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StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2018 Jan-.

Osteoporosis

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Last Update: November 15, 2018.

Introduction

Osteoporosis is defined as low bone mineral density caused by altered bone microstructure ultimately predisposing patients to low-impact, fragility fractures. Osteoporotic fractures lead to a significant decrease in quality of life, with an increased morbidity, mortality, and disability.[1] Over 50% of postmenopausal Caucasian women will have an osteoporotic-related fracture. Only 33% of senior women who have a hip fracture will be able to return to independence. In Caucasian men, the risk of an osteoporotic fracture is 20%, but the one-year mortality in men who have a hip fracture is twice that of women. Black males and females have less osteoporosis than their Caucasian counterparts, but those diagnosed with osteoporosis have similar fracture risks. The aging of the American population is expected to triple the number of osteoporotic fractures. [2][3][4][5]

Etiology

Primary osteoporosis is related to the aging process in conjunction with decreasing sex hormones. The bones have deterioration in microarchitecture leading to loss of bone mineral density and increased risk of a fracture. Other diseases or their treatments cause secondary osteoporosis. Men are much more likely than women to have secondary osteoporosis. Medications that can lead to secondary osteoporosis include glucocorticoids and anti-epileptics. Other medications such as chemotherapy agents, proton pump inhibitors, and thiazolidines are less well studied but suspected to also contribute to osteoporosis.

Disease states that can cause osteoporosis include hyperparathyroidism, anorexia, malabsorption, hyperthyroidism, or overtreatment of hypothyroidism, chronic renal failure, Cushing, and any disease that can lead to long-term immobilization. Secondary amenorrhea for more than one year from various causes including non-estrogen hormonal therapy, low body weight, and excessive exercise can also lead to rapid loss of bone mass.

Risk factors for osteoporosis include increasing age, a body weight less than 128 pounds, smoking, family history of osteoporosis, white or Asian race, early menopause, low levels of physical activity and a personal history of a fracture from a ground level fall or minor trauma after the age of forty. [6][1] Patients afflicted with conditions affecting overall mobility level, such as spinal cord injuries (SCI), can experience rapid deterioration of bone mineral density levels within the first 2 weeks following these debilitating injuries. [7]

Epidemiology

Over 200 million people have osteoporosis and the incidence rate increases with age. Over 70% of those over age 80 are affected. It is more common in females than males. In the developed world, 2% to 8% of males and 9% to 38% of females are affected. Worldwide, there are approximately 9 million fractures per year as a result of osteoporosis. [8] [9][10]

One in 3 females and 1 in 5 males over the age of 50 will have an osteoporotic fracture. Areas of the world with less Vitamin D through sunlight compared to regions closer to the equator have higher fracture rates in comparison to

people living at lower latitudes.

Pathophysiology

Osteoporosis is caused by an imbalance of bone resorption and bone remodeling leading to decreased skeletal mass. In most individuals, bone mass peaks in the third decade, after which bone resorption exceeds bone formation. Failure to reach a normal peak bone mass or acceleration of bone loss can lead to osteoporosis. [1]

Histopathology

Histologic specimens demonstrate markedly thinned trabeculae, decreased osteon size, and enlarged haversian and marrow spaces. [3]

Toxicokinetics

Side effects and costs of treatment are the major considerations when prescribing medications for osteoporosis. It should be noted that intravenous bisphosphonates can be used if a patient is intolerant of oral bisphosphonates before advancing to different treatment options, as they can be tolerated by patients intolerant of the oral dosing.

History and Physical

A comprehensive history and physical includes eliciting potential risk factors attributable to secondary bone loss. A thorough social history also should be obtained with attention to smoking history and chronic alcohol consumption. A family history of osteoporosis also should be noted. The patient should be asked about any prior fractures with focus given to low energy ground level fall mechanisms and any fractures after the age of 40.

The physical exam rarely reveals any changes until osteoporosis is quite advanced. At that point, loss of height and kyphosis is evident from vertebral fractures.

In healthy individuals without risk factors, experts recommend starting to screen women at the age of 65 years of age and men at the age of 70. It should be noted that the United States Preventative Services Task Force did not find sufficient evidence to establish screening for men. Patients with risk factors or a high score on an osteoporosis risk assessment test should be screened sooner.

