# Osteoporosis in Orthopaedics: Review of Literature and Clinical Approach

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**Abstract**

**Osteoporosis affects 8 to 62 percent of women in India, with osteoporotic fractures leading to preventable morbidity and often mortality. Osteoporosis does not have any clinical symptoms and may often present with fracture as the first symptom. Our aim to review the literature and describe a clinical approach in osteoporosis was to help the practitioner and orthopaedic surgeon suspect, diagnose, treat, prevent, monitor, and lead a patient through uneventful surgery. Early diagnosis and effective treatment of osteoporosis can lead to decreased morbidity, mortality, and financial burden on the elderly and also improve their quality of life.**

**Keywords: Osteoporosis, Osteopenia, Teriparatide, Bisphosphonates, Denosumab, Osteoporotic fractures, T score, Monitoring of treatment, Bone turnover markers, Bone density, DXA, BMD, FRAX score.**

## Definition

The definition given by the consensus development conference [Copenhagen, 1990], is now considered as one of the earliest modern definitions of osteoporosis. It defines osteoporosis as 'A systemic skeletal disease, characterized by low bone mass and micro-architectural deterioration of bone tissue with a consequent increase in bone fragility and susceptibility to fracture' [1].

A more recent definition was published by the National Institute of Health Consensus Conference [2001], defined osteoporosis as 'A skeletal disorder characterized by compromised bone strength predisposing to an increased risk of fracture'. They specifically observed that low bone mass in itself has no symptoms unless fracture occurs [2].

World Health Organization [WHO] defines osteoporosis as being present when BMD [Bone mineral density] is 2.5 standard deviations or more below the average value for young healthy women [a T-score of <−2.5 SD]. A second, higher threshold describes "low bone mass" or osteopenia as a T-score that lies between −1 and −2.5 SD. "Severe" or "established" osteoporosis denotes osteoporosis that has been defined in the presence of one or more documented fragility fractures [3,4].

## Demographics

### World demographics

Over 200 million women worldwide suffer from osteoporosis. Prevalence is known to vary with age, size, and race. It is estimated that 25% of women between the age of 70-80 years suffer from osteoporosis. It causes over 8.9 million fractures annually, resulting in an osteoporotic fracture every 3 seconds.

Worldwide, 1 in 3 women over 50 years of age, will experience osteoporotic fractures, as will 1 in 5 men aged over 50 years [2,3,4]. By 2050, the worldwide incidence of hip fracture in men is projected to increase by 310% and 240% in women, compared to rates in 1990 [5].

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### Indian Demographics

Data on the prevalence of osteoporosis among women in India comes from studies conducted in small groups spread across the country. Estimates suggest that, of the 230 million Indians expected to be over the age of 50 years in 2020, 20% are osteoporotic women [6]. The prevalence of osteoporosis ranging from 8% to 62% in Indian women of different age groups has been reported by several studies [7].

Gandhi *et al.* in a study [Mumbai, 2005] done on 200 women [more than 40 years of age] attending Well- Women Clinics, reported a prevalence of 34% osteopenia and 8% osteoporosis [8]. Unni et al. in a similar study in Pune reported 31.4% and 14.3% prevalence of osteopenia and osteoporosis in women in a range of 40-72 years [9]. Similarly, in Delhi, Chhibber et al. reported a prevalence of 29% osteopenia and 62% osteoporosis in women from 60-80 years of age [10].

In a study among Indian women aged 30-60 years from low-income groups, BMD at all the skeletal sites was much lower than values reported from developed countries, with a high prevalence of osteopenia [52%] and osteoporosis [29%]. This was thought to be due to inadequate nutrition. Hospital-based data suggest that these women have osteoporotic hip fractures at a much earlier age than Western women [11].

## Osteoporotic Fractures

Osteoporosis is a skeletal disorder characterized by compromised bone strength, predisposing to an increased risk of fracture.

Of the various types of fractures namely traumatic, pathological, stress, and osteoporotic fractures, the osteoporotic fractures occur following minimal trauma, such as a force equal to or less than falling from standing height. They are therefore also called fragility fractures or low-trauma fractures.

Vertebral body compression fractures, which may occur even with everyday activities like lifting, pushing, pulling etc., constitute the most common osteoporotic fractures, followed by hip and distal forearm fractures [12]. Vertebral fractures may lead to pain, loss of height, deformity, reduced lung function, diminished quality of life, and increased mortality [13].

Hip fractures, which affect nearly 1.6 million people per year worldwide, can lead to 24-30% excess mortality within one year, which is a mortality rate similar to breast cancer [12, 14]. Of these, nearly 50% of hip fracture survivors are permanently incapacitated and nearly 20% require long term nursing care [1, 15].

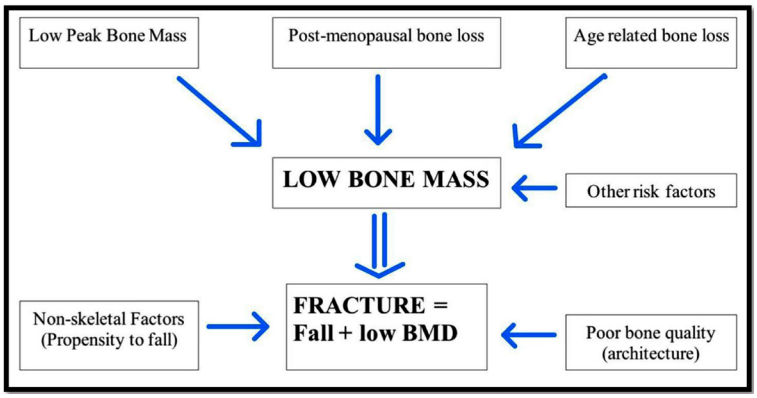


**Fig. 1: Pathogenesis of osteoporotic fractures [16]**

Adapted from Melton LJ and Regis BL. Osteoporosis: Etiology, Diagnosis and Management. Raven Press. 1988,155-179.

Post-menopausal bone loss, low peak bone mass, age, medical co-morbidities, long term medications, poor bone quality, and other non-skeletal factors may contribute to the pathogenesis of osteoporotic fractures [16].

Fractures are precipitated when the body fails to maintain peak bone mass. Peak bone mass is the maximum bone mass or density achieved during a lifetime which is reached when the growth in the size of bones and accumulation of bone mineral has stabilized. Hereditary, gender-related, nutritional, endocrine, mechanical, and habit related factors influence peak bone mass [17, 18, 19].

## Osteoporosis in Clinical Scenario

Osteoporosis itself does not have any clinical symptoms. Symptoms, if any, are caused by osteoporotic fractures. Hence, diagnosis of osteoporosis can be made by the presence of an osteoporotic fracture, or by means of Dual-energy X-ray Absorptiometry [DXA] to calculate Bone Mineral Density [BMD].

### Approach to a patient

**When to suspect osteoporosis?**

The importance of a thorough medical history and physical examination cannot be understated in raising suspicion for osteoporosis as it may show no symptoms.

Advanced age, female gender, menopause, smoking and alcohol consumption, and malnutrition are established risk factors for primary osteoporosis [20,21].

