

# Perspectives In Neuroscience



A Quarterly Publication for Continuing Medical Education

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## Current Management of Osteoporotic Spine Fractures

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This quarterly publication is designed for primary care physicians, neurosurgeons, neurologists, neuroradiologists, and other practitioners. The purpose of this publication is to provide these physicians with current management strategies for dealing with a variety of disorders and conditions in the neurosciences, and to provide up-to-date diagnostic and prognostic information written by specialists in the field. It is estimated that it will take the physician 1 hour to complete the activity. The 10 questions at the end of each lesson are designed to test and evaluate the participants' comprehension of the topic. This CME program is sponsored by the Central Illinois Neuroscience Foundation and funded by grants and donations. This CME activity was planned and produced in accordance with the Illinois State Medical Society's Essential Areas for Continuing Medical Education. The Central Illinois Neuroscience Foundation is accredited by the Illinois State Medical Society to sponsor continuing medical education for physicians. The Central Illinois Neuroscience Foundation designates this activity for a maximum of 1 hour of Category I credit towards the American Medical Association's Physician Recognition Award. It is the intent of the Central Illinois Neuroscience Foundation to assure that its educational mission, and Continuing Medical Education activities in particular, is not influenced by the special interests of individuals associated with its program.

*Dr. Ricardo Vallejo has no financial arrangements or affiliations that would constitute a conflict of interest with any corporation organization and this sponsoring institution.*

### OBJECTIVES

At the conclusion of this CME activity, the participants should be able to:

1. Describe risk factors associated with osteoporosis.
2. Outline the preventative measures that should be discussed with patients at risk for osteoporosis.
3. Identify the current treatment options for patients with or at risk for osteoporosis.
4. Recognize the interventional procedures available for patients suffering vertebral body fractures.

### INTRODUCTION

Osteoporosis is a major health problem that will continue to expand as the average age of United States citizens continues to

rise. Traditionally it has been recognized by the occurrence of its associated complications: non-traumatic fractures of the spine and hip in the presence of low bone mass. This issue of Perspectives in Neuroscience will define both primary and secondary osteoporosis, and identify risk factors and preventative measures that may help avoid the devastating complications associated with this disorder. Current treatment options for traumatic and non-traumatic compression spine fractures will be reviewed.

### DEFINITION

The World Health Organization defines osteoporosis as levels of bone density more than 2.5 Standard Deviations (SD) below the young adult mean. The condition is characterized by low bone mass and microarchitectural deterioration of bone with consequent bone fragility and increased risk of fractures.<sup>14,15</sup> In the presence of reduced bone mass, other contributing factors which increase the risk of fractures include the propensity to fall in the elderly, qualitative changes in bone structure and variability in bone geometry.<sup>16,17</sup>

### EPIDEMIOLOGY

Osteoporosis is now recognized as one of the most common and serious problems facing postmenopausal women and aging persons of both sexes. Progressive aging of the population in developed countries of North America, Europe and Japan and exponential increases in the population of undeveloped countries will result in a corresponding increase in the number of fractures that occur because of the direct relationship of fracture rate to age.<sup>18</sup>

Extrapolation of the results of epidemiologic studies in Rochester, MN, in 1986, estimated that 1.5 million fractures are due to osteoporosis in the United States. These include 700,000 vertebral fractures, 250,000 hip fractures, 250,000 wrist fractures and 300,000 fractures of other limb sites.<sup>18</sup> Caucasian females are especially at high risk for the development of osteoporosis. The lifetime risk for a clinically evident fracture in a 50 year old Caucasian female is 15.6% for vertebral body fracture; 16.0% for hip fracture and 15.6% for wrist fracture, with a conjugated risk of 39.7% for any of them. The risk in African and Asian populations is about half of that for Caucasians.<sup>18</sup>

The prevalence of osteoporosis in men is often overlooked. One third of all hip fractures occur in men, with about 2 million Americans affected and 3 million at risk for this disease. Of all male populations, Caucasian men appear to have the greatest risk for developing osteoporosis.



