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Frequent Asked Questions

Lifetime Treatment and Prevention of Osteoporosis

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What is Osteoporosis?

Osteoporosis is a metabolic bone disease characterized by low bone mass and micro architectural deterioration of bone tissue, leading to bone fragility and a consequent increase in bone fracture risk¹.

The World Health Organization (WHO) cutoff of -2.5 Standard Deviation (SD) Tscore (Tsc) of the mean bone mineral density (mBMD) by Dual X-ray Absorptiometry (DEXA) is used for the diagnosis of osteoporosis². When measuring osteoporosis it is preferable to express Tsc in percentage than in -2.5. It is more comprehensible, the moment we read the computer printout of the measurements and compare it with the previous one.

Is Osteoporosis a new disease?

No, osteoporosis is as old as human civilization. Hippocrates described thinning and tendency to fracture of the bones in the aged. Only the last 50 years, medical science has begun to shed some lights on the nature of the disease.

Why is everybody so concerned about Osteoporosis nowadays?

The electronic media in particular the daily TV advertisements in promoting the sales of milk and milk products daily induce awareness of osteoporosis in the community. This a good thing, but on the other hand it creates misinformation what milk and milk products can do against osteoporosis.

Can food supplements prevent or be used for treatment of Osteoporosis?

No, milk, milk products, and calcium in tablets, liquid, and powder are food components that everybody must take daily to grow and remain healthy until old age. These are not medicines to cure or prevent osteoporosis. To treat and prevent osteoporosis we require adequate nutrition and this includes milk and milk products.

What is Osteopenia?

Osteopenia is one of the osteoporotic grades of the BMD

Table 1 Classification of osteoporotic grades

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0. DEXA > -1 SD of mBMD (mean Bone Mineral Density) is **normal bone**
 1. DEXA -1 to -2.5 SD of mBMD is **osteopenia** (low bone mass)
 2. DEXA < -2.5 SD of mBMD is **osteoporosis**
 3. DEXA < -2.5 SD of mBMD plus > 1 fragility fracture(s) is **severe osteoporosis**
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These measurements are based on the comparison of a patient's BMD with mBMD of healthy women of 25-49 years of age³. Outcome of measurements of BMD cannot differentiate between primary and secondary osteoporosis.

What is a risk factor for Osteoporosis?

A risk factor is a variable that is definitely associated with osteoporosis. Fracture risk increases with $1.5 \geq 3X$ for each SD decrease in BMD⁴. The risk of hip fracture increases in women with increases of the length of the femoral neck⁵.

For Caucasians at 50 years of age the lifetime risk of fracture are 40% and 13% for women and men respectively.

What are the protective factors against Osteoporosis?

Factors that confer protection against development of osteoporosis are a long period between menarche and menopause, past use of the contraceptive pill⁶, and high BMD.

What is the age contribution to hip fracture?

The contribution of Peak Bone Mass (PBM), skeletal, and extra skeletal factors to hip fracture vary with age. The reasons are for any given BMD, the risk of fracture is greater in the elderly, because of an increased tendency to fall, the type of fall, the loss of protective soft tissue covering, and a decreased ability to react appropriately to diminish the force of the impact of falling. This indicates a larger contribution of age to risk of hip fracture compared with BMD in the elderly⁷.

What are the risk factors for Osteoporosis?

The risk factors for osteoporosis are various and complex in their interrelationships and associations in table 2.

Table 2. Risk factors for Osteoporosis**Disease-induced**

Autoimmune diseases	: rheumatoid arthritis, ankylosing spondylitis, systemic lupus erythematosus, reactive arthritis, etc.
Endocrine disease	: primary hyperparathyroidism, thyrotoxicosis, Cushing's syndrome, Addison's disease
Hematological disease	: Multiple myelomas, systemic mastocytosis, lymphomas, and pernicious anemia
Gastrointestinal disease	: mal absorption syndrome, e.g., celiac disease, Crohn's disease, gastrectomy of peptic ulcers
Chronic liver disease	: e.g., primary biliary cirrhosis
Vascular accident	: immobility due to strokes

Drug-induced

Glucocorticoid	: prednisone \geq 7.5 mg/day for > 6 months
Anti epileptic drugs	: phenytoin
Excessive substitution	: thyroxine, hydrocortisone
Anticoagulant	: heparin, warfarin

Age-induced

Genetic factors	: low body mass index and leanness ⁸ , first-degree relatives with low-trauma fracture ⁹ ,
Menstrual status	: early menopause before 45 years of age [*] , previous amenorrhea due to anorexia nervosa, Hyperprolactinemia

Environment-induced inadequate

: cigarette smoke, alcohol abuse, inadequate physical activity, low calcium diet, exposure to sunlight, vitamin D insufficiency, and previous fracture¹⁰

Sex

Women : lower Peak Body Mass (PBM), live longer, and are more prone to fall compared with men.

