A Practical Approach to Osteoporosis Management in the Geriatric Population

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ABSTRACT

Osteoporosis is a medical condition that is seen commonly in elderly patients, and it is associated with a large burden of morbidity and mortality. This article provides a practical approach to the workup and management of osteoporosis in patients 65 years or older.

Key words: osteoporosis, fracture, bisphosphonate, vitamin D, CAROC

INTRODUCTION

It is estimated that osteoporosis may cost as much as $3.9 billion a year in Canada alone.[1] These include costs associated with acute care admissions, rehabilitation, long-term care, drug costs, and productivity losses, among others.[1] There is no longer a belief that osteoporosis is simply a matter of treating bone mineral density values; the priority now is to prevent fragility fractures and their immediate and long-term sequelae.[2] It is now well known that, aside from the pain, morbidity, and financial costs of fragility fractures, there is also an increased risk of mortality due to fractures,[3] and current antiresorptive therapies reduce this risk.[4]

In the United States, it is estimated that 44 million people have osteopenia or osteoporosis.[5] In Canada, by the year 2036, due to rapid ageing of the population, the number of citizens aged over 65 may outnumber children.[6] A previous systematic review revealed that the majority of patients who sustained fragility fractures were not receiving adequate osteoporosis workup and management.[7] In 2007, Bessette et al.[8] found that 81% of fractures sustained by women over age 50 would be considered fragility fractures. Among these women, 79% had either not been prescribed treatment to prevent further fractures or had not been investigated for osteoporosis. A fragility fracture results from a fall from standing height or less; this increases the risk for subsequent fractures by up to 9.5 fold.[9] The strongest association is between a prior and subsequent vertebral fracture, with the risk increasing with the number of vertebral fractures.[10]

The purpose of this article is to supply primary healthcare providers with a reference on how to manage osteoporosis in patients 65 years or older in Canada. The information presented is in keeping with the 2010 recommendations by Osteoporosis Canada.[2]

WHO TO SCREEN

The clinical recommendations are that every patient over the age of 50 should be assessed. Thus, every patient 65 years of age and older should be regularly screened for risk factors for osteoporosis and fragility fractures. This applies for both women and men. In the younger population, there are several risk factors that prompt consideration for bone mineral density testing; these factors do not play a role in the geriatric population. Our recommendation is that all patients aged 65 and over should have a bone mineral density test. This differs slightly from the United States Preventive Services Task Force and the United Kingdom—National Osteoporosis Guideline Group, who recommend bone mineral density testing in women over the age of 65 and men over the age of 70.[11,12]

CLINICAL ASSESSMENT AND TESTING

History taking is especially important for our target population. The purpose of taking a proper history is to identify the factors that increase the risk for low bone mineral density, falls and resultant fractures. This includes a history of falls, the number of falls in the past year, gait, balance difficulties and fragility fractures. Other risk factors that apply to any age group include current glucocorticoid use, excessive alcohol (three or more units per day) and smoking status, rheumatoid arthritis, and a history of a parental hip fracture. The association of caffeine consumption and the risk of osteoporosis has been inconsistent, though one study has shown that a daily caffeine intake of 330 mg (equivalent to four cups of coffee) may increase the risk of osteoporotic fractures in women.[13]

There are a number of non-glucocorticoid medications that are suspected of inducing osteoporosis and/or increasing fracture risk. These include antiepileptic drugs, suppressive

dose thyroid hormones, aromatase inhibitors, gonadotropin-releasing hormone agonists, antipsychotics, selective serotonin reuptake inhibitors, and proton pump inhibitors.[14] There is also literature that certain co-morbidities increase osteoporosis severity, particularly Crohn's disease.[15] The increased osteoporosis severity among other diseases, such as depression, breast cancer, and prostate cancer, may be due to the medications used to treat the disease.[15] Parkinson's disease was found to have an age-adjusted hazard ratio of 2.2 for incident fracture.[16]