Endocrinopathies [e.g. thyroid / parathyroid disorders, Cushing's disease], drug intake [e.g. steroids, chemotherapy, anticoagulants, anticonvulsants], malabsorption syndromes, bone marrow disorders, in-

**Table 1: Routine investigations to identify secondary causes of osteoporosis**

| Test Parameter | Associated diseases |
|---|---|
| Differential Blood Count | Hematological pathology |
| ESR or CRP | Inflammatory / Infective causes of spinal abnormalities |
| Serum Calcium | Increased in primary hyperparathyroidism or other causes of hypercalcemia. Decreased in secondary hyperparathyroidism, malabsorption etc. |
| Serum phosphate | Decreased in secondary hyperparathyroidism, malabsorption etc. |
| Alkaline phosphatase | Increased in osteomalacia |
| Serum creatinine and eGFR | Renal osteopathy |
| Serum protein electrophoresis | Multiple myeloma |
| TSH | <0.3 mU/L - risk factor for fracture |
| Serum vitamin D | Vitamin deficiency, osteomalacia |
| Intact PTH | Differentiate primary, secondary hyperparathyroidism, hypercalcemia of malignancy |
| Testosterone in men | Hypogonadism |
| Bone resorption marker | Evaluation of bone turnover |

1. ESR – Erythrocyte sedimentation rate, CRP – C-reactive protein, eGFR – Estimated glomerular filtration rate, TSH – Thyroid-stimulating hormone, PTH – Parathyroid hormone.

2. Adapted from Pfeilschifter J, Kurth AA *et al.* DVO guideline 2009 for prevention, diagnosis, and therapy of osteoporosis in adults. Osteology; 2011;20[1]:55-74

flammatory disorders [e.g. rheumatoid arthritis, systemic lupus erythematosus], infective disorders [e.g. Tuberculosis, osteomyelitis, pneumonia] and other miscellaneous disorders [e.g. HIV, COPD, renal disease, organ transplantation] can increase suspicion towards secondary osteoporosis [22].

**Simple tests for osteoporosis?**

Routine hematological investigations like complete blood counts, erythrocyte sedimentation rate [ESR], and C-reactive protein [CRP] help to rule out inflammatory or infective causes of osteoporosis.

Serum vitamin D, calcium, phosphorous, alkaline phosphatase, parathyroid hormone and thyroid function tests help identify nutritional and metabolic causes of osteoporosis like osteomalacia, hyperparathyroidism, hyperthyroidism, etc.

Plain radiographs which are easily available, non-invasive, and relatively less expensive help identify and raise suspicion of osteoporosis, but cannot quantify it or help start or monitor treatment for the same.

Thinned out long bone cortices, disappearance of bony trabeculae, decreased height of vertebral bodies are all radiologically suggestive of osteoporosis. Singh et al. graded osteoporosis based on the appearance of bony trabeculae on AP radiographs of the hip [as shown in the figure below]. These however are not reproducible and inter-observer findings often vary.

Conditions like multiple myeloma, metastatic disease, osteomalacia, infection, soft tissue tumors, etc. can often be identified on plain radiographs which may draw attention towards a secondary cause of osteoporosis.

Lateral radiographs of thoracic and lumbar spine help delineate silent old osteoporotic fractures. Silent vertebral fractures and microfractures may lead to progressive deformities like kyphoscoliosis in elderly patients thereby compromising lung function.

Bone biopsy and serum markers of bone turnover, though mentioned in the literature, have limited clinical use in the diagnosis of osteoporosis. They however have a role in monitoring the progress of treatment.

**What is a DXA scan?**

Diagnosis of osteoporosis when suspected due to any of the above risk factors and in the absence of osteoporotic fractures is done by bone mineral density [BMD] evaluation using Dual-energy X-ray Absorptiometry [DXA].

DXA is performed at sites which are most prone to fragility fractures like the thoraco-lumbar spine, hip joints, and distal forearms. It helps not only in diagnosis, quantification, and classification of osteoporosis

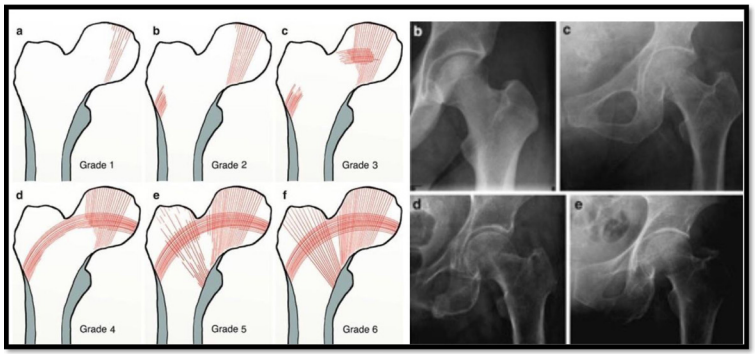


**Fig. 2: Singh's index for trabecular patterns in hip osteoporosis**

Grade 1: Principle compressive trabeculae markedly reduced in number. Grade 2: Only principle trabeculae can be seen, all tensile trabeculae have been resorbed. Grade 3: Break in continuity of principle tensile trabeculae opposite greater trochanter. Grade 4: Principle tensile trabeculae reduces in number. Grade 5: Principle tensile and compressive trabeculae accentuated, Ward triangle prominent. Grade 6: All normal trabecular groups visible.

[Adapted from : Kanakaris NK, Lasanianos NG, et al. Singh index for osteoporosis. Trauma and orthopaedic classifications.]

but also in monitoring response to treatment.

**How do osteoporotic fractures present?**

If not investigated on suspicion, a patient with osteoporosis will often present with osteoporotic low trauma fracture as the first symptom. Pain, swelling, deformity, inability to use limbs, inability to perform a range of movements of involved areas, in sites most prone to fracture are commonest symptoms of osteoporotic fractures. These patients can be administered a DXA scan after healing of fracture for quantification and to monitor treatment subsequently.

Often, osteoporotic fractures may be occult and may present with no symptoms at all. Stooped posture, kyphosis, chest deformity, may lead to high suspicion of vertebral osteoporotic silent fractures. Patients with a previous history of osteoporotic fractures are at increased risk of repeat fractures [23,24].

## Bone Densitometry in Osteoporosis

Bone densitometry is currently the most easily available, and accurate method of assessing osteoporosis in suspected patients. Bone densitometry can be conducted on the central or peripheral skeleton. The central skeleton usually assesses densitometry in the lumbar spine and proximal femur. Peripheral skeleton sites include forearms [Radius], phalanges, tibia or calcaneus.

Central skeleton analysis can be done using Dual-energy X-ray Absorptiometry [DXA] or quantitative computed tomography [QCT]. The DXA scan is the most commonly used WHO-approved modality with reproducible results. It can assess and quantify Bone Mineral Density [BMD] both in forearms and the rest of the body.

DXA scan works on principles of attenuation of X-ray beams and the absorption of electrons in them. Attenuation refers to a reduction in the number and energy of photons in an X-ray beam [i.e. its intensity] when they pass through tissues of different density and thickness. Absorptiometry helps measure the degree of attenuation thereby quantitatively assessing and differentiating tissue density.

The WHO classification of post-menopausal osteoporosis published in 1994, which was intended to assess the prevalence of osteoporosis in a particular population [post-menopausal cohort of Caucasian females] was done using a DXA scan of the spine, hip, and forearm. Results were expressed as a standard deviation from the mean predicted bone mass, in young adult females, which was later expressed as a T-score [25].

T-score, which is used for diagnosis and classification of osteoporosis indicates the number of standard deviations in which a patient's BMD is above or below the average BMD of young adult reference population.