Treatment-induced : immobilization for fractures to heal**How is postmenopausal calcium lost?**

* Calcium absorption in the bowel and reabsorption in the kidney is oestrogen-dependent¹¹. That is why postmenopausal women lose calcium through the urinary tract. This is coupled with inadequate absorption from the bowel. A normal serum level is maintained by adsorption of calcium from the bones. Ultimately, osteopenia, osteoporosis, and fractures ensue if oral and/or parenteral calcium is not supplying this requirement. A higher daily

dosage of calcium is required to maintain intestinal absorption and retain a normal serum calcium level in postmenopausal women.

What is corticosteroid-induced Osteoporosis?

Corticosteroids are notorious drugs for their associated high risk for development of osteoporosis and fractures. Nevertheless, they are required for treatment of chronic diseases such as allergic dermatitis, autoimmune diseases, bronchial asthma, etc. Bone is lost rapidly in patients exposed to daily supra physiological levels of corticosteroids and corticosteroid-induced osteoporosis results.

How does corticosteroid-induced Osteoporosis develop?

Glucocorticoids promote osteoblasts and osteocytes apoptosis (programmed cell death). Osteoclast number, trabecular spacing, and the number of trabeculae are not affected by corticosteroids. The primary effects of corticosteroids are a decrease in the number of osteoblasts and reduced bone formation resulting in a time- and dose-dependent reduction in BMD. As trabecular bone has a higher surface-to-volume ratio compared with cortical bone, the former incurs a greater BMD loss than the latter.

How much BMD is lost after oral corticosteroid?

After only 20 weeks (< 5 months ingestion of prednisone 7.5 mg/day, 8% of spinal bone mass can be lost¹². After 5 years intake of daily 7.5 mg Prednisone, the integral bone mass of the spine and proximal femur falls to 80% of the baseline values¹³. The 5-year probability of fracture was 34% in Caucasian females on ≥ 5 mg/day of prednisone¹⁴. Deflazacort is claimed to be a bone-sparing corticosteroid, but proved to induce bone loss similar to prednisone¹⁵.

Can corticosteroid-induced osteoporosis recovers?

Corticosteroid-induced osteoporosis is reversible after withdrawal of the drug, albeit a long-term recovery is required in losses of > 60% BMD. Recovery to normal bone density may be reached after months to years of euadrenalism^{12,16}. This slow recovery of bone density account for the finding that alternate-day administration of corticosteroid is not bone-sparing¹⁷.

What is the risk of oral corticosteroid?

One-third of the patients experienced osteoporotic fractures after using corticosteroid for 5-10 years or in Cushing's syndrome due to substantial reduction in BMD^{18,19}. Therefore, corticosteroid administration to patients who are in postmenopausal status and reduced physical activity should be no longer than a few months. At least the benefits of corticosteroid ingestion should be weighted against the risk of osteoporotic fractures on long-term administration.

How is Osteoporosis diagnosed?

The patient BMD is measured by DEXA for total forearms, total spine, and total hips or specific location such as the knees, elbows, and shoulders in Tsc expressed in percentages or figure. Whole body BMD can be measured.

What are the clinical symptoms of osteoporotic fractures?

The clinical manifestation of osteoporosis is fragility fracture, which causes symptoms. Hip fracture usually causes pain and immobility. Wrist fracture induces pain and dysfunction. Vertebral fracture is the most frequent osteoporotic fracture, which often occurs with slight or no symptoms at all. The most common sites of fractures (in order of decreasing frequency) are located in the lumbar spine, proximal femur, and distal radius.

What are the indications for treatment of Osteoporosis?

Treatment of osteoporosis is indicated when a DEXA:

1. Tsc < -2.5 SD in the presence of other risk factor in Table 2
2. Tsc < - 1 within 5 years after the menopause
3. Zsc < - 1 at the lumbar spine or proximal femur at any age requires prevention of further bone loss.
4. Zsc < - 2 requires further identification of a major risk factor.

What are primary and secondary Osteoporosis?

