Osteoporosis: Risk Factors, Diagnostic Methods And Treatment Options

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Citation

Abstract
Osteoporosis afflicts more than 25 million Americans, causing 1.3 million fractures yearly at a cost of $10 billion. There are multiple risk factors for osteoporosis including postmenopausal women not on hormonal replacement therapy, chronic medication use (glucocorticoid therapy, heparin), hyperthyroidism, hyperparathyroidism, hypogonadism, secondary amenorrhea, and vertebral abnormalities. Current diagnostic techniques measure bone density via Dual-Energy X-ray Absorptiometry (DEXA) and Quantitative Computed Tomography (QCT) from various sites including the spine, hip and forearm. Therapeutic regimes include estrogen replacement therapy through oral and transdermal routes, calcium supplementation, vitamin D replacement and bone reabsorption inhibitors such as calcitonin or alendronate sodium (Fosamax). Osteoporosis is a treatable, often preventable disease. Preventative and therapeutic treatment should be given before signs occur or as early in the disease as possible.

INTRODUCTION
Osteoporosis is “a disease characterized by a loss of bone below the level required for mechanical support of normal activity and an increased occurrence of nontraumatic fractures”\textsuperscript{1}. In other words, it is a disease that gradually weakens the bones, causing them to become brittle and break easily. Osteoporosis is a metabolic bone disorder characterized by a diffuse decrease in the amount of bone. There are two types: Type I resulting from increased bone destruction (ex. post-menopausal) and Type II from decreased bone formation (ex. excessive steroid use).\textsuperscript{2}

EPIDEMIOLOGY
More than 25 million Americans have osteoporosis and 80% of those are women.\textsuperscript{3} Osteoporosis causes over 1.3 million fractures yearly with 500,000 vertebral fractures, 250,000 hip fractures and 240,000 wrist fractures costing $10 billion annually.\textsuperscript{3} It has been estimated that women at age 50 have over a 40% chance of developing osteoporosis throughout the rest of their lives. The risk of a hip fracture is equal to a combined risk of uterine, breast and ovarian cancer. Of those suffering hip fractures, the mortality rate is 20%, while 50% never fully recover.\textsuperscript{3}

ETIOLOGY
Osteopenia (low bone mass without demonstrable fractures) and osteoporosis result from bone destruction (osteolysis), decreased bone formation or both.\textsuperscript{2} Bone resorption occurs via osteoclasts that destroy bone during the remodeling process through parathyroid hormone (PTH)-mediated cytokines. These cytokines cause calcium resorption from bones while osteoblasts make collagen to form osteoid, a precursor of bone, during remodeling. When bone destruction occurs faster than bone formation, osteopenia and/or osteoporosis can occur.\textsuperscript{2} Osteoporosis occurs more frequently in women, especially in the postmenopausal period as estrogen deficiency causes an increase in the PTH-mediated cytokines.\textsuperscript{2,4} Estrogen may also decrease calcium excretion from the renal system\textsuperscript{5} providing a protective effect against osteoporosis.

CLINICAL MANIFESTATIONS AND RISK FACTORS
Typical symptoms of osteoporosis are back pain (often of sudden onset and associated with vertebral stress compression or compression fractures), loss of height, dorsal kyphosis, and cervical lordosis (known as “dowager’s hump”).\textsuperscript{2} Hip fractures can occur spontaneously or following mild to moderate trauma.\textsuperscript{2} However, osteoporosis often presents as asymptomatic compression of vertebrae that occurs slowly without pain or curvature of the spine.\textsuperscript{2}
A variety of risk factors for osteoporosis exist including endocrine abnormalities, chronic medication use, vertebral abnormalities, and gastrointestinal disorders (see Table 1).2,5,6 The largest population affected is postmenopausal women, especially those not currently receiving estrogen replacement. Premenopausal risk factors include women with surgical menopause, oligomenorrhea, amenorrhea, or anorexia. Underlying physiological conditions, such as hyperthyroidism, hyperparathyroidism, hypercortisolism, and hypogonadism in men, must be considered.2,5,6 Preventable risk factors include smoking, alcohol abuse, high caffeine consumption, and calcium and Vitamin D deficiencies.2,5,6

Table 1: Risk Factors For Osteoporosis

**ENDOCRINE**

- Postmenopausal women not receiving estrogen replacement or not beginning therapy within the first five years after menopause
- Early menopause (before age 45)
- Hypogonadism in men
- Hyperthyroidism
- Primary hyperparathyroidism
- Hypercortisolism (Cushing’s syndrome)

**MEDICATIONS**

- Excessive thyroid hormone replacement
- Long-term glucocorticoid therapy
- Chronic use of certain anticonvulsants, heparin or methotrexate

**VERTEBRAL ABNORMALITIES**

- Ankylosing spondylitis
- Rheumatoid Arthritis
- Degenerative joint disease
- Osteopenia on radiograph
- History of bone fractures
- Patients on osteoporotic therapy to assess response to therapy

**GASTROINTESTINAL DISORDERS**

- Subtotal gastrectomy
- Malabsorptive disorders
- Chronic obstructive jaundice
- Primary biliary cirrhosis
- Severe malnutrition (including anorexia nervosa)
- Crohn’s disease

