The bone clinic

Men and osteoporosis

BACKGROUND While strict criteria have been developed for defining osteoporosis in women (bone mineral density measurements more than 2.5 standard deviations below the mean for young adult normal women, ie. t-score value <-2.5), there still remains a controversy regarding the definition in men. Spinal fractures occur in 5% and hip fractures in 6% of men older than 50 years. There are significant differences between men and women with respect to the pathogenesis of osteoporosis, underlying medical conditions and postfracture sequelae.

OBJECTIVE To provide an overview of the pathogenesis, diagnosis and prevention of osteoporosis in men.

DISCUSSION Osteoporosis is increasingly recognised. Data from the Dubbo Osteoporosis Epidemiology Study suggests that 30% of men in Australia aged over 60 years will suffer from an osteoporotic fracture. It is estimated that 30–60% of men presenting with spinal fractures will have another illness contributing to their bone loss. Osteoporotic fractures in men are associated with higher morbidity and mortality than in women. Lifestyle changes together with daily calcium supplementation should be implemented and vitamin D_3 should be considered in men with osteopenia.

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Osteoporosis is increasingly recognised in men.[1-8] It is estimated that 19% of men older than 50 years will have osteoporosis. Spinal fractures occur in 5% of men (compared to 16% of women) and hip fractures in 6% of men (compared to 18% of women) older than 50 years.[7] Data from the Dubbo Osteoporosis Epidemiology Study suggests that 30% of men in Australia aged over 60 years will suffer from an osteoporotic fracture.[1]

Today the life expectancy for men has increased to a mean age of 76.8 years. With men now living longer, they can be expected to develop multiple coexisting illnesses contributing to bone loss, and an increased likelihood of falling and fragility fractures.[3,9,10] It is estimated that 30–60% of men presenting with spinal fractures have another illness contributing to their bone disease.[2,4-6] The presence of a prevalent spinal fracture increases the risk of future spinal fractures by as much as 10–25 times, depending on the subject's age and the presence of osteoporosis as defined by bone mineral density.[11]

The impact of osteoporosis on individual men and the community is dramatic. The morbidity and mortality after hip fracture is higher in men than in women with 20.7% of men compared to 7.5% of women over 75 years dying after a hip fracture.[7] Mortality in men five years after hip or spinal fracture is about 20% in excess of that expected.[7] The physical functioning significantly deteriorates in elderly men after hip fracture, with one in five requiring a higher level of long term care. The postfracture outcome and prognosis in men appears to be significantly influenced by their pre-existing medical illnesses (comorbidities).[3,9] In Australia in 1995, the financial burden attributed to hip fracture alone in men was $110 million. This estimate did not include the costs associated with loss of quality of life.[12]

Table 1. Factors associated with increased risk of osteoporosis

- Family history
- Medical conditions (*Table 2*)
- Low calcium intake
- Low bodyweight
- Delayed puberty
- Immobilisation
- Lifestyle factors including smoking, high alcohol intake
- Physical inactivity

Table 2. Medical conditions associated with osteoporosis

- Prolonged glucocorticoid therapy (see guidelines on the management of glucocorticoid induced osteoporosis)
- Conditions associated with excess glucocorticoid secretion (Cushing syndrome)
- Primary (testicular failure/orchidectomy) or secondary (hypothalamic pituitary disorders) hypogonadism, including anti–androgens (combined androgen blockade for prostate cancer)
- Post–transplantation
- Chronic cardiopulmonary disorders (congestive heart failure, emphysema/chronic bronchitis, bronchiectasis, cystic fibrosis)
- Chronic neuromuscular disorders (Parkinsonism)
- Malabsorption, hepatobiliary, coeliac and chronic inflammatory bowel diseases
- Rheumatological disorders (rheumatoid arthritis, ankylosing spondylitis)
- Haematological malignancies (myeloma, lymphoma, mastocytosis)
- Primary hyperparathyroidism
- Hypercalciurea
- Thyrotoxicosis
- Anticonvulsant therapy (Dilantin)
- Chronic depression

What causes bone loss in men?

