosis as in low BMD is a major risk factor for fracture. Other major factors are related to falls: the impact of the fall and the frequency of falling. The risk factors for falls can be divided into intrinsic or extrinsic factors. Among the intrinsic factors, poor coordination and poor balance are most important. However, they may in turn be related to a general deterioration in health status, with concomitant conditions leading to multiple drug therapy. This decrease in the neuromuscular function may also include impairment of vision. The extrinsic factors are related to the environment and are dependent on geographic and socioeconomic circumstances, but may include poor indoor lighting, obstacles such as rugs or stairs, weather conditions, and uneven and slippery surfaces. The best predictor of falls is a fall in the previous year; therefore fall hazards need to be identified⁹.

Fracture risk assessment relies on relative risk (RR). Therefore, even if all factors above are associated with an increased risk, they cannot be used with certainty to predict

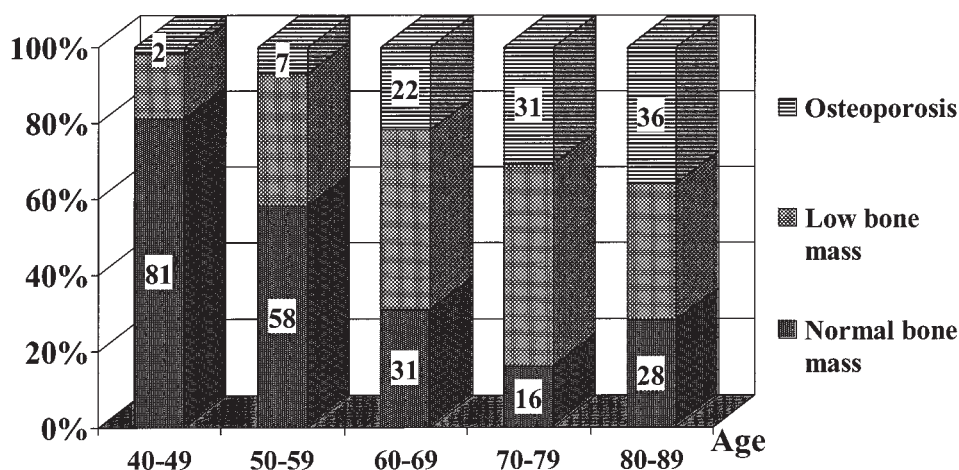


Figure 1. Percentage of women with normal bone mass, low bone mass, and osteoporosis of the hip in the Swedish population (Measurement of bone density, the Swedish Council on Technology, Assessment in Health Care. SBU report 127, 1995).

if a person will fracture or not. Nevertheless, a woman presenting with a previous fracture, bone mass in the osteoporotic range, and multiple falls during the previous year has a high risk for future fractures.

Treatment and Prevention

The main expected outcome of treatment and prevention of osteoporosis is a reduction in the number of fractures, while change in the bone mass is to be regarded as a surrogate measure. The difficulty lies in identifying those who will benefit most from the various interventions. From a societal point of view, primary prevention should be targeted at the population and the measures should be inexpensive and preferably carry additional benefits. However, it is also possible to target the population at risk for prevention strategies. In osteoporosis the fracture risk is low in younger individuals, while it increases with ageing (Figure 2). The message therefore has to be appropriate for the perceived risk within the segment of the population towards which the message is aimed.

Osteoporosis and fracture increase with age, beginning around age 50 years but with a steep increase occurring after age 75, with a mean age of 80 in hip fracture patients. In the general perspective a 50-year-old woman is clearly different from a 75- or 80-year-old woman with regard to physical capacity and general health status. Preventive measures aimed at the population must contain an age-adjusted approach where some basic measures such as adequate calcium vitamin D intake, refraining from smoking, and physical activity are nonspecific and applicable to all ages (Figure 2). In the elderly both intrinsic and extrinsic risk factors for falls become increasingly important. Preventive measures in the elderly therefore include balance and coordination training, appropriate treatment for other medical conditions, and minimizing external hazards causing falls. In children and young adults adequate nutritional intake including calcium and avoidance of early adaptation to a sedentary lifestyle by physical education should have favorable longterm effects by increasing peak bone mass.

