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Review Article

European Guidelines for the Diagnosis and Management of Osteoporosis in Postmenopausal Women

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Abstract

The European Foundation for Osteoporosis and Bone disease (subsequently the International Osteoporosis Foundation) published guidelines for the diagnosis and management of osteoporosis in 1997. This manuscript updates these in a European setting. Here guidance is provided on the assessment and treatment of postmenopausal women with or at risk from osteoporosis. The following areas are reviewed; the role of bone mineral density measurement for the diagnosis of osteoporosis and assessment of fracture risk, general and pharmacological management of osteoporosis, monitoring of treatment; assessment of fracture risk, case finding strategies and investigation of the patients. Here a platform is provided on which specific guidelines can be developed for national use.

Keywords: *Bone mineral density, Diagnosis of osteoporosis, Fracture risk assessment, Treatment of osteoporosis.*

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Introduction

Osteoporosis is defined as a systemic skeletal disease characterised by low bone mass and micro architectural deterioration of bone tissue, with a consequent increase in bone fragility and susceptibility to fracture.[1] The clinical significance of osteoporosis is bone fracture.

Common sites for osteoporotic fractures are Hip, Distal forearm, Spine and Proximal humerus. The remaining lifetime probability of a fracture in women at the menopause at any one of these sites is 40% or more in developed countries.[2] In the year 2000, there were estimated to be 620,000 new fractures at the hip, 574,000 at the forearm, 250,000 at the proximal humerus; and 620,000 spine fractures in men and women aged 50 years or over in Europe. These fractures accounted for 34.8% of such fractures worldwide[3].

Collectively, all osteoporotic fractures account for 2.7 million fractures in men and women in Europe at a direct cost of 36 billionEuros[4] Osteoporotic fractures are a major cause of morbidity in the population. It is widely recognized that osteoporosis and the consequent fractures are associated with increased mortality.

Assessment of fracture risk

The following are clinical risk factors used for the assessment of fracture probability

1. Advancing age
2. Sex- female
3. Low body mass index
4. Previous fragility fracture, particularly of the hip, wrist and spine
5. Glucocorticoid treatment (Less than 5 mg prednisolone daily for 3 months or more)
6. Smoking
7. Alcohol intake 3 or more units daily
8. Secondary cause of osteoporosis
9. Untreated hypogonadism in women e.g. premature menopause, bilateral oophorectomy
10. Prolonged immobility

Investigation of patients with osteoporosis

Bone mineral measurements and diagnosis of osteoporosis

The objectives of bone mineral measurements are to provide diagnostic criteria, prognostic information on the probability of future fractures. Bone measured density (BMD) is the amount of bone mass per unit volume (volumetric density), or per unit area (areal density). Dual-energy X-ray absorptiometry

(DXA) is the most widely used bone densitometric technique.

It is versatile in the sense that it can be used to assess bone mineral content of the whole skeleton as well as of specific sites, including those most vulnerable to fracture [7]

Diagnostic thresholds

The following four general descriptive categories are given below for adult men and women using measurements of DXA at the femoral neck[8]

1. Normal: a value for BMD that is higher than 1 standard deviation below the young adult female reference mean (T-score greater than or equal to −1 SD).
2. Low bone mass (osteopenia): a value for BMD more than 1 standard deviation below the young female adult mean, but less than 2.5 SD below this value (T-score >−1 and <−2.5 SD).
3. Osteoporosis: a value for BMD 2.5 SD or more below the young female adult mean (T-score more than or equal to −2.5 SD).
4. Severe osteoporosis (established osteoporosis): a value for BMD 2.5 SD or more below the young female adult mean in the presence of 1 or more fragility fractures.

Other techniques to measure bone mineral

1. Quantitative ultrasound (QUS)

a Broad band ultrasound attenuation (BUA)

b. Speed of sound (SOS)

2. Quantitative computed tomography (QCT).

General management

Encourage mobility

Immobilization is a very important cause of bone loss. Immobilized patients may lose as much bone in a week when confined to bed as they would otherwise lose in a year. For this reason immobility should, wherever possible be avoided. Exercise forms an integral component of management.[9] But the amount of weight-bearing exercise that is optimal for skeletal health in patients with osteoporosis is not known, Walking is safest & easiest, but does not have an impact on bone density.