Bone loss occurs with ageing in both men and women. In elderly men, this occurs predominantly as a result of decreased bone formation with minimal increases in bone resorption.[13] On bone histomorphometry, this is manifested by trabecular plate thinning and endocortical bone resorption.[14] Recent data suggests that a reduction in periosteal bone formation may also contribute to a smaller bone size (reduced vertebral body and femoral neck width) leading to an increased fracture risk.[15] Longitudinal studies suggest that bone loss in elderly men is approximately 5–10% per decade, with bone loss further accelerating after 75 years of age.[16] Other factors contributing to age related bone loss include:[2,6,17–25]

- physical immobility
- poor nutrition
- reduced calcium absorption (low calcium dietary intakes and diminished intestinal absorption)
- vitamin D deficiency
- increased parathyroid hormone activity
- reduced cytokine and growth factors (such as insulin growth factor I)
- reduced osteoblastic activity and recruitment
- reduction in gonadal function.

Testosterone and osteoporosis

While serum testosterone levels decline with age, this hormone accounts for only 5% of the age and weight adjusted variance in bone loss.[18] An accelerated phase of bone loss similar to that seen in menopausal women has been described in men with hypogonadism secondary to gonadectomy or androgen deprivation.[20,26–28] The classic histomorphometric findings accompanying this disorder includes osteoclast activation associated with trabecular plate perforation and loss of trabecular connectivity.[14] Partial reversibility of the bone loss has been reported following androgen replacement[29–33] or antiresorptive therapy (calcitonin[26] or bisphosphonates[33–34]).

The biological significance of testosterone levels just below or in the low–normal reference range in elderly men remains controversial.[18,35] Hypogonadism per se, with serum testosterone levels in the 'castrate' range, is a major risk factor for osteoporosis.[2–8,28–34] However, the fact that testosterone therapy alone does not restore bone mass in hypogonadal men suggests that other hormonal factors may be important in the pathogenesis of hypogonadal bone loss.[27–32] The recent discovery of a mutation in the aromatase receptor in an osteoporotic man has led to advances in understanding the role of oestrogen in skeletal growth.[36,37]

Osteoporotic risk factors

Osteoporosis results from:

- a failure to achieve a peak bone mass and/or
- secondary causes of bone loss (*Tables 1,2*).

Compared with women, little attention has been paid to the determinants of peak bone mass in men, which include racial, genetic, nutritional, hormonal, medical and lifestyle factors.[2] Puberty has been shown to be a major determinant accounting for at least 40% of peak bone mass acquired between the ages of 9–13 years.[4,6,38] Men with a history of constitutional delay in puberty have significantly reduced spinal and forearm bone mineral density (BMD).[29] At least 60% of men presenting with osteoporosis have a secondary cause (*Table 2*).[2] The remainder have no identifiable medical conditions or risk factors associated with bone loss and are referred to as having primary or idiopathic osteoporosis.

A recent study has demonstrated that men with medical disorders associated with osteoporosis had a twofold increase in the risk of hip fractures (OR=2.9; 1.3–4.3), while conditions linked with an increased risk of falling were associated with an almost sevenfold increase in risk (OR=6.9; 3.3–14.8).[39] These factors together accounted for almost 72% of the hip fractures in men. Other significant risk factors contributing to hip fracture in men include comorbid factors (such as sleep disturbance, impaired mental status and poor appetite), previous stroke with hemiplegia, prior fragility fractures, senile dementia, alcoholism and gastrectomy.[40]

Diagnosis

Both age and BMD are strong predictors of fracture rates and survival.[41–43] Unfortunately risk factors alone have a low sensitivity and specificity in predicting hip fractures (59.6% and 61%, respectively).[42] Bone mineral density measurements therefore remain the gold standard for assessing the severity of osteoporosis and fracture risk. The criteria for diagnosing osteoporosis in women is based on the World Health Organisation recommendation of using a BMD value of more than 2.5 standard deviations below the young normal mean reference range (t-score <–2.5). These criteria, however, have not been standardised in men. Until a final consensus is reached, the diagnosis of osteoporosis in men should use a similar t-score value (<–2.5).[2,7,11,44] To permit more accurate t-score calculations in individual men, bone densitometers should be standardised using software derived from reference databases for 'healthy' Australian men aged 20–40 years.

Interpreting the BMD

The interpretation of BMD in men needs special attention. Advanced spondyloarthropathy, facet joint disease and aortic calcification may falsely elevate spinal BMD as assessed by dual energy X-ray absorptiometry (DXA).[41–45] Bone mineral density reports usually include the mean value for the combined L2–L4 vertebrae. In cases where BMD values are pseudo–elevated, the L1, L2 and L3 vertebrae may need to be analysed separately. Spinal X-rays are required to assess for the presence of extravertebral calcification and asymptomatic spinal fractures (usually defined as greater than 20% reduction of the anterior, posterior or central vertebral height). Quantitative computed tomography (QCT) of the lumbar spine is another option for measuring spinal bone mass.[44] This technique has the ability to accurately define a region of interest not confounded by extravertebral calcification. It is limited, however, by a high precision error (greater than 3–4%) which may render it unsuitable for monitoring changes and also has the potential of an increased radiation exposure.

