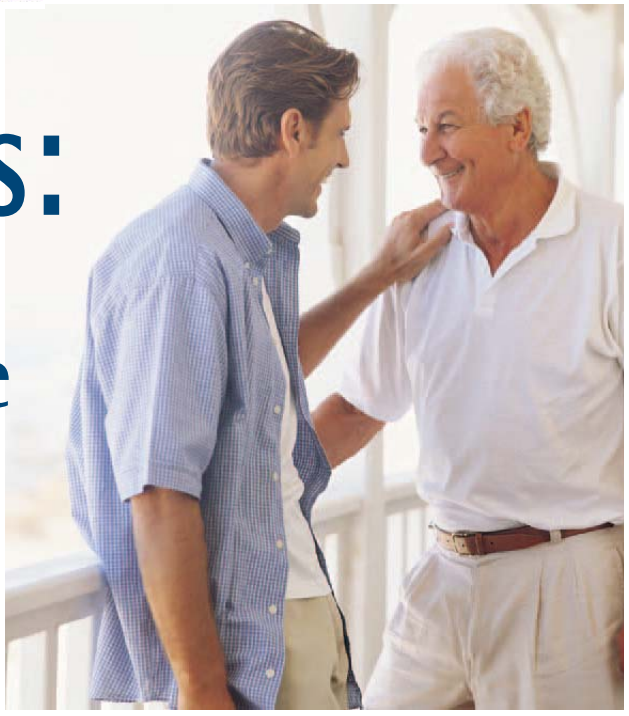
Osteoporosis: Not Just for Women Anymore



By Lisanne G. Laurier, MD, PhD, FRCPC

Osteoporosis is characterized by low bone mass and microarchitectural deterioration that result in an increase in fragility fractures. Although the prevalence of osteoporosis is higher in women, recent population-based studies demonstrate that men are also vulnerable to bone loss, particularly later in life.[1-3]

Men are better able to withstand bone loss because of growth-related differences in skeletal size. Although men have larger (hence stronger) skeletons than women, when corrected for size, the density of bone is similar.

Osteoporosis is the result of an imbalance in bone remodeling. In women, this imbalance is caused by excessive resorption, whereas a reduction in bone formation appears to account for the imbalance in men.[5]

Androgens and estrogens both contribute to bone health. Bone cells express androgen receptors and cortical bone thickness in men is due to androgen-stimulated periosteal bone formation. Even in men, however, skeletal integrity is critically dependent on estrogen.[4] Estrogen biosynthesis in men is catalyzed by the enzyme aromatase, using androgen precursors as a substrate. The local synthesis of estrogen in bone is thought to be responsible for the maintenance of mineralization.

In this article:

1. How does one diagnose osteoporosis in men?
2. What are the differences and similarities of osteoporosis in men and women?
3. What are the risk factors for osteoporosis?
4. What are the management options?

Consequently, men with aromatase deficiency who are unable to convert androgen to estrogen have osteoporosis, and this responds to treatment with estradiol but not testosterone. Moreover, measurements of bone density in younger and older men correlate with circulating levels of estradiol, but not testosterone, and men with vertebral fractures have lower levels of bioavailable estradiol. Although age-related declines in sex hormones contribute to bone loss in both men and women, men do not undergo an accelerated phase of bone loss in mid-life. Bone architecture tends to be better preserved in men, although the overall loss of bone over time may be similar in men and women.[5]

Osteoporosis

Case Presentation

Mr. L. is a 77-year-old man who is physically fit and maintains a 25-acre property in the country. He has a previous history of hypertension, renal calculi, heartburn and osteoarthritis. At a recent family reunion, family members noticed that he was shorter than his older brother, whereas he used to be half an inch taller. Could he have osteoporosis?

Risk Factor Assessment

Mr. L. had no history of fractures or falls. His mother was kyphotic but there was no family history of fractures. He did, however, have osteoarthritis of the knees, ankles and hands. His weight was stable, he was a non-smoker and consumed moderate amounts of alcohol. He had been taking calcium and multiple vitamin supplements for several years.

Over the past four years, he had noted a decrease in libido and a decline in muscle mass.