The appropriate physical examination maneuvers serve two purposes: to assess risk factors for future fragility fractures and to screen for possible undiagnosed vertebral fractures. The elements of the physical exam that are most pertinent to the elderly population include weight measurement, the Get-Up-and-Go Test (which helps assess for proximal muscle weakness, gait, and risk of falls), and screening for vertebral fractures (height loss of > 2 cm, rib to pelvis distance < or equal to 2 fingers' breadth, and an occiput-to-wall distance of > 5 cm). Assessing for vertebral fractures is supported by Grade A evidence.[2] While the guidelines do not necessarily mention performing a cognitive screen, a 2005 study revealed that patients with dementia have a relative risk of 10.1 for having at least one fall in the next year.[17]

The etiology of falls is generally multifactorial. There are many risk factors that have been identified for falls. These include psychotropic medications, gait and balance impairment, functional limitation, home hazards, advanced age, cognitive impairment, and visual impairment.[18]

Baseline biochemical tests are not mandatory unless the patient is found to have lower than normal bone mineral density results. In the event that osteoporosis or osteopenia is diagnosed, then the recommended blood tests include corrected calcium, alkaline phosphatase, creatinine, complete blood count, thyroid stimulating hormone, and a serum protein electrophoresis (only for patients with vertebral fractures). A serum 25-hydroxy vitamin D level is also recommended after the patient has been supplemented with vitamin D for a minimum of three months.

If there is clinical worry about a possible vertebral fracture, lateral thoracic and lumbar spine x-rays should be ordered.

The final step in the workup of a geriatric patient is bone mineral density testing. To facilitate testing for frail individuals who are unfit to be screened with a bone mineral density test, the 2010 Osteoporosis Canada guidelines highlight four categories of patients who are considered high-risk (and don't necessarily require testing for risk assessment). These include patients with

1. hip fractures
2. vertebral fractures
3. more than one fragility fracture
4. one fragility fracture and who are on glucocorticoids (equivalent to prednisone of equal to or greater than 7.5 mg per day for greater than three months in the past year).

HOW TO INTERPRET BMD RESULTS

For simplicity and convenience, we prefer using the Canadian Association of Radiologists and Osteoporosis Canada (CAROC) system.[19,20] The CAROC system is an easy-to-use scoring system that plots a patient's femoral neck bone mineral density T-score against a curve that divides patients into low (< 10%), moderate or high (> 20%) ten-year fracture risk. The 2010 version of the CAROC tool has been validated in Canada (grade A) and is the preferred national risk assessment system for reporting bone mineral density results (grade D).[2] These scoring systems are sex-specific. For a woman over the age of 65, a femoral neck T-score -1.9 or lower places her in the moderate-risk category, while a value lower than -3.5 makes her a high ten-year fracture risk patient.

There are certain caveats when plotting the femoral neck T-score on the CAROC curve. Any fragility fracture after the age of 40, or recent prolonged glucocorticoid use (defined as daily prednisone ≥ 7.5 mg for a cumulative duration of three months or longer over the past year), increases the ten-year fracture risk by one category. If both features are present, the patient becomes high-risk, even with a normal T-score. Any patient who has more than one fragility fracture, or a fragility fracture of the hip or vertebra, is considered at high ten-year fracture risk. If the T-score for the lumbar spine or total hip is -2.5 or less, the patient is at least at moderate ten-year fracture risk.

Certain situations regarding moderate risk patients compel us to treat. These factors include a lumbar spine T-score that is at least one standard deviation less than the femoral neck score, older than age 65 with a prior history of wrist fracture, history of wrist fracture with a T-score lower than -2.5, recurrent falls, low-dose glucocorticoid therapy, and current use of aromatase inhibitors or androgen deprivation therapy.

HOW TO TREAT

The goals of treatment for patients with osteoporosis include bone strengthening, optimizing physical function, prevention of new fractures, and decreasing symptoms of prior fractures.[21]

Non-pharmacologic interventions should be advised to all patients who have osteoporosis. Inactivity and immobility promotes reduced bone mass, and even moderate (or more vigorous) walking programs help reduce the risk of hip fractures.[22] Those who are at high-risk of falls may benefit from a home occupational therapy safety assessment. Smoking cessation and moderation of alcohol intake are also recommended.

