Prevention and management of osteoporosis

Richard Eastell

Abstract

Fractures resulting from osteoporosis are a major public health problem. Physicians should be aware of the chief risk factors for osteoporosis and refer appropriately for bone densitometry. Risk factors include previous fracture, family history of fracture, slender habitus, early menopause, treatment with drugs known to affect bone (glucocorticoids) and diseases known to affect bone (rheumatoid arthritis). The diagnosis of osteoporosis can be made if the bone density *T*-score is −2.5 or below. This information can be used with other risk factors to estimate the 10-year risk of fractures. Patients at the highest risk for fracture benefit from many licensed treatments. These can be given orally (alendronic acid, disodium etidronate, risedronate sodium, ibandronic acid, calcitriol, raloxifene, hormone replacement therapy), subcutaneously (parathyroid hormone, denosumab) or intravenously (ibandronic acid, zoledronic acid) and usually result in an increase in bone mineral density and a reduction in fracture risk. Osteoporosis can be prevented by careful attention to exercise and diet.

Keywords Bone mineral density; kyphoplasty; MRCP; osteoporosis; treatment; vertebroplasty

Key points

- It is worthwhile measuring bone mineral density (BMD) in patients with strong risk factors (e.g. those taking long-term corticosteroids, older patients with low-trauma fractures)
- There is good evidence that treatment prevents fractures in women with vertebral fractures or with BMD *T*-scores of −2.5 or less
- It is usual to give a 5-year course of oral bisphosphonates (or a 3-year course of intravenous bisphosphonates) and then a drug holiday; in more severe cases, it is usual to give a 10-year course of oral bisphosphonates (or a 6-year course of intravenous bisphosphonate)
- Denosumab should be given every 6 months, punctually, and treatment should not be stopped without considering alternative therapy
- Hip fracture can be prevented in frail, elderly patients by calcium and vitamin D supplements

Introduction

Osteoporosis is a systemic skeletal disease characterized by low bone mass and microarchitectural deterioration, with a consequent increase in bone fragility and susceptibility to fracture, particularly of the vertebral body, distal forearm and proximal femur in postmenopausal women.[1] A more practical definition of osteoporosis is based on bone mineral density (BMD). The BMD of the older person is compared with the average BMD of a person of the same gender at age 30 years, and the results expressed in standard deviation units, the so-called '*T*-score'. If the *T*-score is equal to or less than −2.5, osteoporosis may be diagnosed.

Fractures that result from osteoporosis cause considerable morbidity and mortality. Their incidence is increasing in developed countries as a result of the increase in the proportion of elderly people in the population, and an increase in the incidence of fracture within the elderly population resulting, perhaps, from a more sedentary lifestyle.

It is now possible to determine an individual's risk of osteoporosis and fracture accurately, and to monitor their response to treatment by bone densitometry. The prediction algorithm FRAX™ allows estimation of 10-year risk,[2] and treatment guidance can be based on this. Many cases of osteoporosis are preventable, and treatment is effective in reducing the number of further fractures in patients with established osteoporosis.

Diagnostic testing

Investigations

Patients with an osteoporosis-related low-trauma fracture should undergo systematic investigation to identify underlying causes (or secondary osteoporosis) (Tables 1 and 2).[1] Identification of a low-trauma fracture (a fall from standing height or less) of the hip or distal forearm is straightforward. However, identification of vertebral fracture can be difficult because it may not be painful.

Radiology

The most reliable finding on a spine radiograph to support the diagnosis of osteoporosis is the presence of a deformed vertebra. Vertebral fracture is characterized by depression of the endplate and can appear as:

- a wedge deformity (loss of anterior height)
- an endplate deformity (loss of middle height)
- a compression deformity (loss of anterior, posterior and middle height).