T-score = BMD of patient - BMD young-normal reference SD young-normal reference

Z-score indicates the number of standard deviations in which a patient's BMD is above or below average BMD of age-matched reference population.

Z-score = BMD of patient - BMD age-matched reference SD age-matched reference

The WHO recommends the use of T-score over Z-score for diagnosis because bone strength and risk of fracture are related to BMD. Using a Z-score could, on the contrary suggest that osteoporosis does not increase with age and many normal patients may end up having an osteoporotic fracture.

Spine [mostly the lower lumbar vertebral bodies], hip [femoral neck and total proximal femur], and the distal 1/4$^{th}$ of radius are most commonly used for DXA. It's better to analyze BMD at the spine, hip, and radius together as peak bone mass and rate of bone loss are not the same throughout the skeleton. In post menopausal women, the initial rate of bone loss is greater in cancellous bone than cortical bone.

The WHO classification system cannot be applied to T-scores from measurements other than DXA at the femoral neck, lumbar spine, or distal radius [26]. T-scores obtained from technologies other than central DXA are not directly comparable to central DXA as physical principles of the techniques are different and

**Table 2: WHO classification of osteoporosis based on BMD**

| Classification | Bone Mineral Density [Mean level = young adult reference population] | T Score |
|---|---|---|
| **Normal** | Within 1 SD of mean | Equal to or above -1.0 |
| **Osteopenia** | Between 1 and 2.5 SD below mean | Between -1.0 and -2.5 |
| **Osteoporosis** | Equal to or more than 2.5 SD below mean | Equal to or below -2.5 |
| **Severe Osteoporosis** | Equal to or more than 2.5 SD below mean | Equal to or below -2.5 With 1 or more fractures |

WHO: World Health Organization; BMD: bone mineral density; SD: standard deviation

[Adapted from : World Health Organization. Technical report series 843, WHO, Geneva. 1994.]

normative databases are not comparable.

## DXA in other categories of patients

### Pre-Menopausal women

The DXA based WHO classification does not apply to healthy premenopausal women as it was primarily described to express results as a standard deviation from the mean predicted bone mass in young adult Caucasian females [which is expressed as T score].

For women who have not attained menopause, Z scores, rather than T scores are preferred. Z score of -2.0 or lower is defined as 'below the expected range for age' and Z score above -2.0 is defined as 'within the expected range for age'.

The diagnosis of osteoporosis in premenopausal women should not be made based on densitometry criteria alone.

### Children

In children too, diagnosis of osteoporosis should not be made based on densitometric criteria alone. There should be a presence of both a clinically significant fracture history and low bone mineral content [BMC] or bone mineral density [BMD].

Significant fracture history can include long bone fracture of lower extremities, vertebral compression fractures, or two or more bone fractures of the upper extremity.

Low BMD in children is defined as a Z score of less than or equal to -2.0, adjusted for age, gender, and body size as appropriate [27].

BMC and BMD are measured in the spine and total body [not considering head] in children [28].

### Men

Derivation of T scores in men and thereby quantitation of BMD is controversial. Previously it was thought that a separate male database specific to men should be used to determine T scores for men. This thought was questioned as fracture risk should be the same in men and women at a specific BMD. This necessitates that T scores also be the same and therefore, the database used for determination should also be the same. ISCD [International society for clinical densitometry] most recently advised that a uniform [non-race adjusted] female reference be used even for men of all ethnic groups.

In men aged 50 years or more, T-scores should be preferred and in men younger than 50 years of age, Z-scores should be preferred, with a Z-score of -2 or lower defined as "below the expected range for age" and a Z-score above -2 defined as "within the expected range of age"

### Ethnicity

It is known from the literature that changing ethnicity does not affect T-score, but does affect Z-score. ICSD [International society for clinical densitometry] recommends using a uniform Caucasian [non-race adjusted] female normative database for women and men of all ethnic groups

The following table shows us to which groups can the WHO standard database be applied for classification.

## Fracture Risk Assessment

Although the measurement of bone mineral density with DXA is the so-called gold standard for the diagnosis of osteoporosis, it has some technical and statistical limitations [29].

Bone mineral density cannot be used as the sole predictor of bone strength. Less than 50% of the variation in whole bone strength is attributable to variations in bone mineral density [30 - 33].

The majority of patients who sustain fragility fractures, have a T score above -2.5 [34 - 36].

Epidemiological studies have been performed to examine the risk factors that are associated with low bone mineral density and hip fractures [37,38]. National osteoporosis foundation outlined major risk factors for osteoporosis and related fractures, which include age, height, weight, poor health, a personal history of fracture as an adult, a history of fragility fracture in a first-degree relative, low body weight, hyperthyroidism, hyperparathyroidism, current smoking and use of oral corticosteroid therapy [39].

For example, age is a powerful independent risk factor that has largely been ignored in previous clinical guidelines. In women with a T-score of −2.5, the probability of hip fracture is five times greater at the age of eighty years than it is at the age of fifty years [40]. Thus, fracture risk can be assessed more accurately by considering both age and bone mineral density than it can by considering bone mineral density alone. Similarly, other clinical risk factors contribute independently to fracture risk [41].

Several clinical factors are associated with a fracture risk that is greater than what can be accounted for by bone mineral density alone [42]. Fracture risk assessment, therefore, should employ specific risk factors in addition to bone mineral density. It is represented as a gradient and not a threshold. The following diagram

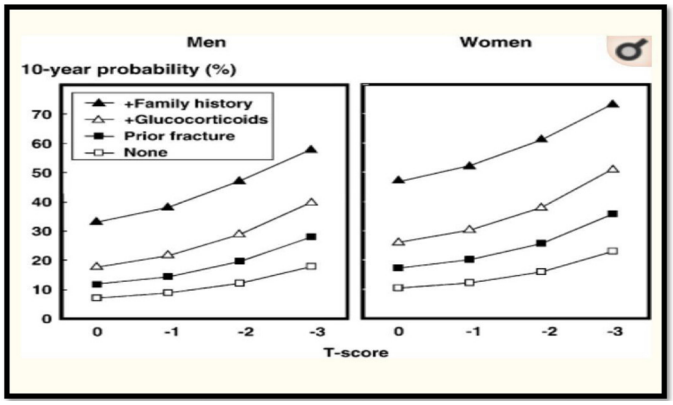


**Fig. 3: Fracture risk gradient based on risk factors**

[Adapted from : Kanis JA. Diagnosis of osteoporosis and assessment of fracture risk. Lancet. 2002;359:1929-36.]

represents the effects of several clinical risk factors on the ten-year probability of a major osteoporotic fracture occurring in 65-year-old white men and women in the United States [41].

### FRAX Model

Efforts have been made to formulate a system to better predict fracture risk because of the limitations of Dual-energy X-ray Absorptiometry [DXA]. Based on a series of meta-analyses undertaken to identify clinical risk factors for osteoporosis, the Fracture Risk Assessment Tool [FRAX] was developed by [2008] [42-44].

It was developed and validated under the direction of Professor John Kanis with the support of many individuals and organizations including the American Society for Bone and Mineral Research, International Osteoporosis Foundation.

FRAX aims to provide an assessment tool for the prediction of fractures in men and women with the use of clinical risk factors with or without femoral neck bone mineral density [BMD]. These clinical risk factors include age, sex, race, height, weight, body mass index, a history of fragility fracture, parental history of hip fracture, use of oral glucocorticoids, rheumatoid arthritis and other secondary causes of osteoporosis, current smoking, and alcohol intake of three or more units daily.