Women with normal dual-energy x-ray absorptiometry scans do not need follow-up dual-energy x-ray absorptiometry scans as studies have shown that most women with normal scores did not progress to osteoporosis. Using these scans to follow up osteoporosis treatment has rarely led to treatment changes as long as compliance with medications can be assessed in other ways.

Evaluation

Patients with a diagnosis of osteoporosis should have laboratory assessment of their renal and thyroid function, a 25-hydroxyvitamin D and calcium level. The World Health Organization (WHO) has established dual x-ray absorptiometry tests scans of the central skeleton is the best test for assessing bone mineral density. A dual x-ray absorptiometry scan can be completed in five minutes with minimal radiation exposure. Dual x-ray absorptiometry scans measure all calcified tissue in the path of the scan and specificity is better than sensitivity.

Peripheral dual x-ray absorptiometry tests and ultrasound measure density in bones not at high risk and do not correlate well to the standard dual x-ray absorptiometry scan of the hip and spine. They are not as useful in diagnosis or treatment decisions.

A dual x-ray absorptiometry scan reports a t-score and a z-score. A t-score reflects the difference between the measured bone mineral density and the mean value of bone mineral density in young adults. It is measured in standard deviations. The WHO has defined normal bone mineral density for women as a t-score within one standard deviation

of the young adult mean. Scores between negative 1 and negative 2.5 reflect a diagnosis of osteopenia. Scores below negative 2.5 reflect a diagnosis of osteoporosis.

Instead of measuring against a young adult mean, a z-score is the number of standard deviations above or below the age-matched bone mineral density. It is useful when suspecting secondary osteoporosis. A score is less than negative 1.5 warrants a workup for secondary causes of osteoporosis.

The low bone density of the hip has the highest predictive value of future fracture. This is because spine bone density can be falsely elevated due to calcification from degenerative joint disease. Density in the spine can still be useful in younger perimenopausal women without significant degenerative joint disease where the spine can show initial osteoporotic changes before it can be detected in the hip.

A validated tool developed by the World Health Organization is the osteoporosis risk assessment tool which gives a ten-year probability of a major fracture. It can be used on men or women and takes into account the body mass index, independent risk factors and some causes of secondary osteoporosis. It is most useful in determining which patients with osteopenia need treatment and in determining which patients younger than the age of 50 would benefit from dual x-ray absorptiometry scanning due to high risk of fractures. It does not have utility for patients who are already being treated for osteoporosis.

Treatment / Management

Recommend lifestyle changes to all patients. Weight-bearing physical activity and exercise that improves balance such as yoga and tai chi should be encouraged. Treatment should be offered to help with both smoking and alcohol cessation. Recommend calcium and Vitamin D3 to all patients, and patients who are vitamin D deficient should have a treatment that raises their levels to be normal.

Patients with a t-score of negative 2.5 or less should receive treatment. It is also indicated for patients with osteopenia (t-score between negative 1 and negative 2.5) who score on the osteoporosis risk assessment test as having a 3% or higher risk of hip fracture. Patients with a personal history of a fragility fracture can be treated without further testing.

There are multiple pharmacologic treatments available. These agents work through either antiresorptive or anabolic means. In women with known osteoporosis, the recommendations are to start treatment with risedronate, alendronate, zoledronic acid or denosumab to reduce the risk of fracture. These treatments reduce fracture both at vertebral and non-vertebral sites. Bazedoxifene, a selective estrogen receptor modulator combined with conjugated estrogen, has been approved by the FDA for prevention of osteoporosis but not for treatment.

Men should be offered bisphosphonates as first-line therapy.

If patients do not tolerate these medications they can try other medications such as teriparatide. Medications that have only been shown to reduce vertebral fractures, such as raloxifene and ibandronate, should be reserved for patients that cannot tolerate any of the previously mentioned medications. For both groups, any secondary cause should be treated. Use of combination therapy of teriparatide and a bisphosphonate or teriparatide and denosumab in patients with severe osteoporosis and hip and vertebral fractures is worth consideration.