Subtle changes of osteoporosis may be identified on spine radiographs (e.g. low density compared with soft tissue, prominence of vertical trabeculae), but these changes are unreliable,

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Factors affecting rate of bone loss

	Nutrition	Body weight	Lifestyle	Genetic
Increase bone loss	Sodium Caffeine	Thinness	Alcohol abuse Cigarette smoking Bed rest	Family history Female sex
Decrease bone loss	Calcium	Obesity	High activity	Race (black)
Unknown effect on bone loss	Phosphate		Normal activity	

	Sex hormones	Diseases	Drug therapy
Increase bone loss	Early menopause Oophorectomy Postmenopause Amenorrhoea	Cushing's syndrome Hyperthyroidism Hyperparathyroidism	Glucocorticoids Thyroxine Heparin Diuretics (furosemide) Aromatase inhibitors
Decrease bone loss			Hormone replacement therapy

Table 1

Diagnostic evaluation of osteoporosis

Establish presence of low-trauma fracture
- Spine radiography

Evaluate degree of osteopenia
- Bone densitometry

Exclude secondary osteoporosis
- Primary hyperparathyroidism (serum calcium)
- Thyrotoxicosis (plasma thyroid-stimulating hormone)
- Multiple myeloma (erythrocyte sedimentation rate, protein electrophoresis, urinary Bence Jones protein)
- Osteomalacia (serum 25-hydroxyvitamin D, plasma parathyroid hormone, serum calcium, phosphate, alkaline phosphatase, 24-hour urinary calcium and creatinine)
- Malabsorption syndrome (full blood count)
- Hypogonadism in men (testosterone)

Evaluate bone turnover
- Biochemical markers
- Bone histomorphometry

Table 2

and the apparent low bone density seen on a radiograph may be a technical artefact introduced by overexposure. Osteoporosis must therefore be confirmed by BMD measurement.

Bone mineral density measurement

BMD measurement has become more reliable and more widely available.

Dual-energy X-ray absorptiometry (DXA) is precise and accurate, involves exposure to only low doses of X-rays and allows the measurement of bones of clinical interest (lumbar spine, proximal femur). In DXA, two energy peaks of X-rays are absorbed to different extents by bone and soft tissue, and the density of bone is calculated, in g/cm^2, using simultaneous equations. The measurement is compared with two reference ranges: one for young adults (aged 30 years; giving a *T*-score) and one for age-matched adults (giving a *Z*-score). These BMD measurements have several uses (Table 3).

Bone turnover

Bone biopsy can be useful in unusual forms of osteoporosis (e.g. idiopathic osteoporosis in young adults). It provides information about the rate of bone turnover and the presence of secondary forms of osteoporosis (e.g. systemic mastocytosis). Patients with high bone turnover usually respond better to antiresorptive drugs (e.g. oestrogen, bisphosphonates, calcium).

Biochemical markers of bone turnover (Table 4) reflect the processes of bone resorption and bone formation (see Bone structure and metabolism on pages xxx of this issue). Markers that are specific to bone (e.g. osteocalcin, N-terminal telopeptides) are useful in predicting individuals at risk of osteoporosis ('fast bone-losers') or in monitoring the effect of drugs used in treatment.

Markers of bone resorption can be particularly useful, as changes in their concentration reflect the reduction in risk of fracture following treatment with bisphosphonates more closely than do changes in measured BMD. The changes in bone resorption markers are usually maximal after 6 months of treatment. This makes them more suitable for treatment monitoring than bone density as changes in density are often not apparent for 2 years. Also, access to bone density facilities can be limited.

Management and prevention

Treating established osteoporosis

The aims of treatment of established osteoporosis are alleviation of symptoms and reduction of the risk of further fractures. Currently available drugs can prevent further bone loss and reduce the risk of further fractures by up to 50%. Drug treatments should be monitored by BMD or bone turnover marker measurements as some patients fail to respond to certain drugs. The rate of bone loss can be accelerated once treatment is stopped; it therefore remains important to measure BMD or bone turnover markers after stopping treatment.

Pain relief: this is provided by analgesic drugs or physical measures (e.g. lumbar support for a limited period of time, transcutaneous nerve stimulator). Fracture pain usually resolves within 3 months, but patients with vertebral fractures can require long-term analgesia because of secondary degenerative disease. During the early phase (6 weeks), some patients can benefit from percutaneous vertebroplasty (injection of bone cement into a collapsed or fractured vertebra) or balloon kyphoplasty (inflation of a balloon within the collapsed vertebral body before stabilization with bone cement). During the later phase (after 6

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