

Prevention and treatment of Osteoporosis, An application of the Institute of Medicine (IOM) continuum of care model

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Abstract

Osteoporosis results from disordered bone remodelling characterized by an imbalance between bone formation and bone resorption carried out by Osteoclasts leading to an increased occurrence of osteoporotic fracture. The absolute and relative rises in the elderly population and increasing unhealthy habits of children and adolescents are causing increases in the incidence of osteoporosis and fragility fractures. The objective of this review is to assess the risk factors and prevention of osteoporosis on all prevention levels; primary, secondary, and tertiary.

The main non-modifiable risk factors are gender and genetic factors while the modifiable risk factors include physical activity, calcium intake, vitamin D, and dietary intake. Primary

prevention of osteoporosis can be started from an early age by optimizing factors that improve bone mass and quality leading to a better bone mineral density. Secondary prevention can be applied through a screening program for early detection which could be implemented on population level or only for high-risk patients, while tertiary prevention is aimed at treatment and rehabilitation. The outcome of a successful prevention program is based on improving the bone mineral density of the population and detecting osteoporosis early and treating it medically to prevent fragility fracture.

Keywords:

Prevention, Fragility fractures, Osteoporosis

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1. Introduction

Osteoporosis is a systemic skeletal disease characterized by low bone mass and micro architectural deterioration of the bone tissue, causing increase in bone fragility and fracture susceptibility. ⁽¹⁾

Osteoporosis is a result of disordered bone remodelling characterized by imbalance between bone formation, carried out by Osteoblasts, and bone resorption carried out by Osteoclasts. ⁽²⁾ This leads to increased occurrence of fractures which are called osteoporotic fractures.

Osteoporosis can cause different formats of fractures ranging from asymptomatic (like morphometric fracture of vertebral body) and passing through partial fractures to unstable comminuted fractures in which restoration of anatomical features of the bone is very difficult. Some of these fractures may lead to painful sequelae, permanent physical disability, or even death

The absolute and relative rises in the elderly population and increasing unhealthy habits of children and adolescents are causing increases in the incidence of osteoporosis and fragility fractures. ⁽³⁾

Osteoporosis is classified clinically into primary or secondary osteoporosis. primary osteoporosis occurs in post-menopausal women and in men without any known underlying cause, and it is age-related. If the osteoporosis is due to an underlying disease or medication, it is called secondary osteoporosis. ⁽⁴⁾

Osteoporosis is diagnosed using Dual-energy X-ray absorptiometry

DEXA based on bone mineral density (BMD) with T-score of ≤ -2.5 at the lumbar spine, total hip, or femur neck testing. With decreasing T-scores, the relative risk for fracture increases. ⁽⁵⁾

2. Bone mineral density

Adult Bone mineral density is considered as the result of two processes, acquiring peak bone mass and strength during adolescence and maintenance of the mass during middle and old ages. Any physiologic and pathologic processes affecting this cycle may result in decreasing bone mineral density. ⁽⁶⁾

Bone remodelling is continuous throughout life. In the first decades of life, bone turnover is tightly regulated to maintain a steady state between bone resorption and bone formation. Bones mass reach peak level around the age of 15–20 years in women and later in men. After this, bone loss becomes more evident and bone resorption exceeds bone formation. Later in life, during menopause in women, decreased levels of oestrogens significantly accelerates bone resorption over formation thus inducing accelerated bone loss. ⁽⁷⁾

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Studies showed that children with low bone mass are more likely to have low bone mineral density in adulthood unless effective intervention are done. Studies also reported that late-maturing females have lower BMD compared with their early maturing peers. The higher the BMD during childhood, the higher in adults and less risk of osteoporosis and fragility fractures. This suggests starting interventions to improve bone quality among young age group, so they achieve their maximum peak bone mass and proceed to adulthood with better bone quality. ^(8,9)

3. Factors controlling BMD during childhood

These factors can be either modifiable or non-modifiable.

3.1 Non-modifiable (Genetics and sex)

Up to 80 % of the variability in bone mass and risk of osteoporosis can be explained by genetics. BMD is lower for daughters of women with osteoporosis.

Males have greater Bone mass than female. These differences are more apparent with the onset and progression of puberty.

3.2 Modifiable factors

Studies showed the factors that improve BMD, these include physical activity, calcium intake, vitamin D, dairy consumption, high protein and fat diet, zinc, magnesium, Vitamin C, and diet rich in fruits and vegetables.