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Data from 1986 calculated 492,000 hospitalizations, 4,290,000 hospital days, 83,000 nursing home stays with an average of 1 year, and 2.3 million physician visits, as a direct cost of osteoporotic fractures. The direct economic cost in 1986 was around 5-10 billion dollars per year.<sup>19</sup>

Although most of the mortality associated with osteoporosis is due to hip fractures, a high incidence of co-morbidity should not be neglected. Patients affected with hip fractures may develop pressure ulcers, pneumonia, urinary tract infection and severe depression. Despite the fact that not all vertebral body fractures are symptomatic, about one third of the patients complain of severe pain with associated loss of height and kyphoscoliosis. All these symptoms, as well as the therapies which may include potent analgesics and prolonged bed rest, interfere with the patient's daily activities and may lead to severe depression.

## ETIOLOGY

Throughout childhood and adolescence, bones grow in length and density. Maximum height is achieved approximately at the age of 20, but peak bone density is attained about age 30. Many factors affect the development of osteoporosis, including heredity, diet, sex hormones, physical activity, smoking, general health and the use of certain medications. After age 40 to 50, cortical bone is lost at a rate of 0.3 to 0.5% per year. Near menopause, women start to experience an accelerated loss of cortical bone superimposed to on the age-related loss. Females are more affected by osteoporosis than men, probably due to smaller and less dense bones as well as to hormonal changes.

There is a close relationship between estrogen deprivation and the development of osteoporosis. Estradiol, formed primarily by the ovaries, decreases drastically after menopause. It has been demonstrated that estrogens inhibit the secretion of interleukin 1 (IL-1) and tumor necrosis factor? (TNF?) which enhance osteoclastic activity. These cytokines may also stimulate the production of IL-6, the most important cytokine in the recruitment of osteoclasts in the abnormal bone remodeling in postmenopausal osteoporosis. The loss of bone is not uniform, as demonstrated by dual-energy x-ray densitometry. Rate of bone loss is greater in the metacarpals, the femoral neck, and the vertebral bodies.

Besides menopause, other risk factors for osteoporosis are included in Table 1:

**Table 1: Risk factors for osteoporosis**

Female sex	Surgical bilateral oophorectomy
Chronic use of steroids	White or Oriental race
Hemiplegia	Sedentary lifestyle
Thin body habitus	Psychotropic drugs
Chronic kidney disease	Increasing age
Smoking	Malnutrition
Low calcium intake	Alcohol abuse
Low testosterone	

## CLASSIFICATION

In some situations, osteoporosis is a manifestation of another disease, like Cushing's syndrome or osteogenesis imperfecta. However, most commonly, no other disease is apparent. Type I, or primary, osteoporosis occurs in postmenopausal women and is characterized by an accelerated and disproportional loss of trabecular

bone. It affects more frequently the vertebral bodies and the distal forearm. Decreased parathyroid function may be compensatory to an increase in bone resorption.

Type II, or secondary, osteoporosis occurs in women and men over the age of 70 and is associated with loss of both cortical and trabecular bone. It occurs more frequently in the femoral neck, proximal humerus, proximal tibia and pelvis.

For secondary causes of osteoporosis see Table 2.

**Table 2: Secondary causes of osteoporosis**

Cushing's disease	Use of certain drugs, e.g.:
Multiple myeloma	corticosteroids
Inflammatory bowel disease with associated malnutrition	chemotherapeutic agents
Chronic renal failure	heparin
Prolonged immobilization	barbiturates
	valproic acid
	gonadotropic releasing hormones
	aluminum-containing antacids in excess

## DIAGNOSIS

Osteoporosis is a generalized disorder of the skeleton, but the major sequelae result from fractures of the hip, vertebral bodies, wrist and humerus. Most often the diagnosis is only suspected when a complication is noted. Early detection is based on patient's risk factors, history, physical signs and radiological testing.