FRAX calculates the ten-year probability of a major osteoporotic fracture [in the proximal part of the humerus, the wrist, or the hip or a clinical vertebral fracture] and the ten-year probability of a hip fracture calibrated to the fracture and death hazards [39,45].

FRAX tool can be accessed online. Following is a picture showing the chart for the input of data and format of results in the United States' version. It helps clinicians enter particulars of the patients and calculate a fracture risk score to guide them at the time of beginning treatment.

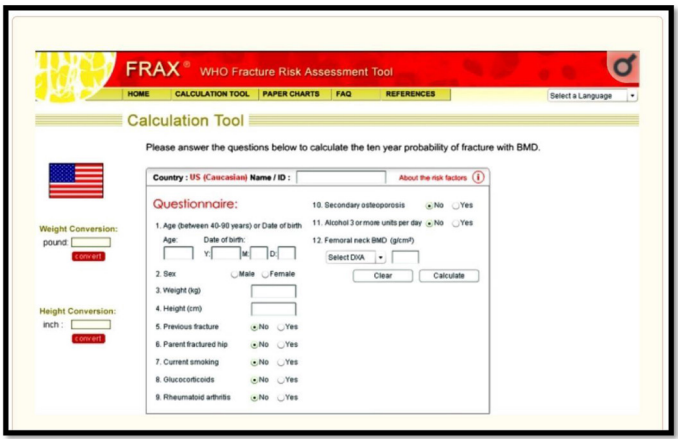


**Fig. 4: Online calculation of FRAX score**

[Adapted from : Unnanuntana A, Gladnick BP et al. The assessment of fracture risk. J Bone Joint Surg Am. 2010;92[3]:743-753.]

### Limitations

FRAX tool for assessment of risk fractures does have a few limitations. It can be applied only to previously untreated patients limited to ages 40 - 90 years. It cannot be applied to pre-menopausal women.

Parameters that affect the risk of fracture like falls, rate of bone loss, bone turnover, medications, use of glucocorticoids and family history of fractures other than maternal hip fractures are not considered [29].

## Clinical Management of Osteoporosis

Despite major advances in diagnosis and therapy, most patients with osteoporosis do not receive evaluation or treatment. Even patients who have had a fragility fracture, often are not further investigated or treated for osteoporosis, despite high mortality, morbidity, and economic burden.

The goals of prevention and treatment are focused on decreasing fracture risk and proper fracture management. Fracture risk can be decreased by stabilizing and increasing bone mass, maintenance, or improvement of bone quality and fall prevention.

### I: Non-pharmacological treatment

1. Dietary Calcium and Vitamin D
2. Exercise [weight-bearing and muscle-strengthening]
3. Smoking and excess alcohol control
4. Fall prevention

**Calcium supplementation**

Daily dietary intake of calcium is often found in-

**Table 3: Recommended daily calcium intake by age and gender**

| | Recommended daily Allowance [mg] | Upper limit [mg] |
|---|---|---|
| 9 - 18 yrs [Boys/Girls] | 1300 | 3000 |
| 19 - 50 yrs [Women] | 1000 | 2500 |
| > 50 yrs [Women] | 1200 | 2000 |
| Pregnancy | No adjustments | No adjustments |
| 19 - 50 years [Men] | 1000 | 2500 |
| 50 - 70 yrs [Men] | 1000 | 2000 |
| > 70 yrs [Men] | 1200 | 2000 |

[Adapted from : dietary reference intakes for calcium and vitamin D. Institute of medicine. 2011. The National Academic press : Washington DC]

sufficient to meet the needs to prevent osteoporosis. The National Osteoporosis Foundation recommends a daily dietary intake of 1200 mg of calcium for women above 50 years of age and men above 71 years of age to be adequate. It has further observed that there is no evidence, that taking more than 1200-1500 mg calcium per day is beneficial. The following table shows the recommended calcium intake per day as suggested in 2010 by the Institute of Medicine in the National Academic Press.

Evidence strongly suggests that calcium supplementation reduces bone loss and thereby reduces the incidence of fractures. Calcium supplementation is the first simple step in promoting bone health. Varying studies in the literature have reported the effect of calcium supplementation on an increased risk of myocardial infarction and cardiovascular events. At the moment, no consensus has been reached.

**Vitamin D**

Deficiency of Vitamin D is common due to low exposure to sunlight, less effectiveness of skin to produce vitamin D with advancing age and low dietary intake. The National Osteoporosis Foundation recommends a daily dietary intake of 800-1000 IU of vitamin D per day for adults above 50 years of age.

The American Association of Clinical Endocrinologists recommends that serum Vitamin D levels of 30-50 ng/ml are optimal for most patients. For many patients, vitamin D supplementation of 1000-2000 IU per day is required to maintain 30 ng/ml of 25-OH-D.

The Institute of Medicine in Washington in 2011, observed that practically all persons whose serum vitamin D levels are 20 ng/ml and above have sufficient vitamin D. Their recommended daily allowances for 97.5% of the population were as follows.

- 0-12 months of age - 400 IU Daily
- 1-70 years of age - 600 IU Daily
- Over 70 years old - 800 IU Daily

Tang *et al*. in 2007 observed that the best results towards improving bone health were achieved by maintaining an intake of 1200 mg of calcium and 800 IU of vitamin D together daily. It reduces fracture risk and reduces the rate of bone loss significantly as compared to taking calcium supplementation alone [46].

**Regular exercise**

A systematic review of 18 randomized control trials done by Bonaiuti et al. in 2002, found that aerobics, weight-bearing and resistance exercises, effectively and significantly increased bone mineral density at the spine across all ages. They further observed that walking as a form of exercise significantly improved BMD at the hip [47].

Feskanich *et al*. [2002] published an 11-year study of 61,200 post-menopausal women and found that hip fracture risk decreased by 6% for every 3 METRs [Metabolic Equivalent of Task] per week increase in activity [48].

**Falls**

It is estimated that 30% of people above 65 years of age suffer at least one fall per year. 10% of these falls result in serious injuries and 2% lead to fracture [49].

Prevention of falls can lead to the prevention of significant morbidity and mortality through the reduction of osteoporotic fractures in the elderly. Some ways of prevention of falls are:

- Correction of visual and hearing impairment
- Optimization of medications
- Bathroom grab-bars and non-skid mats
- Avoiding carpets and slippery mats
- Keeping away electric and toy cords
- Nightlight in bedroom and bathrooms
- Hand-rails on steps and stairs
- Walking aids if needed
- Exercise for strength and balance
- Good footwear

## II: Pharmacological Treatment

Pharmacological treatment of osteoporosis is aimed towards increasing bone mass, improvement of bone architecture and strength and reduction of fracture risk.

According to the National Osteoporosis Foundation recommendations [2008], treatment of osteoporosis should be considered for

1. Patients with a history of hip or vertebral fracture,
2. Patients with a T-score of −2.5 or lower at the femoral neck or spine, and
3. Patients who have a T-score of between −1.0 and −2.5 at the femoral neck or spine and a ten-year hip fracture risk of ≥3% or a ten-year risk of a major osteoporosis-related fracture of ≥20% as assessed with the FRAX tool [50,51].

Medications for osteoporosis can be anti-resorptive, anabolic or quality altering which targets different aspects of bone physiology such as reducing bone loss, increasing mineral deposition in bones, or increasing trabecular and tensile strength of bones.