Factors that have negative effects on bone mass during childhood include sedentary lifestyle, high consumption of cola and caffeinated beverages, and contraception. While the negative effects of smoking and alcoholism on BMD early in life are controversially reported by the studies. ⁽⁹⁾

4. Prevention of osteoporosis

Prevention of osteoporosis can be achieved on three levels of prevention including primary, secondary, and tertiary prevention. ⁽¹⁰⁾

The aim of Primary prevention of osteoporosis is directed to non-osteoporotic individuals, while secondary prevention of osteoporosis indicates early detection of the disease with preventing osteoporotic fractures. Both primary and secondary prevention include preventing behaviours. Tertiary prevention is directed toward treatment and rehabilitation of patients with fragility fractures.

4.1 Primary prevention

Primary prevention of osteoporosis can be started from early age by optimizing factors that improve bone mass and quality leading to a better

BMD. ⁽⁹⁾ Population based comprehensive approach should be applied as a primary prevention. These include promoting physical activity, nutrition, and behavioural interventions like sun exposure, falls screening, avoiding smoking, and alcohol restriction. These should be applied at all disease stages from primary prevention during childhood and adolescent up to the tertiary prevention of elderly who had fragility fractures. Pharmacologic intervention can be applied aiming for primary prevention in patients with risk factors. ⁽¹⁰⁾

Some Studies reported lack of public awareness about the diagnosis and risk factors of osteoporosis and fragility fracture. Therefore, it is necessary to promote awareness among the general population for behaviours that improve their bone quality using different approaches like Public seminars, posters, local press, television programs, and school education. ^(11,12) As Improving patient's awareness through education program has been found to be an important part in prevention programs of osteoporosis. ⁽¹³⁾

4.2 Secondary prevention

4.2.1 screening

Osteoporosis screening is based on measuring BMD usually by DXA, that is then used to predict fracture risk. Studies showed that low BMD predicts occurrence of osteoporotic fractures. As treatment of osteoporosis reduce the risk of fracture, screening and treating osteoporosis reduce fracture risk significantly.

One of the most common tools used for screening is quantitative ultrasound densitometry. Even though results of ultrasound are less than to that of DEXA, quantitative ultrasound densitometry is used for community-based screening programs due to the portability of the equipment and no radiational hazard. ^(14,15) *The Fracture Risk Assessment Tool (FRAX)* is a tool that can be used to predict the 10 years risk of major osteoporotic fractures or hip fractures based on clinical risk factors, with or without using bone mineral density. ⁽¹⁶⁾

Guidelines recommend starting screening of postmenopausal women at 65 years of age. Screening for women with age range 50-64 is recommended, if their risk of fracture (assessed using FRAX) is equal to or greater than that of a white woman without risk factor with 65-year-old. The recommended interval of screening as suggested by literature for those with normal BMD or mild osteopenia (T-score, -1.01 to -1.49), is 15 years. For women with moderate osteopenia (T-score, -1.50 to -1.99), screening could be every 5 years, and for women with advanced osteopenia (T-score, -2.00 to -2.49), screening should be performed yearly. ⁽¹⁴⁾

The American College of Physician recommends (DEXA) for men with increased risk of osteoporosis who may benefit from drug therapy. The male osteoporosis risk estimation score (**MORES**) is a scoring system that helps the clinicians in identifying patients with increased risk of osteoporosis who must be referred for DEXA. It includes three variables: age, weight, and history of chronic

obstructive pulmonary disease. Studies found that MORES score of 6 or more has sensitivity of 93%.⁽¹⁷⁾

4.2.2 Nonpharmacologic therapy

Nonpharmacological management includes adequate vitamin D intake and calcium, weight-bearing exercise, cessation of smoking, limitation of alcohol and caffeine consumption, and avoiding falling.

It is recommended that dietary calcium intake must be limited to 1gm daily for men between 50-70 years of age and to 1.2gm daily for women more than 50 years age and men older than 71 years of age. The recommended daily intake of vitamin D is about 600 IU for women and men above 50 years of age and 800 IU for women and men older than 70 years.⁽¹⁸⁾

4.2.3 Pharmacologic therapy

American Association of Clinical Endocrinologists (AAACE) strongly recommends pharmacologic therapy for the following patients:

- 1-Those with low bone mass or osteopenia with a history of fragility fracture of the spine or hip
- 2- Those with a T-score ≤ -2.5 in the spine, total hip, femoral neck, or 33% radius.
- 3-Those with a T-score between -1.0 and -2.5 in the femoral neck, total hip, spine, or 33% radius, if the FRAX 10-year probability results for major osteoporotic fracture is $\geq 20\%$ or if the 10-year probability of hip fracture is $\geq 3\%$ in the U.S population or according to country specific threshold.⁽¹⁹⁾

Bisphosphonates

They act by binding to hydroxyapatite in bone matrix, thus inhibiting osteoclast mediated bone resorption through multiple mechanisms.⁽²⁰⁾ Adverse effects of bisphosphonates include Barrett's oesophagus and gastrointestinal disturbances such as esophagitis, dyspepsia, and oesophageal varices. Rarely, atrial fibrillation, osteonecrosis of the jaw, or renal failure may occur, so intravascular bisphosphonate should be avoided in patients with low glomerular filtration rate.