Bone density is now most commonly measured by dual-energy x-ray absorptiometry (DXA), although quantitative CT may also be used. Bone mass has been shown to correlate with skeletal fragility and fracture risk. DXA can measure bone density at any skeletal site with a precision of 1-2%.<sup>18</sup> Bone mass is typically compared to the peak bone mass achieved in a person's second and third decade of life. Deviations from the peak are described in standard deviations (SD). For each 1 SD decrease in bone density of the femoral neck there is a 2.4-fold increase in age-adjusted hip fracture risk.<sup>20</sup> Cross sectional studies have shown that fractures occur most often in individuals with low bone density, independently of the age, race, sex, or the site measured.

Indications for bone mass measurement are included in Table 3<sup>21</sup>:

**Table 3: Indications for bone mass measurement**

1. Estrogen deficient woman (s/p oophorectomy or post menopausal)
2. Individuals receiving long term glucocorticoid therapy or methotrexate
3. Individuals with primary hyperparathyroidism
4. Individuals with vertebral abnormalities
5. Follow up assessment of response to osteoporosis drug therapy
6. Prolonged use of excessive thyroid replacement
7. Prolonged immobilization
8. Rheumatoid arthritis or ankylosing spondylitis

## THERAPY

### Prevention

Given the magnitude of the problem, the only cost-effective approach is prevention. The first priority is to eliminate major risk factors. This should include educational programs for health professionals and lay people, campaigns to decrease alcohol and tobacco abuse, unnecessary use of steroid hormones and excessive use of thyroid hormones. Supplementation of the diet with calcium and vitamin D may be indicated except in a small subset of the population affected by hypercalcemia or active kidney stone disease. Weight bearing exercises can also be helpful in building and maintaining bone mass.

### Drug therapy

Drug therapy aiming to decrease bone mass turn over include the following:

1. Hormone replacement therapy (HRT) in the form of estradiol 17 $\beta$  should be considered in perimenopausal women. Despite the many benefits of HRT, including relief of menopausal symptoms and decreased risk of ischemic heart disease, the desire to avoid menstruation and concerns regarding uterine and breast cancer may prevent some patients from accepting this therapy. The addition of progesterone to HRT may offset the risk of uterine cancer, but with prolonged use of estrogen (>10 years), there may be an increase risk of developing breast cancer. The ultimate decision should be made on a case by case basis after discussing the benefits and risks with the patient.
2. Biphosphonates (Alendronate, Pamidronate, Risedronate), are agents that inhibit the activity of osteoclasts. In clinical trials they have been shown to slow bone loss, increase bone density and reduce fracture risk. Side effects are uncommon and include: esophageal irritation, abdominal or musculoskeletal pain, nausea and heartburn.
3. Calcitonin inhibits the activity of osteoclasts and bone resorption. It does not build bone mass, but slows bone loss. Calcitonin may partially relieve pain in patients with bone fractures. Salmon calcitonin is the most frequent form used, and may be given subcutaneously, intramuscularly or nasally.
4. Selective estrogen receptor modulators (SERMs) act as weak estrogen in some organ systems as well as estrogen antagonist in others. Its use has been shown to increase bone mass density at the spine, hip and total body, but to a lesser extent than HRT or biphosphonates. Raloxifene, the first SERM approved by the FDA, decreases the risk for ischemic heart disease but fails to relieve hot flashes. Unlike HRT, raloxifene does not cause vaginal bleeding or breast tenderness.

### Interventional therapies for vertebral body fractures

Vertebral fractures are associated with significant declines in health and functional activity. Osteoporosis, whether age related or secondary to the use of steroids, is the most common cause of vertebral body fractures in the United States.<sup>1</sup> VBF may also be secondary to tumor infiltration. The most frequent malignant lesions of the spine include osteolytic metastasis and myeloma. Prolonged survival with current cancer therapy prolongs life expectancy, but increases the chance for these patients to develop metastatic vertebral involvement and collapse.