Physical Examination

Mr. L. stood 5'10" tall, a loss of 4 inches from his peak adult height. He weighed 162 pounds. He had a mild dorsal kyphosis but had no focal tenderness in his spine and a good range of motion.

Investigations

His BMD results showed a T score of -2.5 in the lumbar spine and -3.3 in the femoral neck (a T-score equal to or greater than -2.5 defines osteoporosis).

X-rays of the spine show compression fractures at T 8, 9, 10, 11, L1 and the superior end plate of L4. Osteophytes were present throughout the spine. The low BMD in the presence of vertebral fractures is indicative of severe osteoporosis.

He underwent additional investigations to exclude secondary causes of bone loss including TSH, total and free testosterone, calcium, PTH, vitamin D, creatinine, hemoglobin, liver biochemistry, PSA, and serum protein electrophoresis all of which were normal.

Diagnosis

Bone densitometry (DEXA) is the gold standard for diagnosing osteoporosis. Each 1 standard deviation (SD) decrease in bone mineral density (BMD) confers a 1.5- to 2-fold increase in fracture risk. The reference T-scores for most densitometry machines are derived from data in women. Since men have larger skeletons than women and correspondingly higher BMD values, there has been some debate about whether the diagnostic criterion for osteoporosis (T < 2.5) underestimates the degree of bone loss in men. Nonetheless, the risk of fracture seems to be comparable in men and women for any given BMD.[6] DEXA-generated Z-scores, on the other hand, are matched for age and sex. A low Z-score suggests bone loss in excess of that predicted for age, and warrants further investigation.

BMD values may be falsely elevated due to degenerative arthritis in the lumbar spine, previous

Dr. Laurier is member of the Division of Endocrinology, Department of Medicine, The University of Western Ontario and The Lawson Research Institute, St. Joseph's Health Care, London, Ontario.

Table 1

Risk Factors for Osteoporosis

- Previous history of fragility fracture
- Hypogonadism
- Low body mass index
- Prednisone therapy > 7.5 mg daily for > 6 months
- Malabsorption
- Gastric surgery
- Celiac disease
- Pancreatic steatorrhea
- Chronic liver disease
- History of hip fracture in a parent
- Hyperthyroidism
- Hyperparathyroidism

Table 2

The ADAM Questionnaire[7]

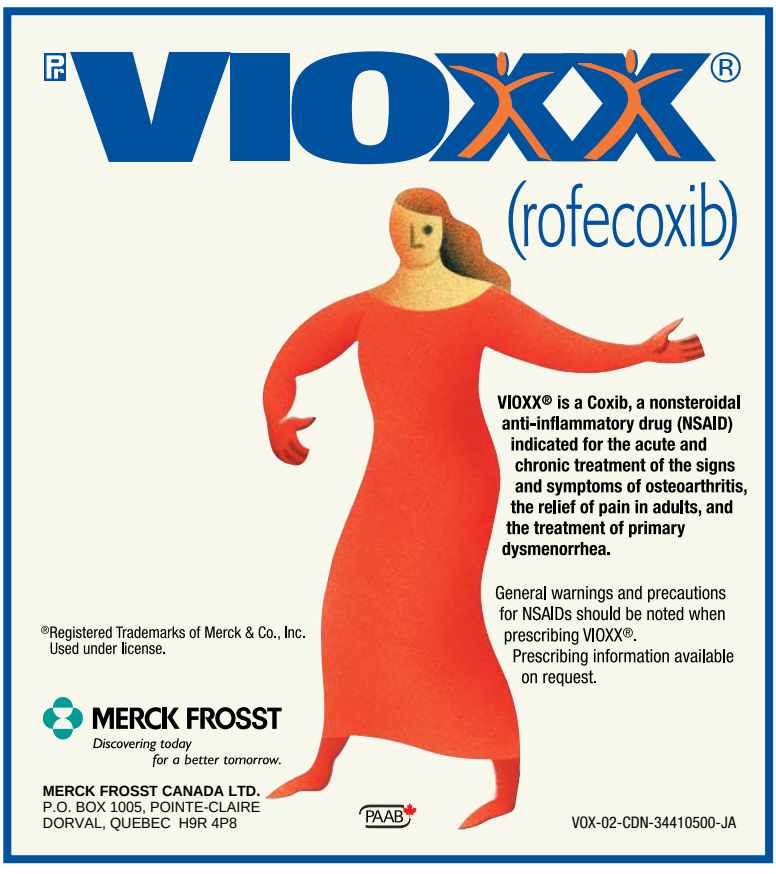
1. Do you have a decrease in libido (sex drive)?
2. Do you have a lack of energy?
3. Do you have a decrease in strength, endurance or both?
4. Have you lost height?
5. Have you noticed a decreased enjoyment of life?
6. Are you sad, grumpy or both?
7. Are your erections less strong?
8. Have you noted a recent deterioration in your ability to play sports?
9. Are you falling asleep after dinner?
10. Has there been a recent deterioration in your work performance?