It is estimated that one-third of falls can be prevented with falls prevention strategies.[18] Among the particular exercise programs, challenging balance training (particularly tai chi) may help to reduce the risk, fear, and number of falls,[23,24] core stability exercises are recommended for those with a prior vertebral fracture, and resistance training (appropriate for functional capacity) is recommended even for those who are at-risk for osteoporosis. Combining weight bearing

exercises with strength training will help prevent bone loss.[24] A Bayesian approach revealed that hip protectors decrease the risk of incident hip fractures in elderly nursing home residents,[25] and these protectors should be considered in patients at high-risk for falls.

The recommendations regarding calcium and vitamin D supplementation may cause confusion. With reference to vitamin D, most of the circulating vitamin comes from exposure to sunlight, not from diet. Certain factors, such as use of sunscreen, darker skin colour, and being elderly, decrease the efficiency of vitamin D production in the skin. We aim for a serum 25-hydroxyvitamin D level of 75 nmol/L, which likely cannot be maintained during the Canadian winter without supplementation.[26] The American Geriatrics Society Workgroup on Vitamin D Supplementation for Older Adults also concluded that a serum 25-hydroxyvitamin level of 75 nmol/L should be a minimum goal for elderly adults (particularly frail ones).[27] For every 1,000 IU of vitamin D_3, the average serum 25-hydroxyvitamin D level will rise by approximately 20 nmol/L.[28] In elderly patients at moderate risk for vitamin D deficiency, we typically supplement with 1,000 IU of vitamin D_3 daily. Higher doses may be required, and doses up to 2,000 IU a day are considered safe. For elderly patients who would be at risk for fractures due to vitamin D deficiency (typically those with comorbid conditions that inhibit absorption of the vitamin D supplement or patients with ongoing bone loss or recurrent fractures despite adequate treatment), higher supplemental doses may be required, and serum 25-hydroxyvitamin D levels can be used to guide dosing.

There is extensive discussion regarding the timing and necessity of measuring serum vitamin D levels. Testing should be conducted three months after initiating therapy and should not be repeated once the recommended level of 75 nmol/L is reached (unless there is a change in clinical status). Ongoing bone loss or new fragility fractures would be considered a change in clinical status. The American Geriatrics Society Workgroup recommends monitoring of serum 25-hydroxyvitamin D levels in individuals who take medications that bind vitamin D, who are obese, who have malabsorption syndromes, or who limit their overall vitamin D intake.[27]

The daily total intake of elemental calcium should be 1,200 mg. When possible, we try to encourage patients to achieve their daily target through calcium-rich foods, but acknowledge that not all geriatric individuals can, or want to, change their diet.

The evidence behind vitamin D and calcium supplementation is strong. It increases bone mineral density, reduces falls, and decreases the risk of hip and non-vertebral fractures in elderly, institutionalized individuals.[29] Community-based clinical trials with calcium and vitamin D supplementation have poor compliance and tend to be negative,[30] though a 2005 meta-analysis on vitamin D supplementation of 700–800 international units a day did reduce the risk of hip and non-vertebral fractures in both ambulatory and institutionalized individuals.[31]

Most trials that examine high doses of vitamin D are not properly designed to assess long-term harms.[32] The studies that investigated whether vitamin D and/or calcium supplementation led to an increased risk of certain malignancies were either inconsistent or not relevant to our patient population.[33]

The purported association between calcium supplementation and cardiovascular disease is controversial. One reanalysis of the Women's Health Initiative database revealed an increased hazard ratio for those patients who were assigned to calcium supplementation (and were not taking calcium supplements at the time of randomization).[34] It is important to determine how much calcium a patient is receiving in their diet before deciding on the supplementation dose. For women over the age of 50, and men over 70 years of age, an appropriate recommended dietary intake is 1,200 to 2,000 mg/day of elemental calcium.[35] Dietary calcium intake may have less adverse cardiovascular effects than supplements because they are taken in less concentrated boluses and are absorbed more slowly since they are eaten with fat and protein.[36]

ANTIRESORPTIVE MEDICATION

The decision to initiate antiresorptive therapy depends on the patient's overall risk. Those who are at high ten-year fracture risk should be treated. Those who fall into the moderate-risk category should be managed on a case-by-case basis. They should undergo a comprehensive evaluation to determine if there are any other factors that might lead the physician to consider therapy (for example, repeated falls, disorders associated with osteoporosis, women receiving aromatase-inhibitor therapy). Patients who are in the low-risk category generally do not require any further therapy, aside from lifestyle modifications (exercise, smoking cessation, falls prevention) in addition to optimization of their calcium and vitamin D intake (diet and supplemental).