Primary osteoporosis is caused by loss of BMD by advanced age in men and women and insufficiency of estrogen

after menopause. Secondary osteoporosis is caused by various risk factors in table 2, e.g., disease, drug, therapy, and environment-induced ones. In men secondary causes of osteoporosis are more common (55%), e.g., hypogonadism, corticosteroids abuse, myeloma, and chronic alcoholism.

What is Remaining Lifetime Fracture Probability (RLFP)?

BMD represents a composite, cumulative index of previous and current skeletal life. A single measurement of BMD, at a point in time, provides information about current fracture risk. This information may be adequate for therapeutic decisions making, but not sufficient for prevention decisions making. Therefore, the concept of Remaining Lifetime Fracture Probability (RLFP) was introduced, which takes into account previous and current major risk factors.

How to treat Osteoporosis?

Treatment of osteoporosis is lifetime and dependent on the percentages of BMD lost. The mean annual increase of BMD by oral bisphosphonates is around + 1.5%. A BMD loss of more than < -85% at 80 years of age will take 20 years of oral bisphosphonates to increase to + 30% of bones. By this time the patient has reached the age of 110 years to achieve BMD loss of -55% from -85%. Intravenous bisphosphonate (Zoledronic Acid) solves the problem by annual increase of BMD of > 30%.

When do you apply intravenous (IV) Zoledronic Acid (ZA) in osteoporosis (BMD more than \leq - 50%)?

Personal communication: IV ZA is applied when

1. DEXA BMD is – 80%. The IV ZA a 4 mg is administered 3X, every week once. After 3 months another DEXA measurement is taken.
2. If BMD is – 60% another Seri of IV ZA a 4 mg is given 3X, every fortnight once. Another DEXA measurement is taken after 3 months
3. When the BMD is –50% the IV ZA can be repeated 3X, once every month if there is a previous osteoporotic fracture. Otherwise therapy is switched to oral bisphosphonates.

How do you monitor the BMD in IV ZA therapy?

Three months after IV ZA the BMD measurement should be repeated. A good response but BMD still < - 50%, the Seri of 3X IV ZA should be repeated. Notwithstanding that the increase of BMD may continue longer than 3 months. The IV ZA therapy must not be given in > 3 Series in 1 year as annoying anorexia may last > 1 month.

How do you treat Osteoporosis by oral route?

When BMD is < -50% once weekly oral bisphosphonate plus adequate daily mineral and calcium (calcium taken at bedtime has a greater effect on bone resorption)²⁰ and vitamin, regular weight bearing exercises, avoidance of cigarette smoke and excessive alcohol consumption. Further prevention of falls, improving cognitive function, and provision of hip protective devices in the elderly is recommended.

How do you monitor the BMD during lifetime oral therapy?

Initially, the BMD should be measure once every 6 months to see a good response to oral therapy. After 2 years monitoring could be done once annually or even biannually.

What about Hormone Replacement Therapy (HRT)?

Estrogen replacement therapy for osteoporosis is now a controversial issue and has been abandoned by women in the USA. The risk of mamma and cervical carcinoma by long-term application of HRT is real. Hormone replacement therapy is now not recommended to postmenopausal women.

What is the way out?

One of the tissue specific estrogen analogs, Raloxifene (RLX), has been used in the last 5 years with beneficial effects on the bone (fracture risk reduced), heart (myocardial infarct), and brain (stroke), but without stimulating the endometrium or without breast and cervical cancer risk²¹.

What therapeutic agents are available for treatment of osteoporosis?

Calcitriol, calcitonin²², bisphosphonates (intestinal absorption < 10% on an empty stomach), Raloxifene, fluoride

salts, anabolic steroids, ipriflavone, and alfacalcidol should not be utilized without measurement of BMD, except in those with previous osteoporotic fracture. The Series of IV ZA should be applied only when BMD is more than - 80% or - 50% plus previous osteoporotic fracture(s) (Personal communication).

What is the goal of the treatment of Osteoporosis?

The goal of therapy of osteoporosis is to halve the risk of a fracture and a new fracture should not discourage continuing treatment.

Why is Osteoporosis detected only after a fragility fracture?

Many people with osteoporosis remain unrecognized and untreated until a fracture occurs. There are no signs and symptoms until the bone breaks. Osteoporosis is called the silent thief who steals your bone (BMD) stealthily until it breaks.

Can Osteoporosis be treated?

Yes, osteoporosis can be treated and fracture prevented. However, osteoporosis is hardly treatable after a fracture and treatment is very expensive.

Can Osteoporosis be prevented?

Osteoporosis is lifetime cheaply preventable in appropriate lifestyle and adequate nutrition

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