Nutrition

There is a high prevalence of calcium, protein and vitamin D insufficiency in the elderly. Intakes of at least 1,000 mg/day of calcium, 800 IU of vitamin D and of 1 g/kg body weight of protein can be recommended in the general management of patients with osteoporosis.[10]

Major pharmacological interventions

The most commonly used agents in Europe are raloxifene, the bisphosphonates alendronate, ibandronate and risedronate. Until recently, hormone replacement treatment is also widely used.

Selective oestrogen-receptor modulators

Selective oestrogen-receptor modulators (SERMs) are non-steroidal agents that bind to the oestrogen receptor and act as oestrogen agonists or antagonists, depending on the target tissue. Raloxifene is the only SERM available for the prevention and treatment of postmenopausal osteoporosisIt prevents bone loss.[11]

Limitation

1. There was no significant reduction of non-vertebral fractures.

2. The only severe (but rare) adverse event was an increase in deep venous thromboembolism.

3. The overall risk benefit ratio of Raloxifene is favourable & the drug is approved widely for the prevention & treatment of postmenopausal osteoporosis

Bisphosphonates

Bisphosphonates are stable analogues of pyrophosphate They are potent inhibitors of bone resorption and produce their effect by reducing the recruitment and activity of osteoclasts and increasing their apoptosis. Alendronate 70 mg once weekly and risedronate 35 mg once weekly are the most commonly used bisphosphonates worldwide. It reduces the incidence of vertebral, wrist and hip fractures by approximately half in women with prevalent vertebral fractures.[12] The overall safety profile of Bisphosphonates is favourable. Oral bisphosphonates are associated with mild gastrointestinal disturbances, and rarely cause oesophagitis.

Other pharmacological interventions

Hormone replacement therapy (HRT)

Oestrogens reduce the accelerated bone turnover induced by the menopause, and prevent bone loss at all skeletal sites &

decrease the risk of vertebral and non-vertebral fractures. The combined use of conjugated oestrogen and medroxy progesterone acetate was associated with a 30% increased risk of coronary heart disease (CHD) and breast cancer, and with a 40% increase in stroke.[13,14] Thus, HRT is no longer recommended as a first-line treatment for the prevention and treatment of osteoporosis.

Calcitonin

Calcitonin is an endogenous polypeptide hormone that inhibits osteoclastic bone resorption.[1,2] For clinical use it can be administered either by injection or nasal application.[15] It likely reduces the risk of vertebral fracture. The drawbacks of repeated injections and the high costs of the nasal formulation preclude the long-term use of calcitonin as a first-line treatment of osteoporosis.

Peptides of the parathyroid hormone (PTH) family

Intermittent administration of PTH (e.g. with daily subcutaneous injections) results in an increase in the number and activity of osteoblasts, leading to an increase in bone mass and in an improvement in skeletal architecture at both cancellous and cortical skeletal sites. The recommended doses are 20 μg of teriparatide daily as subcutaneous injection. The most common reported adverse events in patients treated with teriparatide are nausea, pain in the limbs, headache and dizziness.

Strontium ranelate

Strontium ranelate is a recently registered agent that is marked for the treatment of postmenopausal osteoporosis, to reduce the risk of vertebral and hip fractures. Strontium ranelate both inhibit bone resorption & stimulates bone formation. The recommended daily dose is one 2-g sachet once daily by mouth.

Monitoring of treatment with densitometry

The goal of drug therapy in a patient with osteoporosis is to significantly increase bone strength, in order to decrease the risk of fracture. Alendronate was attributed to an increase in BMD at the lumbar spine and hip and causes 16% of vertebral fracture risk reduction.[16] Raloxifene causes 4% of the vertebral fracture risk reduction.

Monitoring of treatment with biochemical markers of bone turnover

Several markers have been developed over the past 20 years that reflect the overall rate of

bone formation and/or bone resorption. The most informative ones for the investigation of osteoporosis are osteocalcin and procollagen I N-terminal extension peptide (P1NP) for assessing bone formation, and type I collagen – and C-telopeptide breakdown products to assess bone resorption.[15] Antiresorptive therapies such as calcitonin, estrogen, SERMs and bisphosphonates induce a significant decrease in bone markers that return to the premenopausal range within 3–6 months for the resorption markers and within 6–9months for markers of formation.

Conclusion

From the above discussion, a platform is provided on which specific guidelines can be developed for national use.

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