Diagnosis and management of osteoporosis

Ralston SH, Fraser J. Diagnosis and management of osteoporosis. 
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OSTEOPOROSIS IS A COMMON CONDITION CHARACTERISED BY LOW BONE MINERAL DENSITY (BMD) and an increased risk of fragility fractures.

It affects up to 30% of women and 12% of men at some point in their lives. The threshold for osteoporosis is defined operationally as BMD at the spine or hip 2.5 SD or more below the population average in young healthy individuals (T-score <-2.5), where BMD has been assessed by dual energy X-ray absorptiometry (DEXA).1

A large number of factors have been identified that increase the risk of osteoporosis and/or fragility fractures, see table 1, p16. Two of the most important risk factors are increasing age and female gender, although other common and potentially modifiable risk factors include long-term corticosteroid therapy, chronic inflammatory disease, malabsorption and untreated premature menopause.

‘Vertebral fractures are easily missed’

CLINICAL PRESENTATION
Osteoporosis is a clinically silent disease and may not present until it is quite advanced since low levels of BMD do not cause symptoms. A common presentation is with a low trauma fracture, often of the spine, wrist, or hip although almost any bone can fracture as the result of osteoporosis.

Peripheral fractures are easily diagnosed, but vertebral fractures (see figure 1, above) are easily missed. Sometimes they present with back pain after lifting a heavy object but often the presentation may be more insidious with chronic back pain, height loss and kyphosis. Height loss of more than 5 cm should raise the suspicion of vertebral fractures.

While fractures are the hallmark of osteoporosis, the majority of patients with fragility fractures do not have osteoporosis, at least as defined by low BMD on DEXA examination.2
Osteoporosis

CLINICAL ASSESSMENT

History and examination
The patient should be asked about:
- Family history of osteoporosis (particularly parental hip fracture)
- General medical history, focusing on possible secondary causes of osteoporosis
- Smoking
- Alcohol intake
- Previous fracture
- Age at menopause
- Height loss

Clinical examination should include height and weight to assess body mass index and check for height loss. Other clinical signs may include kyphosis in patients with multiple vertebral fractures and local tenderness on percussion over the site of a recent vertebral fracture.

Fracture risk assessment
The diagnosis of osteoporosis can be confirmed by DEXA but this should only be performed in patients who have a fracture risk > 10%.

Risk factor
- Vertebral fractures are generally diagnostic of osteoporosis

A limitation of both tools is that they underestimate the risk of vertebral fractures.

Bone densitometry
Bone densitometry by DEXA is helpful in confirming the diagnosis and for assessing who will benefit from treatment. According to recent SIGN guidance evaluation by DEXA should be considered if the ten-year risk of major osteoporotic fracture is more than 10%.

The rationale for this recommendation stems from clinical trial data which has shown evidence of benefit for treatment in patients with osteoporosis on DEXA who have a fracture risk > 10%.

The NICE fracture risk assessment guidance did not suggest a threshold at which DEXA should be considered.

If the BMD T-score values by DEXA at the lumbar spine, femoral neck or total hip are at or below -2.5 then the diagnosis of osteoporosis is confirmed.

‘DEXA is helpful for assessing who will benefit from treatment’

Vertebral fractures are generally taken as diagnostic of osteoporosis, even if spine BMD values are not in the osteoporotic range. This is particularly relevant in elderly patients where co-existing osteoarthritis and aortic calcification are common resulting in falsely elevated spine BMD values.

While DEXA is not strictly necessary in patients with vertebral fracture it is helpful in providing a baseline upon which to assess response. This is useful in patients who suffer a fracture during treatment (see below).

Other investigations
Other investigations are indicated to determine if there is an underlying cause.

Table 1

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for the osteoporosis and to determine if there are any contraindications to specific treatments. A typical screen includes tests for coeliac disease (TTG antibody), thyrotoxicosis (TFT), myeloma and monoclonal gammopathy of uncertain significance (serum protein electrophoresis and urinary Bence-Jones protein); renal impairment (urea and electrolytes; liver disease and alcohol excess (liver function tests), osteomalacia and hyperparathyroidism (serum calcium phosphate) and male hypogonadism (serum testosterone and gonadotrophins).

In our experience the most common secondary causes of osteoporosis are occult coeliac disease, monoclonal gammopathy of uncertain significance and hypogonadism.

MANAGEMENT
The management of osteoporosis consists of identifying and treating any underlying causes, correcting lifestyle factors that might contribute to the osteoporosis or risk of fractures and instituting drug treatment where appropriate, see table 2, p18. Although correction of secondary causes of osteoporosis is generally beneficial, expert advice should be sought before initiating testosterone replacement in male patients with hypogonadism because of the increased risk of cardiovascular disease.8

Who should be treated?
The best evidence is in postmenopausal osteoporosis where various treatments have been shown to reduce the risk of further fractures in patients with osteoporosis on DEXA and/or those with pre-existing low trauma vertebral fractures.

FIGURE 2
Pathway for diagnosis and management of osteoporosis, adapted from SIGN 142.
parenteral therapy should be considered. The first-line treatment is intravenous zoledronic acid 5 mg once a year, although denosumab 60 mg every six months subcutaneously is equally effective.

Parenteral therapy is usually initiated in secondary care. It is common for patients to experience a transient flu-like illness for 2-3 days after the first dose of zoledronic acid, but this does not usually recur with subsequent infusions. There is a risk of hypocalcaemia with both parenteral preparations but that can be minimised by ensuring that the patient is given calcium and vitamin D supplements prior to and during therapy.