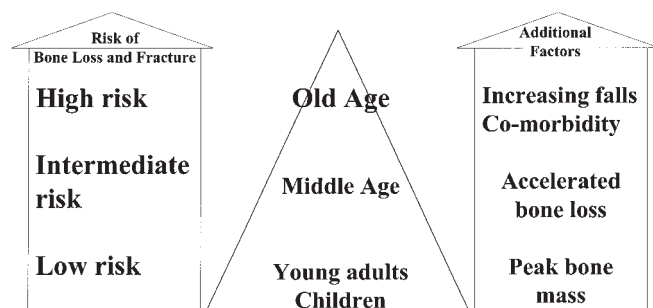


Figure 2. A model of risk increase for bone loss and fracture in relation to age, the dominant risk factor for fracture. The additional factors are expandable to described risk factors.

Pharmacological treatment. Pharmacological treatment to target those at highest risk of fracture. At present, osteoporosis remains undiagnosed and untreated also in those at highest risk, i.e., persons with previous fractures. Effective treatment, increasing bone mass and decreasing fracture rate, is available, although the antifracture effect is evident only in those at highest risk. The pharmacological agents available primarily decrease bone resorption, leading to a secondary gain in bone mass, while novel therapies may also increase bone formation.

Calcium is the basic building block of bone and is necessary for bone mineralization. Adequate calcium intake is necessary; a recent Cochrane review estimated the antifracture effect to RR 0.77 (99% CI 0.54–1.09) for vertebral fractures and 0.86 (0.95 CI 0.43–1.72) for nonvertebral fractures; however, results were nonsignificant because of too small a sample size¹⁰. Vitamin D is a requisite for efficient calcium uptake. Addition of vitamin D to calcium has an additive effect and also significantly reduces hip and nonvertebral fractures in the very elderly after 3 years of treatment^{11,12}.

Bisphosphonates directly act on bone by binding to hydroxyapatite and inhibiting osteoclasts. Alendronate, a second generation bisphosphonate, was the first bisphosphonate for which a clear antifracture effect was seen in large, randomized, controlled trials. Three major trials have shown a reduction in vertebral deformities of about 50% and prevention of nonvertebral fractures has been demonstrated as well. The findings of the studies imply that treatment with alendronate is most efficient in reducing fractures in those at highest risk of new fractures either by having a previous fracture or from bone density confirming osteoporosis¹³. Alendronate also appears to be effective in men with osteoporosis, with a decrease in the incidence of vertebral deformities after 2 years of treatment and a corresponding increase in bone mass¹⁴. Bone density increases at all sites during alendronate treatment. When compared with placebo the mean increase over 3 years is about 6% in the lumbar spine, 4–4.5% in the femoral neck, and 4.5–5% in the total hip measure. The recently available 70 mg once weekly dosage regimen shows an increase in bone mass similar to daily dosing. The antifracture effect is assumed to be consistent with the reduction seen in earlier studies¹⁵.

Risedronate is a third-generation bisphosphonate with a higher potency. In randomized controlled studies vertebral fractures were reduced by 41% and nonvertebral fractures by 39% for up to 3 years¹⁶. Risedronate also has an effect on hip fracture incidence, but this is evident only in women with low bone density and not in elderly women where treatment was based on risk factors alone. The effect on bone density is similar to that of alendronate, producing a 4–6% increase in spinal and femoral bone mass after 3 years of treatment.