Osteoporotic compression fractures occur in more than 500,000 patients per year in the United States and are more frequent than hip fractures.<sup>2</sup> In the United States, VBF account for 150,000 hospital admissions, 161,000 physician office visits, and more than 5 million restricted activity days annually. Women with clinically diagnosed

VBF have a 15% higher mortality rate than women who do not.<sup>3</sup> One third of VBF are clinically manifested. The estimated prevalence of vertebral fractures increases steadily with age, reaching 40% in 80 year old women.<sup>3</sup> According to Kado et al., women with VBF were 2 to 3 times more likely to die of pulmonary causes than those without fractures. This finding could not be explained by long-term corticosteroid or tobacco use. Severe kyphosis was a strong predictor of pulmonary deaths perhaps due to underlying lung disease and decreased respiratory reserve.<sup>3</sup> There is 9% decrease in predicted force vital capacity per vertebral fracture.<sup>4</sup> Osteoporotic vertebral fractures also affect the musculoskeletal system and cause chronic pain, functional disability, changes of mood and impairment in quality of life.<sup>5</sup>

Despite the efforts to prevent osteoporosis, by the early use of calcium and vitamin D supplements, exercise, smoking cessation and biphosphonates and calcitonin treatment, compression fractures, requiring pain control are still a major health problem. Therapeutic options for compression fractures include acetaminophen, non-steroidal anti-inflammatory (NSAIDs), narcotic analgesics and bracing. This conservative therapy may be useful in some patients, but carries the risk of significant side effects related to the use of these medications in elderly patients. The added risk of protracted immobilization predisposes secondary complications like atelectasis, pneumonia, and/or pulmonary embolus.<sup>1</sup>

An area of growing interest is minimally invasive surgical management of acute vertebral body fractures (VBF).

Acrylic cements have been used for augmentation of weakened bones for decades.<sup>5</sup> The first image guided percutaneous vertebroplasty was described by Deramond and Galibert in France in 1987.<sup>6</sup> There are two current methods for the injection of cement into the fractured vertebral body.

Percutaneous vertebroplasty (PVP) consists of passing an 11 gauge cannula percutaneously through the pedicle into the vertebral body. Once in the junction of the anterior third with the two posterior thirds of the vertebral body, cement is injected into the body to increase strength and support. Patients usually require only sedation and local anesthetic at the site of needle placement for the performance of this procedure. Jensen et al.,<sup>7</sup> reported 90% pain relief in 29



**Figure 1.** Sagittal MRI, T2 image, showing cement in the vertebral bodies of L4 and L5.



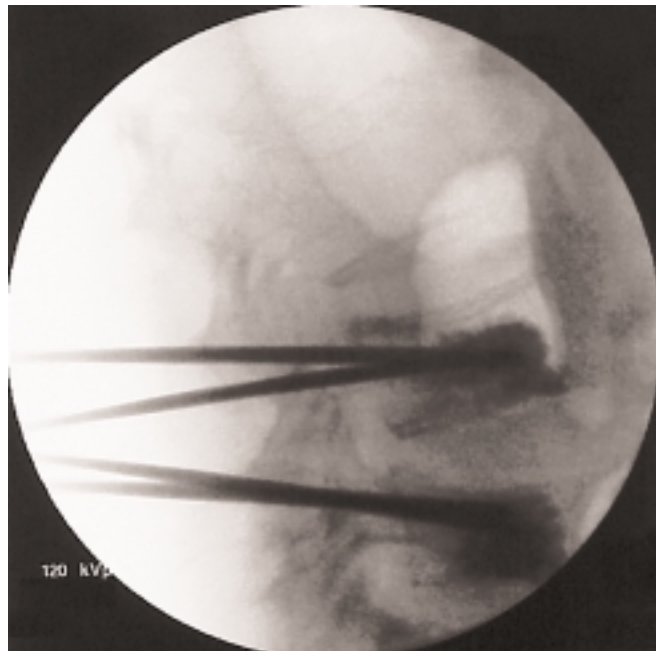
patients treated with PVP for osteoporotic VBF. Complication rates are low, usually 1-2%, and most often are non-neurological and transient.<sup>7,8</sup> Despite the high rate of cement extrusion (30-73%), neurologic sequelae are uncommon, and thermal injury to the neural structures, does not appear to occur.<sup>9,12</sup> Transient radiculopathy has been reported in 3-6% of patients and has been successfully treated in the majority of cases with steroids and anti-inflammatory medications.<sup>9</sup> Recently the cement viscosity for this technique has been increased in order to decrease extrusion of the cement. Other complications related to vertebroplasty include: radiculopathy, spinal stenosis(0.5%), and pulmonary embolus.