**Bisphosphonates**

Bisphosphonates are anti-resorptive drugs, which increase BMD at various skeletal sites and thereby reduce the risk of fractures.

Bisphosphonates inhibit osteoclasts thereby causing a rapid decrease in bone resorption, followed by a late decrease in bone formation. This leads to the refilling of remodeling space and an increase in secondary remineralization. Eventually, BMD increases and fracture risk decreases. Bisphosphonates however, do not affect trabecular thickness [52].

Alendronate, Risedronate, Ibandronate, and Zoledronic Acid are regularly available and time tested, oral and injectable forms of bisphosphonates. Their routes of administration and frequency are outlined in the table below.

Bisphosphonates like alendronate, risedronate, and ibandronate have some dosage specifications which sometimes make it difficult for patients to follow. For oral administration, they have to be given on an empty stomach, in a sitting position with lots of water intake. This is done to prevent high chances of gastric irritation. The intestinal absorption of bisphosphonates is poor.

Zoledronic acid is administered IV over a 20-minute infusion annually. There is a high risk of acute phase reactions towards zoledronic acid and therefore the patients often need to be monitored over a period of 24 hours [53]. It has proven adverse effects in patients with renal and cardiac disease. It is contraindicated in renal patients with high creatinine values and a creatinine clearance of less than 35 [54].

Bisphosphonates are known to cause other side effects like musculoskeletal pain, hypocalcemia, acute-phase reaction, esophageal cancer, and osteonecrosis of the jaw. It is advisable to not start dental treatments when on bisphosphonate therapy and conversely not to start bisphosphonate therapy while undergoing dental treatments [55].

Effects of Bisphosphonates are known to last as long as 6 months after cessation of therapy which can work as an advantage for longer cover till other therapies can be instituted. The effect of zoledronic acid may last for one year and no reversal of the effect or antidote is currently available.

Bisphosphonates are known to cause incomplete or complete insufficiency fractures in long bones when administered for a long period. Allison, McKenna et al found that the highest incidence of atypical femur fractures in highly compliant patients on bisphosphonate therapy to be in the range of 1 - 3 percent after 3 to 5 years of therapy [56,57].

Bisphosphonates breaks are recommended for patients who are on long term therapy for osteoporosis. A patient with mild osteoporosis and low risk may be advised a drug holiday after 4 - 5 years of treatment and improvement in BMD scores. In patients with high fracture risk, a drug holiday of 1 - 2 years may be considered after 10 years of treatment. During a drug holiday if there is a significant decrease in BMD, then irrespective of time since the stoppage of treatment, the second phase may be started [58].

Treatment with bisphosphonates leads to a decrease in bone turnover markers. [The significance of bone turnover markers in monitoring of treatment is discussed further under 'Monitoring of treatment'.]

**Table 4: Dose and regimen of various bisphosphonates for osteoporosis therapy**

| Drug | Daily | Weekly | Monthly | Annually |
|---|---|---|---|---|
| **Alendronate** | 10mg oral | 70mg oral | - | - |
| **Risedronate** | 5mg oral | 35mg oral | 150mg oral | - |
| **Ibandronate** | - | - | 150mg oral monthly<br>3mg IV 3 monthly | - |
| **Zoledronic Acid** | - | - | - | 5mg IV |

**Calcitonin**

Calcitonin belongs to the class of anti-resorptive biological agents and is commonly available as a nasal spray. They lead to a relatively less increase in BMD and primarily reduce

the risk of vertebral fractures. There is no evidence to support the role of calcitonin in reducing hip or non-vertebral fracture risk. Calcitonin also inhibits osteoclasts towards causing its antiresorptive effect.

Calcitonin is preferably given via nasal sprays in the following way. 1 spray [200 IU] is given daily in alternate nostrils with calcium and vitamin D supplementation. Alternately, 100IU injectable dose can be given subcutaneously or intra-muscular daily.

Calcitonin is thought to have an analgesic effect and is often prescribed in vertebral body osteoporotic fractures. It helps improve osteoporosis and also helps decrease pain as most osteoporotic vertebral fractures are treated conservatively.

Because of its nasal route of administration there is often a chance of inadequate administration of dose and thereby loss of compliance. It causes nasal irritation frequently and occasionally can cause epistaxis.

There isn't clear literature on the risk of cancer following calcitonin administration for the treatment of osteoporosis. European medicines agency committee for medicinal products for human use and the US FDA has recommended that calcitonin no longer be used for osteoporosis due to its increased overall cancer risk. These results and recommendations have not yet been published in peer-reviewed journals.

Treatment with calcitonin leads to a decrease in bone turnover markers.

**Teriparatide [rhPTH: 1-34]:**

Teriparatide is a partial analog of parathyroid hormone which causes an increase in BMD at the spine and the hip. It also decreases fracture risk at the spine, hip, and non-vertebral regions.

Being an anabolic hormone, it improves and strengthens bone microarchitecture. It causes an increase in bone volume, periosteal diameter, cortical thickness, and endocortical diameter thereby improving cortical bone. In trabecular bone, it uses an increase in bone volume, trabecular thickness, and connectivity thereby improving cancellous bones. Teriparatide not only improves BMD towards the treatment of osteoporosis but is also known to aid in fracture healing.

Teriparatide is administered as a subcutaneous injection 20 mcg [8 units] every day from a pre-filled metered syringe, much like insulin. Serum parathyroid hormone levels should be ascertained to be normal before administration or beginning of teriparatide therapy.

The treatment is expensive as compared to some other agents for the treatment of osteoporosis. The syringe and medication require refrigeration and safe storage. Teriparatide can be given at a stretch only for 2 years, as after that its effect becomes catabolic and leads to bone loss and destruction.

Apart from more tolerable side effects like dizziness, leg cramps, and hypercalcemia, it is also known to cause osteonecrosis of the jaw and increased incidence of some tumors.

Treatment with teriparatide leads to an increase in bone turnover markers.

**Denosumab:**

Denosumab is a fully human monoclonal antibody that binds and inhibits RANK-ligand, thereby causing the anti-resorptive strengthening of bone. It leads to an increase in BMD at the spine and hip and reduces the risk of fracture at the spine, hip, and non-vertebral bones.

It is given as a single subcutaneous injection of 60 mg every 6 months.

It is thought to be similar in action to Bisphosphonates. The advantages of denosumab over bisphosphonates are, that denosumab is given as a subcutaneous injection once in 6 months, instead of every day which has better compliance. Its effect stops nearly immediately after discontinuation of therapy which may be considered both ways as an advantage or disadvantage. Disadvantages of denosumab are that it is expensive as compared to bisphosphonates and not anabolic unlike teriparatide.

It is also known to cause hypocalcemia, osteonecrosis of the jaw, and other side effects similar to bisphosphonates. Chances of infection are higher with the administration of Denosumab as compared to bisphosphonates.

Treatment with denosumab leads to a decrease in bone turnover markers.

**Raloxifene:**

Raloxifene is a selective estrogen receptor modulator [SERM], which is anti-resorptive in effect and increases BMD at the spine and hip. Like calcitonin, it reduces the risk of vertebral fractures but has no proven benefit in hip and non-vertebral fractures.

Raloxifene, when given 60 mg daily through the oral route of administration, not only increases BMD towards the treatment of osteoporosis but also reduces the relative risk of invasive breast cancers.

Treatment with raloxifene leads to a decrease in bone turnover markers.