Estrogen replacement. In women, bone loss begins after

estrogen withdrawal at menopause. Estrogen plays an important role in the regulation of bone metabolism, and it is therefore logical to use estrogen substitution to maintain bone mass. Unfortunately, the effect on fracture by estrogen replacement therapy has not been conclusively studied in prospective randomized controlled trials. Nevertheless, a recent metaanalysis identifying 22 studies with data on fractures suggests an overall reduction in nonvertebral fractures in women below the age of 60 years (RR 0.67; 95% CI 0.46–0.98) after at least 12 months of hormone replacement therapy (HRT)¹⁷. Numerous studies have indicated beneficial effects on bone mass, with an increase of about 2–4% in spinal bone mass up to 3 years, but with a lesser effect on hip bone mass. A major concern with HRT treatment is the risk of breast cancer. A risk increase equal to a 2.3% increase of breast cancer with each year of HRT treatment indicates that the duration of HRT should stay within 5–10 years or the risk may outweigh the benefits¹⁸.

Raloxifene is a selective estrogen receptor modulator conferring beneficial effects on bone. Raloxifene reduces vertebral fractures by about 30% over 3 years¹⁹. No effect was seen on nonvertebral fractures. In contrast to estrogen treatment the number of new breast cancer cases was lower in the group of patients treated with raloxifene, indicating an additional beneficial effect²⁰.

Parathyroid hormone (PTH) has a dual effect on bone. When given continuously, the resorptive effect predominates, similar to that seen in primary or secondary hyperparathyroidism. The anabolic effect on bone is seen with intermittent dosing. The primary effect of PTH is on trabecular bone and therefore the most pronounced effect is seen in spinal bone density²¹. In clinical studies of postmenopausal women with previous vertebral fractures recombinant human PTH reduced vertebral fractures by 65–69% (99% CI 0.22–0.55 and 0.19–0.50) over 21 months²². The availability of an anabolic agent such as PTH provides an additional treatment option for severe cases of osteoporosis when other agents give insufficient results or when side effects prohibit their use.

Increasing knowledge of mechanisms regulating bone metabolism provides potential sources for new therapeutic agents including blockage of cytokine activity by anti-tumor necrosis factor- α or anti-interleukin 1 (IL-1) or anti-IL-6 by factors affecting osteoclast attachment such as RANKL or osteoprotegerin. Another agent, strontium ranelate, may also have an anabolic effect on bone and therefore be of potential use²³.

Fracture treatment and rehabilitation. In patients with established osteoporosis the aim is to reduce pain and disability caused by fracture. A primary goal is to limit the impairment related to the structural damage, i.e., the fracture, regardless of fracture type. Adequate fracture treatment aims to restore anatomical continuity, the basic requirement if function is to be regained or loss of function minimized.

In addition, adequate fracture treatment diminishes fracture-associated pain. Fracture treatment can be either conservative, with plaster casts or braces, or surgical. For certain fractures, such as vertebral or pelvic fractures, fracture treatment will focus on pain control and mobilization. Good immediate fracture care, including early involvement of physical and occupational therapy, can diminish functional limitations and maintain activities of daily living. It will also allow for a fracture patient's continued participation in family life and in society. Continued rehabilitation and the outcome of rehabilitation are dependent on collaboration between the individual and society. The ability of the individual is determined by factors such as general health status, frailty, mental capacity, and age, while society contributes social and home assistance and adaptation services. Society also has the responsibility to make adjustments in the external environment, diminishing the risk of falls.

CONCLUSION

Osteoporosis is a general health problem, and the number of fragility fractures is expected to increase as a result of demographic changes, with increasing numbers of elderly and very elderly. Fractures cause significant morbidity and may lead to longterm disability and limitation of function, which in turn decrease quality of life. General preventive measures include: regular physical activity, adequate supplies of calcium and vitamin D, smoking cessation, and removal of fall hazards. Individuals at risk of osteoporosis can be identified through risk assessment and should have access to diagnostic bone mass measurements. Persons at high risk, with low bone mass, previous fracture, and with a tendency to fall, should be evaluated for pharmacological treatment. Pharmacological agents such as bisphosphonate, raloxifene, and PTH reduce fracture risk by 30 to 50%. In those with fracture it is essential that adequate fracture treatment is available in order to limit the functional impairment from structural deficiencies. A multidisciplinary approach is necessary for patient rehabilitation to realize the best functional and social outcome (Table 3).

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