A new technique for the treatment of vertebral body fractures, kyphoplasty, was developed in 1997. This procedure involves the percutaneous bilateral placement of inflatable bone tamps into the fractured vertebrae, with the subsequent expansion of the balloons to create a bone free space for the injection of the cement. Because the created space is void of bone, it allows the injection of the cement under low pressure and therefore the use of more viscous cement. Professed advantages of kyphoplasty include height restoration, decrease of kyphosis and less risk for extrusion of cement. Recent studies have shown minimal or no effect in height. Complications rate are around 1.2%, and include epidural hematoma, transient fever and paralysis.<sup>13</sup>

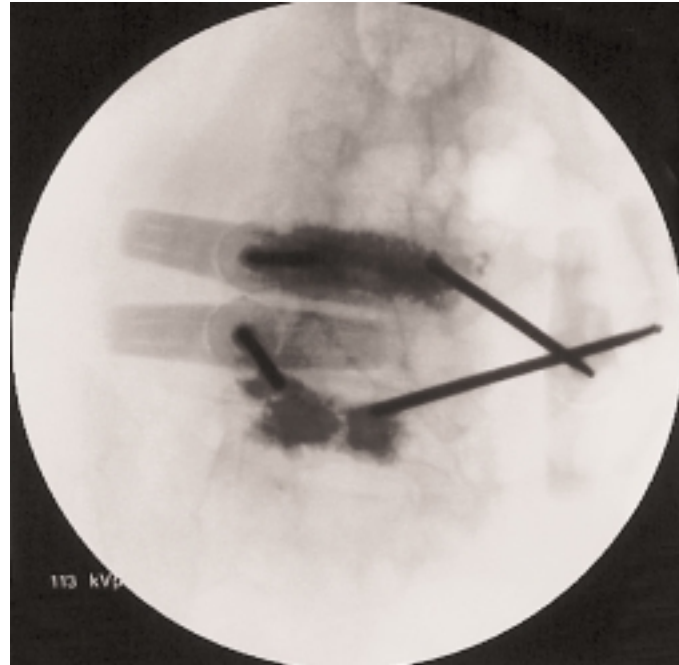
The mechanism by which cement injection into the VBF produces pain relief is not clear and may include thermal necrosis and chemotoxicity of the intraosseous pain receptors, and mechanical stabilization and neurotoxicity mediated by the monomer of the cement.<sup>10,11</sup>

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**Figure 2.**  
Lateral fluoroscopic view. Needles tip at the level of the junction of the anterior third with the two posterior thirds of the vertebral body. Real time cement injection, confirms lack of cement extravasations.



**Figure 3.**  
AP fluoroscopic view with cement injected at both sides of the vertebral body. Occasionally, one side injection is enough, for the cement to spread in the fractured site.

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## Continuing Medical Education Questions

- Osteoporosis is defined by a low bone calcium concentration.  
 True     False
- Women are more prone to develop osteoporosis due to smaller and less dense bones, as well as hormonal changes.  
 True     False
- The risk of osteoporosis in males is minimal.  
 True     False
- Caucasian males appear to have the greatest risk for development of osteoporosis.  
 True     False
- Dual-energy x-ray absorptiometry (DXA), is currently the most frequently used test to measure bone mass.  
 True     False
- The bone mass reported by DXA in a specific patient, is compared with bone density average for the same age group, to determine the risk of osteoporosis.  
 True     False
- Hip fractures are a more frequent complication of osteoporosis, than vertebral body fractures.  
 True     False
- The risk of complications from vertebroplasty is about 1-2% and most often non-neurological and transient.  
 True     False
- The success rate for vertebroplasty, in terms of pain relief is around 90%.  
 True     False
- Suggested mechanisms for pain relief after percutaneous injection of cement into the fractured vertebral body includes: thermal necrosis and chemotoxicity of the nociceptors, and mechanical stabilization.  
 True     False

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