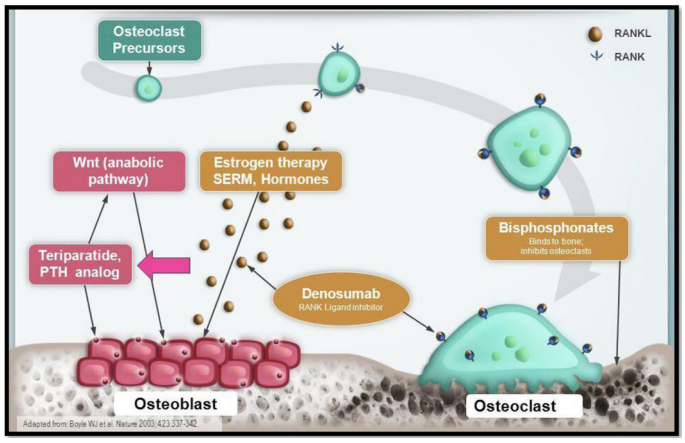


**Fig. 5: Mechanism of action of various osteoporosis therapies [59]**

PTH – Parathyroid hormone; SERM – Selective estrogen reuptake inhibitor; RANK – Receptor activator of nuclear factor; RANKL – RANK kappa-B ligand; Wnt – Wingless-int signaling.

[Adapted from : Boyle WJ, Simonet WS et al. Osteoclast differentiation and activation. Nature. 2003;423[6937]: 337-342.]

Following is a diagram showing the pathways of action of various drug modalities for the treatment of osteoporosis.

## Duration of Treatment

The optimal duration of treatment in women with post menopausal osteoporosis is not yet clear.

Strong and consistent evidence suggests that the anti-resorptive effect, which is assessed by BMD, BTM, or histomorphometry persists for at least 7 years for risedronate and at least 10 years for alendronate. Evidence also suggests that there is significant fracture risk reduction with the use of bisphosphonates for 3 - 5 years. There is no evidence to suggest that patients become refractory to treatment with bisphosphonates. On the other hand, bisphosphonates are known to decrease the risk of breast cancer, stroke, and overall mortality.

Black *et al* found that continued Alendronate treatment for 10 years is associated with further gains in spine BMD as compared to 5-year administration and further prevention in loss of BMD at the hip. [60]. They also found that there was a significant decrease in the incidence of morphometric vertebral fractures, clinical vertebral fractures, and non-vertebral fractures when alendronate was administered for 10 years instead of 5. Patients with high fracture risk for vertebral fractures may benefit from IV administration of zoledronic acid for 6 years instead of 3.

A postmenopausal patient with a low risk of fracture and osteoporosis may be given a drug holiday of 1 year after 3 - 5 years of therapy and a high-risk patient may be given a drug holiday of 1 - 2 years after 10 years of bisphosphonate therapy.

It is essential that teriparatide therapy cannot be given more than 2 years at a stretch as it converts the effect of the drug to catabolic.

More research is needed regarding the use of Denosumab for a long period like 10 years and its efficacy and side effects thereof.

Anti-resorptive drugs especially bisphosphonates need to be given a drug holiday to prevent bisphosphonate induced atypical fractures and other side effects from occurring as stated above. Many people have recommended a change of drug choice and conversion to raloxifene or teriparatide during a drug holiday for patients at a high risk of osteoporotic fractures.

Combination and sequential therapy with more than one agent have been explored. Literature has found it hard to justify the use of two anti-resorptive agents together even though they yield slightly additive effects on BMD, as the effect on fractures in not documented, costs increase and potential side effects increase as well.

Researchers studied various simultaneous and combination therapies and found that [61-64]:

1. For teriparatide and alendronate, monotherapy with teriparatide gave a better BMD response than combination therapy.
2. For teriparatide and raloxifene, combination therapy gave a better BMD response than monotherapy.
3. For teriparatide and zoledronic acid, combination therapy gave more benefit in the early 6 months but this benefit was not sustained.
4. For teriparatide and denosumab, combination therapy gave a greater BMD increase than either alone.

**Table 5: Regions of action with specific effect of routinely prescribed medications**

| Medication | Spine | Hip |
|---|---|---|
| Alendronate | +++ | ++ |
| Risendronate | +++ | ++ |
| Ibandronate | +++ | ++ |
| Zolendronic Acid | +++ | ++ |
| Calcitonin | - | - |
| Raloxifene | + | [+] |
| Denosumab | +++ | ++ |
| Teriparatide | ++++ | + |

[Adapted from : Osteoporosis Essentials : Densitometry, diagnosis and management; An IOF-ISCD International course]

5. Most simultaneous combination therapies were not convincing yet [61-64].

Many studies supported the use of teriparatide and anti-resorptive drugs sequentially to be able to give drug holidays and still maintain the effect of increased BMD by the primary drug used.

## Treatment Failure

The efficacy of drug treatment in osteoporosis ultimately depends on the demonstration of a reduction in the risk of fracture.

Failure of treatment may be inferred when two or more incident fractures have occurred during treatment when serial measurements of bone remodeling markers are not suppressed by antiresorptive therapy and where bone mineral density continues to decrease.

The available evidence does not permit a firm assessment of the success or failure of a treatment. The recommendations available as of today are based on expert opinion that provides the lowest level of evidence. Three parameters that modify fracture risk and that are commonly measured in clinical practice are incident fractures, changes in BMD, and changes in markers of bone turnover and form the basis of recommendations.

### Incident Fracture

Sustaining a fracture is always an undesirable outcome, but treatments do not eliminate fracture risk; they reduce it. Thus, it is difficult to infer that a fragility fracture occurs while on treatment for at least 6 months since its initiation means that treatment has failed. Conversely, the absence of an inter-current fracture is no arbiter of successful treatment. In clinical trials, a second or third fracture during therapy is generally markedly reduced by 80–90 % in comparison to the placebo-treated [65].

Also, the natural history of fracture events is that after the index fracture, the fracture risk decreases progressively with time [66-68]. These observations provide the rationale for the working group to recommend that the occurrence of a second fragility fracture be used to infer that treatment has failed. It is important to note that not all fracture sites are associated with osteoporosis [69,70]. These include fractures of the hand, skull, digits, feet, and ankle which appear to be less responsive to interventions for osteoporosis [71].

### Bone mineral Density

An increase in BMD represents a favorable response to treatment and, conversely, that a decrease in BMD during the course of treatment is a sign of failure of treatment. The principal problem in assessing this issue is that rates of bone loss or gain are most often modest compared to the errors incurred in the measurement of BMD. Thus, a change in areal BMD is, as expected, a weak predictor of fracture risk reduction [72-75].

The change in BMD that can be confidently detected is termed the least significant change [LSC]. LSC depends upon the precision error of the technique applied and the confidence needed to assume a change. To be 95 % confident that a decrease in BMD has taken place, a change of 4 –5 % should have been observed.

### Markers of bone turnover

The treatment of osteoporosis with anti-resorptive agents is associated with an early decrease in markers of bone resorption and a later decrease in markers of bone formation.

In the case of teriparatide [or PTH 1-84], the principal index of response is an increase in indices of bone formation. Several studies suggest that, in general, the larger the decrease in turnover markers with antiresorptive agents, the greater the reduction in fracture risk [76-82]. Thus, failure to observe a change in these response variables might be considered as a failure to respond to treatment.