There are no randomized studies regarding monitoring of treatment with follow-up dual x-ray absorptiometry scans. Several studies show that women had reduced fractures with treatment independent of follow-up bone mineral density.

Recommendations for duration depend on the specific type of medication used for treatment. Some agents such as teriparatide or hormonal-based therapy, need immediate follow-up treatment with another agent or bone mass is lost quickly after discontinuation. There is the ongoing debate about the bisphosphonates with studies underway to determine if drug holidays after five years of therapy or continuous therapy is of most benefit to reduce the fracture.

Pharmacotherapy Options [3]

Pharmacotherapy agents work through either anti-resorptive or anabolic means. Bisphosphonates are the most commonly prescribed medication class. These drugs are divided into non-nitrogen and nitrogen-containing compounds. The latter are considered first-line therapy. The nitrogen-containing compounds inhibit farnesyl pyrophosphate synthase and ultimately inhibit osteoclast resorption and induce osteocyte apoptosis. Common agents include:

- Alendronate may reduce the rate of hip, spine, and wrist fractures by 50%
- Risedronate may reduce vertebral and nonvertebral fractures by 40% over three years
- IV zoledronic acid reduces the rate of spine fractures by 70% and hip fractures by 40% over three years

Other Medication Classes [1]

- Conjugated estrogen-progestin hormone replacement (HRT)
- Estrogen-only replacement (ERT)
- Salmon calcitonin (Miacalcin, Fortical)
- Selective estrogen receptor modulators (Raloxifene) - Raloxifene is an agonist to estrogen receptors on bone and reduces osteoclast resorption
- Anabolic (Teriparatide) - Teriparatide is a recombinant form of parathyroid hormone (PTH) that stimulates osteoblasts to produce more bone. Teriparatide is now FDA approved for osteoporosis treatment in males and females
- RANKL inhibitors (Denosumab) - Denosumab is a monoclonal Ig2 that targets RANKL and inhibits its ability to bind to RANK and results in the inhibition of osteoclast activation

Treatment and Follow-up Considerations [1][11][12][13]

Treatment duration varies depending on the class of medication utilized. Agents such as teriparatide and hormonal-based therapy require immediate follow-up treatment with another agent upon stopping the medication, otherwise, bone mass is rapidly lost. Clinicians also must remain cautious against the prolonged use of uninterrupted bisphosphonate therapy beyond a 3- to 5-year period. Patients should also be made aware of these potentially morbid adverse events, and they should be counseled to seek immediate care if they are experiencing any symptoms of thigh discomfort

Any patient on bisphosphonates for any given time period and presenting with mild thigh discomfort should have the following treatment workup:

- Educate on the risks of and immediately stop all weight-bearing activity
- Obtain full-length femur and hip radiographs. Thigh pain may be indicative of an impending pathologic, atypical femur fracture. Attention should be directed to the subtrochanteric and diaphyseal regions of the femur, particularly the lateral cortex which often demonstrates evidence of periosteal reaction
- Immediately discontinue bisphosphonate use
- Refer to an orthopedic surgeon for prophylactic surgical fixation

Enhancing Healthcare Team Outcomes

Osteoporosis is a major public health problem affecting millions of elderly individuals. Besides causing fractures, the disorder leads to severe psychosocial and financial consequences for the patient. The condition has many risk factors and is best managed by a multidisciplinary team of healthcare workers. Patient education is vital as many patients are

unaware of the serious consequences of the disorder. Early prevention can help reduce the high morbidity. Patients should be urged to modify their lifestyle and remain compliant with the medications prescribed. In addition, the patient should be urged to quit smoking and abstain from alcohol. The outcomes in patients with osteoporosis are guarded. Close to 250,000 hip fractures occur each year as a result of osteoporosis, and once admitted, there is a mortality rate exceeding 20%. Men with a hip fracture, in general, have a much higher mortality than women. Even after recovery, many patients lose their independence and close to 30% require nursing home care. Full recovery rarely occurs and the overall quality of life is poor. Many patients develop secondary complications like pressure sores, deep vein thrombosis, and nosocomial infections.[14][15]

Questions

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Bookshelf ID: NBK441901 PMID: 28722930