**MISCELANEOUS**

- Family history of osteoporosis
- Alcoholism
- Smoking
- Immobilization
- Chronic Obstructive Pulmonary Disease
- Systemic mastocytosis
- Disseminated carcinoma

**DIAGNOSTIC EVALUATION**

Conventional x-ray techniques cannot detect problems until there is at least 30% bone mass loss, whereas bone densitometry can detect significant changes earlier. Bone densitometry measures the calcium content of bone and requires no preparation, injection or medication and is painless, safe and noninvasive. Bone density studies can effectively diagnose and monitor osteoporosis, estimate future risk of fracture, and assess the effect of glucocorticoid or excessive thyroid hormone use. Densitometry is also used to assess surgical necessity in patients with primary hyperparathyroidism.

Bone densitometry measures bone density from various sites such as spine (L1-L4), hip, and forearm. Bone mineral density (BMD) of patients is compared with the mean peak BMD of young adults of same sex and given in terms of standard deviation. One to two standard deviations below normal is considered osteopenia, while greater than two standard deviations is indicative of osteoporosis. This can provide the diagnosis of osteoporosis years before fractures.
occur.

Two common bone densitometry methods are Dual-Energy X-ray Absorptiometry (DEXA) and Quantitative Computed Tomography (QCT). DEXA safely and precisely assesses skeletal mineral content of hip and spine by noninvasive, 2-dimensional projection system. It has short scan times (10-15 minutes), low radiation exposure (approximated to be less than a dental roentgenogram), improved spatial resolution for easier identification of the vertebra and better precision. All of this can enhance the prediction of bone strength and fracture risk. QCT offers a cross-sectional view of the vertebrae only and requires up to 100 times the radiation dose of DEXA. Accuracy may be decreased in patients with severe osteopenia and/or kyphosis because of difficulty in positioning the patient. Currently, ultrasound and MRI are not conclusive in diagnosis.

**TREATMENT**

Several modalities are available to prevent and/or treat osteoporosis. The most effective form of prevention to date is estrogen replacement. Common routes of administration are oral and transdermal; percutaneous and subcutaneous routes are also available. Recommended dosages are: oral dosage- Premarin™ 0.625 mg/d (conjugated equine estrogen), Estrace™ 1 mg/d (micronized estradiol), or Estinyl™ 20 ug/d (ethinyl estradiol) and transdermal-Estraderm™ or Climara™ patch delivering 0.05 mg/d of 17 B- estradiol. Progestin should also be given continually to women without surgical menopause to decrease or eliminate monthly bleeding and reduce the increase risk of endometrial cancer with unopposed estrogen.

Although calcium does not protect against osteoporosis on its own, 1500 mg/d of calcium supplementation should be taken daily along with Vitamin D 400 IU/d in adults and 800 IU/d for elderly women. Calcium supplementation improves peak adult bone mass. However, controversy exists as to the overall effectiveness of calcium administration alone. Vitamin D is necessary for intestinal calcium absorption and for bone precursor formation in the osteoblasts. Exercise is also very important as it initiates the bone-remodeling process by stimulating bone cells and building bone mass. Although no precise exercise program has been established, programs combining aerobic, muscle strengthening and weightbearing activities increase muscle strength and skeletal stability which helps decrease the risk of falls.

Patients exhibiting osteoporotic changes on estrogen replacement therapy, those with contraindications for estrogen (ie. endometrial or breast cancer, thrombosis during treatment, hepatitis, or liver disease) or males should have other methods implemented to inhibit bone resorption. Calcitonin, a polypeptide hormone secreted by the parafollicular cells of the thyroid gland5, used to be the main modality to prevent reabsorption of bone. It is given in a synthetic injectable form as Calcimar™ at a daily dosage of 100 units SQ or IM. Calcitonin is now available in a nasal spray as Miacalcin™ Nasal Spray, 200 units intranasally daily in alternating nostrils. Transient side effects include nausea and flushing, however an added benefit of calcitonin is that of a skeletal analgesic, as many patients with osteoporosis suffer from back pain.

A fairly recent addition to the market is Fosamax™ (alendronate sodium), a synthetically made bisphosphonate, that suppresses osteoclast-mediated bone resorption. It is given orally as a 10 mg tablet and it is imperative the medication be taken on an empty stomach every morning with eight ounces of water thirty minutes prior to other medications, food, or liquids. The patient should remain in an upright position during the first thirty minutes to prevent the pill from remaining in the esophagus causing irritation and/or ulceration. Patients should be given these instructions both verbally and in writing when prescribed to prevent side effects caused by improper consumption or possible interference with absorption.

Patients can be treated simultaneously with hormonal replacement therapy and Fosamax™ (alendronate sodium) or Calcimar™/Miacalcin™ (calcitonin) when appropriate. Treatment progress can be monitored on a yearly basis via bone densitometry studies.

**CONCLUSION**

Osteoporosis is a treatable disease and in some cases, preventable. If treatment is begun early, patients can be spared pain and suffering and likely lower the overall health cost incurred from treatment of osteoporosis complications (ex. hip and spinal fractures). Preventative and therapeutic treatment should be given before signs occur or as early in the disease as possible.

**References**

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