ADAM: Androgen Deficiency in Aging Males

compression fractures, spinal deformity (*i.e.*, scoliosis), or calcification in the abdominal aorta. This may account for significant heterogeneity in the BMD measurements at different lumbar levels, contributing to errors in the total lumbar score. Men who have lost height, exhibit postural changes, have a history of back pain, or who are over the age of 65 should have X-rays of the thoracic and lumbar spine to document anatomic abnormalities, and these need to be taken into account when interpreting BMD measurements.

Etiology

Secondary causes of osteoporosis account for 50% of cases of osteoporosis in men (vs. 20% in women) and should be excluded with appropriate investigations. The most common secondary causes of bone loss are hypogonadism, glucocorticoid administration and malabsorption syndromes (Table 1). The ADAM (Androgen



Practice Pointer

- Secondary causes account for approximately half of all cases of osteoporosis in men.
- Identifying and treating secondary causes is crucial to optimal management.
- The most common causes of secondary osteoporosis are hypogonadism, glucocorticoid administration and malabsorption syndromes.
- Laboratory tests (*i.e.,* PTH, TSH, calcium) can help confirm or rule out secondary causes.

Deficiency in Aging Males) questionnaire[7] may be used to elicit clinical evidence of hypogonadism (Table 2).

Men who are at risk for osteoporosis based on clinical risk factors should have their bone density assessed.

Investigations

Blood tests should include calcium, albumin, phosphate, parathyroid hormone (PTH), vitamin D, thyroid-stimulating hormone (TSH), creatinine and liver biochemistry. Anti-transglutaminase or anti-endomyseal antibody should be measured to screen for occult celiac disease. In individuals who appear malnourished and who present with significant bone loss, consider ordering a 72-hour collection for fecal fat to exclude pancreatic steatorrhea.

Fracture Risk

The lifetime risk of sustaining an osteoporotic fracture is 13% in men and 40% in women.[8] Standardized mortality ratios are higher for men than women for all fracture types (3.4 vs. 2.0). Mortality rates are particularly high for men who fracture over the age of 80.[9]

Case Discussion

Aside from the obvious loss of height, this gentleman has no objective clinical evidence for osteoporosis. Nonetheless, he has severe osteoporosis with multiple silent vertebral compression fractures, attesting to the insidious nature of this disease. Although his total and free testosterone levels are normal, he has symptoms suggestive of hypogonadism, pointing to a possible etiology for the bone loss.

It is important to emphasize that androgen levels may undergo significant fluctuations in older men. A single measurement of total and free testosterone may not provide an adequate assessment of gonadal status.[15] The ADAM questionnaire (Table 2), along with serial determinations of free testosterone, or a measurement of bioavailable testosterone would assist in deciding whether this man would benefit from androgen replacement.

He is already on calcium and vitamin D supplements. The amount of vitamin D in a multivitamin is 400 IU; this should be augmented with a supplement to achieve a daily level of 1000 IU per day. Less efficient absorption of vitamin D in older individuals, coupled with a relative resistance to the effects of vitamin D on calcium metabolism warrants higher levels of replacement in this population.

He should be treated with a bisphosphonate. Although all of the available bisphosphonates have been shown to prevent vertebral fractures only alendronate and risedronate have been shown to protect against hip fractures. In view of the fact that this man also has significant bone loss in the femoral neck one of these two latter medications would be preferable.

Practice Pointer

- Vitamin D supplementation is indicated for all patients; calcium supplementation should be used for men with inadequate dietary intake
- The medications used to treat osteoporosis in women are thought to be effective for treating osteoporosis in men.
- Bisphosphonates, calcitonin and raloxifene redress bone imbalance by inhibiting bone resorption.