Unlike bisphosphonates, denosumab can be used in patients with renal impairment but great care must be exercised in this patient group because of the high risk of hypocalcaemia which may be serious or even fatal. These patients are best treated in secondary care.

‘Make sure oral bisphosphonates are being taken when the patient has fasted’

Teriparatide (the 1-34 fragment of parathyroid hormone; TPTD) is highly effective in the treatment of vertebral osteoporosis and has been shown to be superior to oral bisphosphonates in preventing vertebral fractures, both in randomised trials and observational studies.15

Therapy with TPTD is usually initiated in secondary care either as primary treatment for severe osteoporosis or as rescue therapy in patients who have failed to respond to other agents. Following a two-year course patients are switched to antiresorptive therapy to maintain the increase in BMD.

Duration of therapy

It is unclear how long patients should remain on treatment. This is because drugs such as bisphosphonates and denosumab suppress the normal process of bone renewal and repair. For most drugs there is good evidence of safety and efficacy for up to five years. After that point the need for ongoing therapy should be reviewed.16

If the patient still has osteoporosis or has suffered fractures there may be benefit in continuing therapy for another five years in patients at high risk of vertebral fracture.17

For zoledronic acid most centres give a course of three years and a spell off therapy for three years based on research which showed no difference in clinical fracture rates in patients treated for three years compared with six.18

Long-term adverse events related to oversuppression of bone turnover include atypical subtrochanteric fractures and osteonecrosis of the jaw, although these are very rare and in the vast majority of patients the benefits of therapy outweigh the risk. There is no evidence that ‘drug holidays’ reduce the risk of the complications related to oversuppression of bone turnover.

Patients who fracture while on treatment

None of the treatments currently available are completely effective at preventing fractures. The results are best for vertebral fractures, relative risk (RR) reduction 50-75%; quite good for hip fractures (RR reduction 40%) but modest for non-vertebral, non-hip fractures (RR reduction 20-25%).

Some patients may suffer fractures while on anti-osteoporosis therapy. If this occurs it is important to check compliance (and with oral bisphosphonates to make sure the treatment is being taken when the patient has fasted). If the medication is being taken correctly therapy should be continued and the patient informed that fractures can still occur even though the treatment is working.

‘Some patients may suffer fractures while on anti-osteoporosis therapy’

If two or more fractures occur during therapy, then a repeat BMD measurement should be requested provided at least two years has elapsed since the last scan. Measurements at shorter intervals are seldom informative because of limitations in the precision of DEXA. If the repeat DEXA shows significant bone loss (more than 4%) then an alternative treatment should be considered. Most often this will involve changing from an oral to a parenteral medication.

Special groups

The management of male osteoporosis follows the same general strategy as for...
Osteoporosis is a common condition characterised by low bone mineral density (BMD) and an increased risk of fragility fractures. It affects up to 30% of women and 12% of men at some point in their lives. Two of the most important risk factors are increasing age and female gender, although other common and potentially modifiable risk factors include long-term corticosteroid therapy, chronic inflammatory disease, malabsorption and untreated premature menopause.

The diagnosis of osteoporosis can be confirmed by DEXA but this should only be performed in patients who have an increased risk of fracture on the basis of clinical risk factors. DEXA should be considered if the ten-year risk of major osteoporotic fracture is more than 10%. If the BMD T-score values by DEXA at the lumbar spine, femoral neck or total hip are at or below -2.5 then the diagnosis of osteoporosis is confirmed. Vertebral fractures are generally taken as diagnostic of osteoporosis, even if spine BMD values are not in the osteoporotic range.

Oral bisphosphonates are the first-line treatment. The most widely used agent is oral alendronic acid, 70 mg once a week, with calcium and vitamin D supplements. Oral risedronate 35 mg once a week has similar anti-fracture efficacy. If oral bisphosphonates are contraindicated or not tolerated then parenteral therapy should be considered. The first-line treatment is intravenous zoledronic acid 5 mg once a year; although denosumab 60 mg every six months subcutaneously is equally effective. Teriparatide (the 1-34 fragment of parathyroid hormone; TPTD) is highly effective in the treatment of vertebral osteoporosis.

There is evidence that fractures occur in glucocorticoid-induced osteoporosis at higher levels of BMD than in postmenopausal osteoporosis so therapy should be considered in patients with a BMD T-score of <-1.5. Although it is useful to have a DEXA scan before starting treatment to provide a baseline value to assess response, this investigation is not absolutely necessary to initiate bone protective therapy especially in those aged above 65 since the vast majority of these patients will have a T-score of <-1.5 or below. In younger individuals where BMD is likely to be higher DEXA is useful in determining if bone protective treatment is needed immediately or if it could be delayed until the T score falls below -1.5.

REFERENCES
12. Ralston SH, de Lala G, Fangerup DJ. NICE on osteoporosis. Women over 75 with fragility fractures should have DEXA. Br Med J 2009;338:b3340

Useful information
National Osteoporosis Society
Information and advice for patients and healthcare professionals including downloadable fact sheets on treatments for osteoporosis
www.nos.org.uk
International Osteoporosis Foundation
Statistics on the epidemiology of fractures. Also provides a detailed dietary calcium calculator
www.iofbonehealth.org
University of Edinburgh
Provides a quick and easy dietary calcium calculator
www.cgem.ed.ac.uk/research/rheumatological/calcium-calculator

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