The role of bone markers in monitoring response to treatment has been reviewed by the International Osteoporosis Foundation, the International Federation of Clinical Chemistry and Laboratory Medicine, recommends that serum C-telopeptide of type I collagen [βCTX] and serum procollagen I N-propeptide [PINP] are considered as reference markers [83].

The working group proposes that a decrease in βCTX and PINP less than the LSC at 95% confidence is considered as an indicator of failure to respond to treatment with anti-resorptive agents and that an increase in PINP less than the LSC at 95% confidence is considered as an indicator of failure to respond to treatment with parathyroid hormone peptides.

No evidence is available on the effectiveness of alternative treatments when one has been deemed to have failed. Almost no studies have explored the issue and, therefore, the available data is scarce [84]. Some data based on indirect comparisons or surrogate endpoints can be of help [85-88]. Three general rules, based on the opinion of the working group, are recommended:

1. A weaker anti-resorptive is reasonably replaced by a more potent drug of the same class.
2. An oral drug is reasonably replaceable by an inject-

ed drug.

3. A strong anti-resorptive is reasonably replaceable by an anabolic agent.

## Monitoring Treatment of Osteoporosis

Since osteoporosis does not have any symptoms, and the earliest presentation of osteoporosis is fragility fractures, our goal of treatment is to reduce the occurrence of fragility fractures. A decrease in the incidence of fragility fracture during therapy does not necessarily mean treatment is effective. Conversely, fracture occurrence during therapy does not necessarily indicate the failure of treatment.

Serial measurement of BMD is necessary as a significant loss in BMD may be an indication for treatment and is associated with an increased fracture risk [89]. In patients already receiving treatment, it is necessary to monitor response to therapy and an increase or stable bone density is associated with fracture risk reduction [90].

It is recommended to test BMD typically 1 year after initiation or change of therapy, with longer intervals once the therapeutic effect is established. A follow-up of BMD testing should be done when the expected change in BMD equals or exceeds the least significant change. In conditions associated with rapid bone loss such as steroid therapy, testing more frequently is appropriate.

It is recommended to compare BMD values and not T-scores between two successive studies, as T-scores depend on normative database which may change with DXA machines and also with software upgrades. It is also recommended to compare BMD changes between two studies for specific sites individually.

### Clinical assessment of response to treatment

In a patient on treatment in whom no new fractures have occurred, BMD has increased and bone markers have decreased with anti-resorptive treatment, to the extent as expected from the intervention used, fracture risk is likely to be attenuated and the treatment should be maintained.

If these response criteria are not fulfilled within a year of starting treatment, modification of treatment should be considered. This includes a review of adherence, which is the most likely reason for a poor response and a search for occult secondary causes of osteoporosis [91, 92].

If adherence cannot be further improved and other causes of secondary osteoporosis are excluded, it is recommended that treatment be changed in the following circumstances [*]:

1. Two or more incident fragility fractures
2. One incident fracture and Elevated serum βCTX or PINP with or without a significant decrease in BMD.
3. No significant decrease in serum βCTX or PINP and a significant decrease in BMD.

{[*]1. Fractures of the hand, skull, digits, feet, and ankle are not considered as fragility fractures.

2. The overall decline in BMD should be in the order of 5 % or more in at least two serial BMD measurements at the lumbar spine or 4% at the proximal femur.

3. The sequential measurement of markers of bone turnover should use the same assay. A significant response is a decline of 25% from baseline levels for anti-resorptive treatments and a 25% increase for anabolic agents [PTH] after 6 months. For anti-resorptive treatments, if baseline levels are not known, a positive response is a decrease below the average value of young healthy adults. It is assumed that the response is similar between men and women.

4. Falls are an important driver of fracture. Therefore, this problem should be considered when analyzing the response to treatments.}

## Perioperative Treatment of Osteoporosis

Zoledronic acid at a dose of 5 mg administered as a yearly 15-minute intravenous infusion with the first dose being given within 90 days after hip fracture surgery significantly reduced any new clinical fracture by 35%, clinical vertebral fracture by 46% and non-vertebral fracture by 27% after a mean follow-up of 1.9 years. There was also a significant 28% reduction in all-cause mortality in the active treatment group [93].

Whether fracture healing is affected or not by anti-osteoporosis treatment is one of the most important concerns of the orthopaedic surgeon, in particular with regard to bisphosphonates that suppress bone-turnover. Animal models of fracture demonstrate that bisphosphonates delay remodeling of callus, which became larger in size but stronger in structural strength [93].

Well-designed randomized clinical trials in humans to address this important issue are lacking. A small cohort study that compared radiographic fracture healing of the distal radius in 43 patients pre-

scribed bisphosphonate therapy at the time of fracture with 153 control subjects revealed that bisphosphonate use was associated with a longer time to radiographic union [55 ± 17 days vs 49 ± 14 days]. The differences in healing time were nonetheless small [<1 week] and considered clinically insignificant [93].

Joong *et al.* in their study found that there was no delay in the healing of proximal humerus fractures fixed by locking plate fixation despite early administration of bisphosphonates. One possible explanation is the healing mechanism of proximal humerus fractures treated with locking plate fixation. The difference between cancellous and cortical bone could be another reason. In a fracture of compact long bones, where fracture bone debris must be absorbed to allow room for new bone formation, a resorption process is critical initially. However, proximal humerus fractures involve cancellous bone, in which the space for new bone formation is larger than that in compact bones. Therefore, we speculate that the healing of proximal humerus fractures stabilized by a locking plate may not be suppressed by a reduction in the resorption process by BPs owing to the spacious environment offered by cancellous bone [94].

Recently, several authors have reported that the early initiation of BPs does not delay the healing of fractures fixed by a plate or by nailing [95,96].

Eriksen *et al*. reported that the administration of zoledronic acid for more than two weeks after surgical treatment for low-energy hip fractures increased hip BMD scores and significantly reduced the risks of subsequent vertebral and hip fractures, while also decreasing mortality [97]. Dirschl et al. reported that the loss of femoral neck BMD in patients with a hip fracture was five times greater than that found in a normal population. They recommended pharmacological or some other forms of intervention during the first critical year following a hip fracture to prevent accelerated bone loss and reduce the risk of subsequent fractures during this period [98].

Li *et al* published a systematic review and meta-analysis of randomized clinical trials consisting of 10 studies with 2888 patients [2014]. They found that early administration [less than 3 months from surgery] of bisphosphonates [BPs] after surgery did not appear to delay fracture healing time either radiologically or clinically including nonunion or delayed union. Furthermore, the anti-resorptive efficacy of bisphosphonates given immediately after surgical repair should positively affect the rate of subsequent fractures. However, the bone mineral density [BMD] of total hips did significantly improve after 12 months of treatment with BPs. And most bone turnover markers of patients in the study group were significantly decreased [99].

## Surgery & Fracture Healing in Osteoporosis

Osteoporotic patients differ from normal subjects in bone mineral composition, bone mineral content, and crystallinity.

Poor bone quality in patients with osteoporosis presents the surgeon with difficult treatment decisions towards surgical treatment of osteoporotic fragility fractures or high trauma fractures that occur in patients with osteoporosis. Few studies have investigated the effects of osteoporosis itself on the bone healing process. Fracture healing has been assumed to be the same in osteoporotic bone and normal bone.

Much effort has been expended on improving therapies that are expected to preserve bone mass and thus decrease fracture risk. However, less importance has been given to investigating fracture healing in osteoporosis. Current studies mainly focus on preventing osteoporotic fractures.