In large, population-based cohort studies, the incidence of clinically diagnosed vertebral fractures in men is approximately half the rate observed with women. However, the prevalence of radiographically documented vertebral deformity among men between the ages of 50 and 80 is much higher, and quite similar to rates observed in women (10-20%).[16,17] Previous vertebral fractures and a low BMD are highly predictive of vertebral fracture risk. Although vertebral fractures are asymptomatic in two-thirds of cases, they are associated with a 2.4-fold increase in mortality. The relative five-year survival after a vertebral fracture is 0.84 in women and 0.72 in men.[18]

The lifetime risk of sustaining a hip fracture is 11% in men versus 23% in women. One third of all hip fractures occur in men. Mortality after hip fracture is higher in men than in women (32% vs. 22%). U.S. data from 1995 show that the cost for treating hip fractures in men was $2.7 billion. By 2035 the projected number of hip fractures in men will equal the prevalence of hip fractures among women today due to anticipated increases in life expectancy.[19]

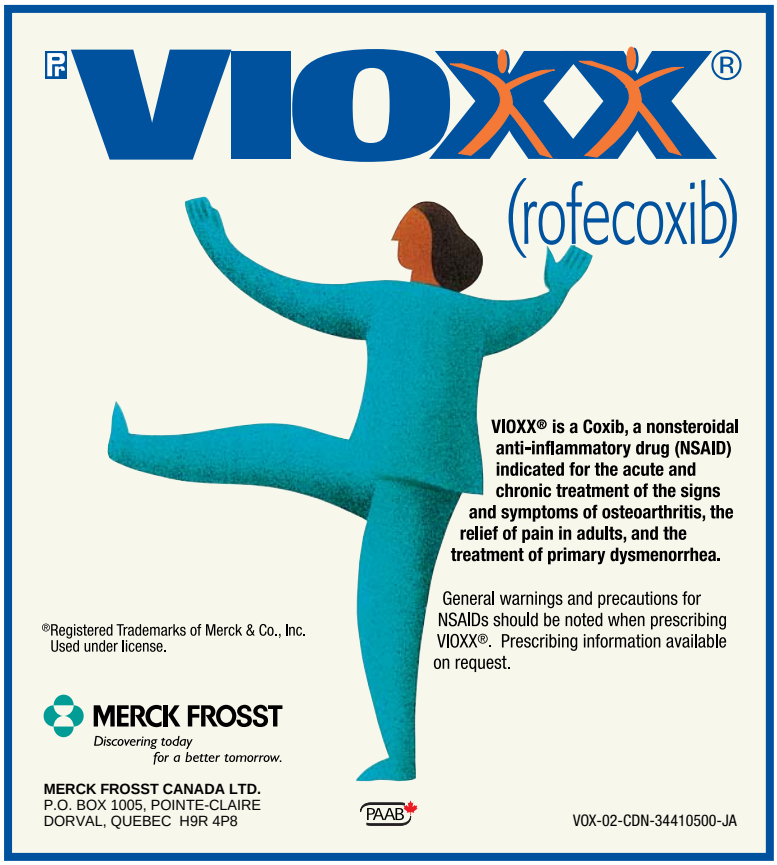


Table 3

Table Defining Osteoporosis by BMD

Normal	BMD is within 1 SD of young adult value (T-score cutoff -1)
Low Bone Mass (Osteopenia)	BMD is between 1 and 2.5 SD below young adult value (T-score between -1 and -2.5)
Osteoporosis	BMD is 2.5 SD or more below that of young normal (T-score cutoff -2.5)

BMD = Bone mineral density
SD = Standard deviation

Management

The following general principles should guide the management of osteoporosis in men:

- Exclude and treat secondary causes;
- Androgen deficiency should be treated with an appropriate parenteral (delatestryl), oral (andriol) or transdermal (androgel) formulation;
- Calcium supplements (500 mg - 1500 mg elemental calcium) should be recommended if dietary calcium consumption is inadequate; and
- All patients should be advised to take vitamin D (400 IU - 1000 IU daily). Higher doses should be considered in the elderly and during the winter months.