Denosumab is a human monoclonal antibody that act by binding specifically to human RANKL leading to inhibition of osteoclast formation and activation, decreasing bone resorption.

It has a long its anti-resorptive effects that last 4–6 months so it can be used once every 6 months. It can be considered as a first-line medication in patients who are intolerant to oral bisphosphonates or those with renal failure.⁽²⁰⁾

Hormone replacement therapy HRT

Hormone replacement therapy reduces the incidence of all osteoporotic fractures, including hip and vertebral fractures, even in women without a high risk of fracture. HRT should be considered for the prevention and treatment of osteoporosis in postmenopausal women, younger than 60 years. It is not recommended to be started after 60 years for the sole purpose of osteoporosis prevention. Low and ultralow dose of HRT was shown to be effective in postmenopausal women for prevention of osteoporosis. These drugs can be

started in patients older than 60 years since it has a safer profile.

Selective oestrogen receptors modulators (raloxifene and tamoxifen) bind with oestrogen receptor as agonists or antagonists according to the target tissue. Raloxifene is used for preventing osteoporosis in postmenopausal women. It has the advantages of reducing the risk of the thromboembolic events and endometrial hyperplasia when compared with tamoxifen. ⁽²¹⁾

Calcitonin can be used for the treatment of osteoporosis in postmenopausal women for more than five years when alternative drugs are not feasible. ⁽¹⁸⁾

Teriparatide (parathyroid analogue) It is anabolic or bone building drug. It stimulates bone formation more than resorption resulting in net increase in bone mineral density.

A recent meta-analysis has shown statistically significant effect of teriparatide in reducing the risk of vertebral and non-vertebral fractures. ^(22,23)

Strontium ranelate

It has a mixed anabolic and antiresorptive effects. It acts by inhibiting bone resorption and inducing bone formation causing increases in BMD. ⁽²⁴⁾

Drugs selection

Risedronate, alendronate, zoledronic acid, and denosumab are found to have broad spectrum antifracture efficacy (vertebral and nonvertebral fracture) and should be considered initially for most patients who are indicated for treatments.

Those who have low or moderate risk of fracture (like young postmenopausal women with

moderately low T-score and no prior fractures) can be managed with oral agents. Injectable agents such as zoledronic acid, teriparatide, or denosumab are considered initially for patients with high risk fracture (like old women who have very low T-score or had multiple hip or vertebral fractures), those with upper gastrointestinal problem and may not tolerate oral route, those with lower GI issues that prevent proper absorption, or poor patient compliance. ⁽¹⁹⁾

4.3 Fragility fractures

If Patients presented with fragility fractures, careful assessment (comprehensive history and physical exam) should be done. These are directed toward patients overall clinical features, mechanism of injury, and factors that contribute to the injury. Fracture stability and anatomical position are important in guiding management.

In typical fracture fixation, failure occurs at the level of hardware, while the cause of failure in fragility fracture is mainly at the interface of bone and implants. ⁽²⁵⁾

4.3.1 Vertebral fractures

They are among the most important fragility fracture. They occur suddenly with rapidly progressing pain, out of proportion to the trauma, continuous and with weight bearing.

The management in acute stages includes conservative approaches such as rest, minor and major pain killers, and using corsets. Pain usually begins to subside within 1-3 weeks and then disappears after few months. Transpedicular injections of a synthetic material that is like

cement within the fractured vertebral body may cause immediate cessation of pain.

vertebroplasty and kyphoplasty are used to stabilize the vertebral fractures. In vertebroplasty, cement is injected under high pressure with high risk of leakage and pulmonary embolism. In kyphoplasty, the cement is injected under low pressure after introduction of balloon which is inflated then within the vertebral body allowing partial reduction of the deformity. As the injection is done under low pressure, there is a lower risk of pulmonary embolism. Both procedures should be recommended for patients who had intractable pain for weeks. ⁽²⁶⁾

4.3.2 Fractures of the distal radius

They are the second most common osteoporotic fracture, with the highest incidence among postmenopausal female older than 50 years of age.