Fracture healing is a complex process of bone regeneration, involving a well-orchestrated series of biological events that follow a definable temporal and spatial sequence that may be affected by both biological factors, such as age and osteoporosis, and mechanical factors such as stability of the osteosynthesis.

In recent years, literature has provided evidence of altered fracture healing in osteoporotic bone, which may have important implications in evaluating the effects of new osteoporosis treatments on fracture healing. However, the mechanics of this influence of osteoporosis on fracture healing have not yet been clarified and clinical evidence is still lacking [100].

Osteoporotic bone differs from normal bone in its reduced bone mass and deterioration of its architecture, leading to bone fragility and increased fracture risk as a consequence of the imbalance between bone formation and bone remodeling. Compromised bone strength affects anchorage of the implants and, at the fracture site, the impaired bone ingrowths and late remodeling could impair the strength of the callus and bony union [100].

Animal studies have been conducted on ovariectomized rodent animal models with a tibia or femur osteotomy. Despite some contradictory results, more studies support a delay in ossification, a decrease of 20% to

40% in the callus area, and a reduction of around 20% in bone mineral density. Mechanical properties of the callus were also disrupted, with decreased strength, decreased peak failure load, and decreased bending stiffness. The architecture was modified with thinning and disruption of the trabeculae and a decrease in connectivity [101].

Clinical data on bony healing and fracture union in osteoporosis are controversial. The failure rates of fixation in patients with osteoporosis range from 10% to 25% [102]. Despite significant effects in several clinical studies, there is so far no high level of evidence that osteoporosis, per se, increases the incidence of fracture nonunion. Cohorts of patients are heterogeneous, and randomized studies comparing osteoporotic patients with non-osteoporotic patients are missing.

Osteoporosis is closely linked with aging. Fracture healing in the elderly is compromised by the decline in the capacity of bone formation.

The loss of osteoblasts in the aging skeleton has been attributed to a decrease in the number of mesenchymal stem cells and their ability to differentiate in progenitors toward the osteoblastic lineage [103]. Due to the augmentation of life expectancy, the absolute number of fragility fractures and its corollary, the absolute number of delayed union or nonunion, increase and the consequences are an augmentation of the mortality and morbidity in this population. The main determinants for deficient fracture healing can be divided into biological and surgical factors [102].

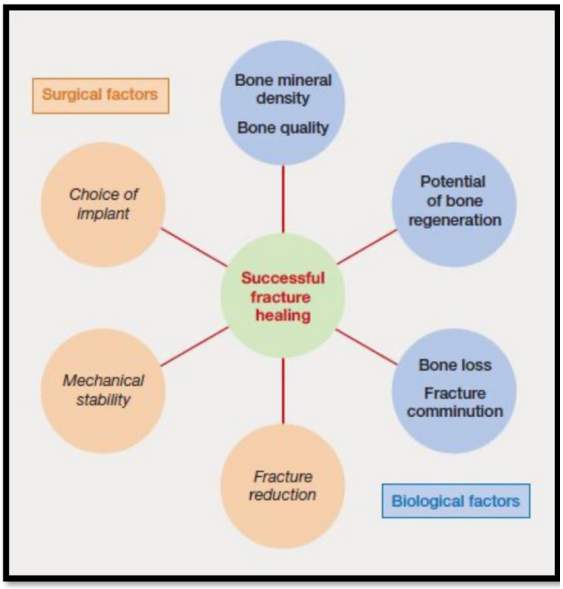


**Fig. 6: Factors influencing fracture healing in osteoporotic bones**

[Adapted from : Giannoudis P1, Tzioupis C et al. Fracture healing in osteoporotic fractures: is it really different? A basic science perspective. Injury. 2007;38[1]:590-599.]

The treatment of fragility fractures in the elderly remains challenging for the orthopaedic surgeon. The poor quality of bone and frequent fracture comminution make a fixation of osteoporotic fractures difficult, despite the development of new fixation devices like locked plating or locked intramedullary nailing, both having revolutionized fracture fixation in weak bone.

Augmentation with cement or bone substitutes may fill the bone void or enhance the strength of the fixation. As in hip fractures, where the indications of arthroplasty have been well described for a long time, some complex epiphyseal fractures [shoulder, elbow, knee], may benefit from primary prosthetic replacement. This option of replacement, instead of fixation, in comminuted articular fractures of the shoulder, the knee, or the elbow, has faster and better functional results in very elderly people, compared with a mechanically poor fracture fixation [104].

## Our Recommendations [Based on the authors' routine practice and protocols]

1. Osteoporosis by itself does not have any symptoms. The first symptom of osteoporosis may be an Osteoporotic fracture.
2. Osteopenia with added risk factors and frank osteoporosis even without risk factors must be treated.
3. T score obtained by BMD through DXA scan at all three sites [Spine, Hip and Distal radius] is gold standard for diagnosis and classification of osteoporosis.
4. Interpretation of DXA in pre-menopausal women, children, men < 50 yrs. and patients of foreign ethnicity are different as outlined above.
5. Sequential DXA [From the same machine & Software] is recommended at 1 year from starting therapy and thereafter as needed. It is better to rely on actual BMD scores rather than T score to monitor treatment.
6. Bone turnover markers and BMD [Not T score] help monitor treatment.
7. Fracture risk in osteoporosis can be determined using the FRAX model [Easily available online].
8. We consider age above 60 yrs., previous large bone fracture, history of large bone osteoporotic fracture in a close relative, steroid intake and renal dialysis to be high risk for osteoporotic fractures in our pa-

tients.

9. We recommend ensuring Calcium and Vitamin D stores are always supplemented before or concomitantly, with the beginning of therapy and throughout therapy.
10. We recommend starting Alendronate / Risedronate therapy for most patients on OPD basis as it is oral and easily available. [Particulars of oral intake need to be explained in detail]
11. We recommend IV Zoledronic acid administration for patients who are comfortable taking injectable medication and admitted / daycare patients to the advantage of once a year dosage and better compliance.
12. We recommend bisphosphonates not be given in patients with renal and cardiac disease as conclusive literature is yet unavailable.
13. We prefer to give teriparatide in elderly patients, patients undergoing long bone fracture surgery, and patients with previous long bone or vertebral fractures who currently have T scores in osteoporotic range.
14. We recommend alternation of teriparatide [12 - 18 months] and bisphosphonates [3 - 5 years] in whichever order necessary, especially during the drug holiday period.
15. We recommend usage of Calcitonin nasal spray along with bisphosphonate or another line of treatment for its analgesic and spine specific action in patients with osteoporotic vertebral fractures.
16. We recommend the usage of Denosumab only for admitted patients or as an alternative to bisphosphonates because of higher expenses.
17. We prefer to give bisphosphonates after 6 weeks of fracture treatment. For some patients who might travel or would be unavailable for follow up, we suggest IV zoledronic acid at the time of discharge post-surgery. Teriparatide can be started as soon as the next day after surgery.
18. We do not use raloxifene or other SERMs in our routine practice.
19. We prefer to repeat DXA scans at 1, 3, 5, and 10 years after initiation of treatment, or earlier if deemed necessary.
20. We recommend following strict principles of osteosynthesis, respect towards fracture biology and soft tissues, and the use of established fracture fixation and stabilization techniques while dealing with osteoporotic fractures and fractures in osteoporotic patients.

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