Bone Mineral Density Measurements. Appropriate BMD thresholds for medical intervention have been less well defined in men compared to women. Extrapolating from recommendations in women, a T-score of -1.5 might be an appropriate threshold for intervention in men with clinical risk factors, whereas in those without risk factors, a T-score greater than -2.0 might be more appropriate (Table 3).

Medication. Although there are few therapeutic trials in men with osteoporosis, the available evidence suggests that medication used to treat osteoporosis in women are also effective in men. With the exception of parathyroid hormone, all of the available treatments for osteoporosis produce clinical benefit by inhibiting bone resorption.

Bisphosphonates. Etidronate, alendronate and risedronate have been shown to increase BMD in men. There is, however, a paucity of information with respect to fracture prevention in men. In a recent clinical trial of osteoporosis in men, alendronate decreased the incidence of vertebral fractures but had no impact on non-vertebral fractures.[10] Risedronate has been shown to reduce the incidence of vertebral fractures at 1 year in men treated with glucocorticoids.[11]

Nasal calcitonin. Nasal calcitonin increases BMD in men with osteoporosis. Its effect on vertebral fractures has been inconsistent, perhaps due to the small sample size in these studies.[12]

Raloxifene, a selective estrogen receptor modulator, is being explored as a therapeutic agent in men, but the data to date are very preliminary.[13]

Parathyroid Hormone (PTH). The intermittent administration of low dose PTH has been shown to significantly increase bone density in men with idiopathic osteoporosis.[14] Although at the present time PTH is only available in Canada on a clinical trial basis, it is poised to emerge as an important therapy for osteoporosis in the future.

Summary

Osteoporosis in men is more common than previously thought and is associated with considerable morbidity. Since the clinical manifestations of bone loss are often subtle, a heightened awareness among physicians that osteoporosis in men is an important health issue — this is an important step to making this diagnosis. A clinical assessment coupled with a BMD and radiographic images of the spine will lead to timely and appropriate therapy in men at risk. CME

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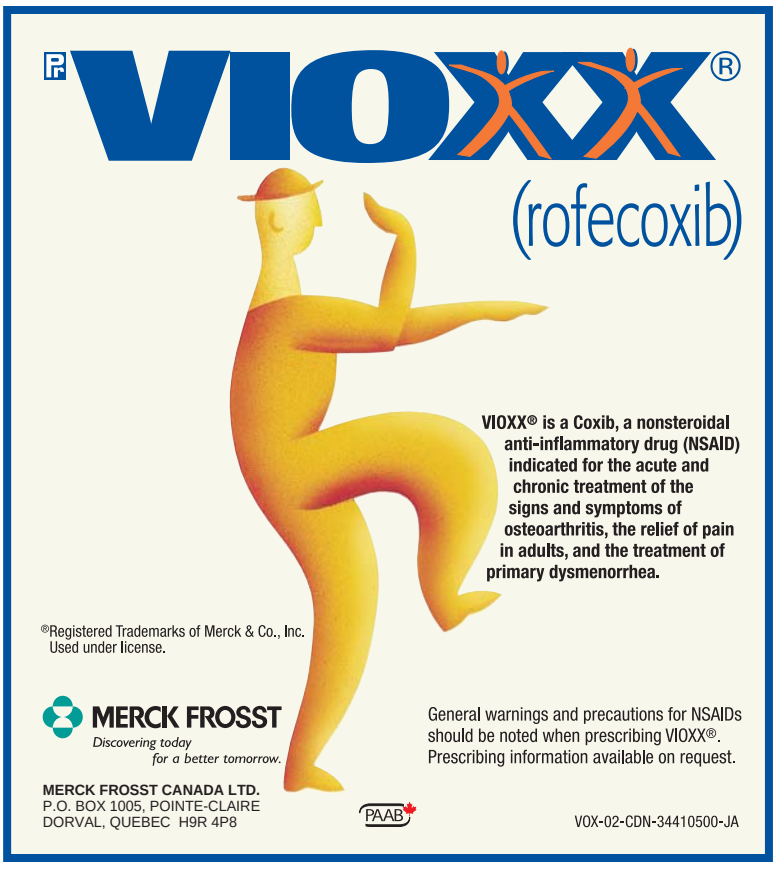
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