Femoral neck DXA may therefore be more appropriate for diagnosing osteoporosis and for monitoring bone mass in elderly men in whom pseudo–elevations in BMD are evident. In a recent study the relative risk of hip fracture in men was 3.0 (1.7–5.4) for each standard deviation decrease in femoral neck BMD.[46]

While men are more susceptible to traumatic fractures, it remains imperative to measure BMD in all men who have:

- radiological evidence of bone demineralisation
- significant risk factors or
- aged over 50 years with a history of an atraumatic fracture.

A Medicare rebate is available for bone densitometry in these subjects.

Prevention of osteoporosis

Effective antifracture therapies for men presenting with osteoporosis are limited. It is therefore essential to consider preventative measures in men at high risk (*Table 1*) or with BMD t–score values equal or less than –1.0. General practitioners play an important role in not only identifying patients who are at risk, but also in educating patients in lifestyle changes to reduce this risk. Although medical intervention may be required in some individuals, patients should be informed of the importance of maximising peak bone mass in childhood and adolescence, as well as maintaining a stable bone mass throughout adult life. Smoking should be avoided and alcohol intake limited. Any reversible medical factors should be treated (*Table 2*).

Diet and supplements

A diet consisting of adequate general nutrition, calcium and vitamin D is especially important in elderly patients.[47,48] The National Institute of Health consensus statement[47] outlines the recommended calcium requirements for men (1500 mg daily). Calcium rich foods, and especially dairy products such as milk, ice cream, cheese and yogurt are readily absorbed.

Vitamin D plays an important role in maintaining skeletal integrity and preventing hip fractures.[50] Vitamin D_2 is only present in minimal amounts in the diet. Cholecalciferol (vitamin D_3) is predominantly formed by the action of ultraviolet radiation on the skin. Vitamin D_3 is metabolised in the liver and in the kidney, to active metabolites responsible for promoting intestinal calcium absorption, and thereby reducing negative calcium balance. Both ageing and the use of sunblock creams limit the ability of the skin to make vitamin D. Chronic liver and renal diseases inhibit the hydroxylation of vitamin D_3. Nutritional supplementation is therefore necessary for those individuals at risk of vitamin D deficiency, usually with serum 25 hydroxyvitamin D below 40 nmol/L). These include:

- the chronically ill,
- frail and elderly patients
- patients with chronic hepatobiliary disorders, and
- those treated with anti-epileptic medications.[52]

Simple vitamin D_3 is available in Australia as ergocalciferol (Ostelin 1000 IU per capsule). Weight loss and low intakes of energy and protein also result in osteopenia and should be avoided in nonobese individuals.[47]

Exercise

Regular weight bearing exercise (this would include ball sports, walking, running, hiking, aerobics etc.) should be encouraged in children and adolescents.[51] High impact activities (such as jumping and running) have a greater effect on maintaining bone than low impact activities. Activities which do not involve supporting the body weight against gravity (swimming and cycling) are less effective.

Conclusion

Osteoporosis is a significant problem, affecting 19% of men over 50. Osteoporotic fractures have a high morbidity in men and result in mortality 20% greater than expected for age. Men presenting with spinal fractures frequently have an underlying medical condition contributing to their bone loss. It is therefore essential to identify and treat these medical conditions so as to reduce the fracture risk. Patients with primary or idiopathic osteoporosis need to be identified and treated with both lifestyle intervention programs in addition to anti-osteoporotic therapies.

References

References are available for this article. Email **afp@racgp.org.au** or phone 03 9214 1546.

SUMMARY OF IMPORTANT POINTS

- Osteoporotic fractures affect up to 60% of women and 30% of men aged over 60 years.
- Osteoporotic fractures in men are associated with a poor outcome, a greater than 20% excess in mortality than expected and a considerable cost to the community.
- All men 50 years and older presenting with a fracture should be considered as having osteoporosis and should undergo bone densitometry.
- Exercise is important. The benefits obtained may extend beyond osteoporosis to include other age related conditions such as hypertension, heart disease, diabetes, arthritis etc.
- The cause of osteoporosis in men should always be defined and specific disease processes should be treated appropriately.
- While primary prevention of fractures remains crucial, treatment to ensure that further fractures do not occur is equally important.

REPRINT REQUESTS

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