These fractures are managed in the elderly in majority of cases by closed reduction and cast fixation for 4 to 6 weeks. If it is unstable, then it is necessary to recur to surgery. The

available options include the insertion of K- wires percutaneously and cast, the closed reduction and stabilization with external fixator or the open reduction and internal fixation with plate and screws. ⁽²⁷⁾

4.3.3 Proximal humerus fractures

These are common fragility fractures. They can often be managed conservatively, with only about 15% treated surgically. Conservative management include sling immobilization with early gentle range of motion and physiotherapy.

The best option for surgical intervention includes closed reduction and percutaneous fixation. Up to 20% of patients who had displaced, complex fractures, or fracture dislocations, the open reduction and internal fixation or humeral prosthetic replacement are indicated. ⁽²⁷⁾

4.3.4 Proximal femur fractures

They can be classified into two main groups: intracapsular and extracapsular. Each type has subtypes which also can be described as stable (non-displaced or minimally displaced) and unstable (displaced).

Intracapsular fractures are usually treated surgically with 3 cannulated screws inserted percutaneously or hip replacement (partial or total). The intertrochanteric fractures are usually treated with screw-plates such as the Dynamic Hip Screw. ^(27,28)

5. Prevention approach

Osteoporosis prevention should be applied as comprehensive approach targeting low and high-risk patients, figure (2) below, which was built according to the Institute of Medicine IOM continuum of care model with modifications, ⁽²⁹⁾ is showing prevention of osteoporosis applied on three levels.

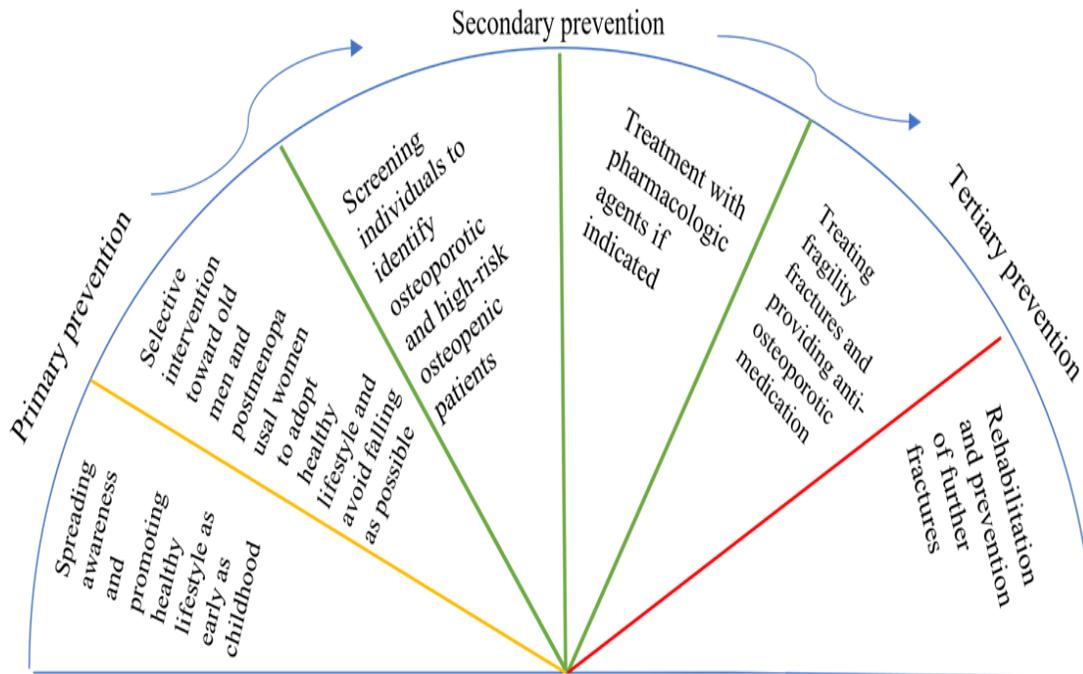


Figure (1) Application of prevention on three levels primary, secondary and tertiary

6. Conclusions

Osteoporosis represents an important public health problem. The main outcome of osteoporosis is fragility fractures. These are recognized as a significant causes of morbidity and mortality especially for old age patients.

Interventions directed toward preventing osteoporosis should be initiated early for children and adolescents. Starting public education about the risks and prevention of osteoporosis is a key step in successful prevention program. Screening programs should be carried as recommended for high risk patients to detect the disease early. Patients with osteoporotic fragility should receive care directed toward their fracture

as well as receiving treatment to prevent further fractures

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