Bisphosphonates, the most commonly used antiresorptive therapy, are generally well tolerated and, for most patients who suffer from osteoporosis, the treatment benefits outweigh the risks.[37] The bisphosphonates reduce the incidence of new vertebral fractures by up to 50%, non-vertebral fractures by 20%, and hip fractures by 40%.[38] The time to onset of benefit for the bisphosphonates is around six months for clinical vertebral fracture prevention, and 18 months for hip fracture prevention.[39]

In post-menopausal women, alendronate, risedronate, and zoledronic acid are all appropriate first-line therapies for the prevention of vertebral and non-vertebral fractures (including hip). The choice of which particular medication to use can be determined by patient preference. Risedronate and alendronate are available orally; they both can be taken daily or weekly, with risedronate also having a once-monthly pill. Risedronate also has a once-weekly pill that can be taken with food. Zoledronic acid is available as a once-yearly intravenous infusion.

An important topic is the long-term safety profile of bisphosphonates. Bisphosphonate binding to skeletal bone

is unsaturable, so that the medication accumulates over time, and may be released even after therapy has been stopped.[40] The likelihood of atypical femur fractures is low, even in women who have received treatment for up to a decade.[37] Nonetheless, these concerns have led to the idea of a drug holiday after several years of therapy.

Not much data exist to guide decisions regarding duration of drug holidays. For those who have moderate ten-year risk of fracture, it may be reasonable to discontinue intravenous bisphosphonate use after three years and oral bisphosphonate use after five years. So long as there has not been a significant loss of bone mineral density (or fracture) on subsequent testing, the holiday may be continued for up to five years. The FLEX trial showed that ten years of alendronate therapy did not significantly reduce the risk of non-vertebral fractures, compared to five years of alendronate therapy. The benefit in continuing alendronate therapy for ten years occurs in the population whose femoral neck T-scores are -2.5 or less, who have a lower incidence of novel vertebral fractures.[41] Patients who are at high-risk for future fractures should be treated for up to ten years before a shorter drug holiday can be offered (typically two years at the most). Patients should be monitored for significant bone loss or novel fractures. The other option is for those at high-risk for future fractures and who are receiving antiresorptive therapy to switch to bone formation therapy after five to ten years of use. For all patients, regardless of risk, the decision of when to hold bisphosphonates and for how long should be made on a case-by-case basis.

Denosumab is a fully human monoclonal antibody RANKL inhibitor. This ultimately prevents the differentiation and function of osteoclasts, and leads to increased bone mass.[42,43] It is administered as a subcutaneous injection every six months. For patients who cannot take oral bisphosphonates (typically due to gastrointestinal side effects or the need to take on an empty stomach), denosumab has been shown to have similar bone mineral density improvements as alendronate.[44] Unlike bisphosphonates, which incorporates into bone, denosumab does not, and cessation of therapy may lead to a more rapid decline of bone mineral density compared to bisphosphonates. A 2012 review shows that denosumab is efficacious and safe as a first-line treatment for postmenopausal women, particularly those who cannot take bisphosphonates.[21] While rare, cellulitis was significantly more common in patients receiving denosumab compared to placebo; it occurred in 12 out of 3,886 patients in the FREEDOM trial, compared to one in 3,876 patients in the placebo arm.[42] Atypical femur fractures, although rare, have also been observed with denosumab therapy.

In July 2013, Health Canada decided to withdraw calcitonin nasal spray from the Canadian market after a review of risks and benefits. Those who were treated with nasal calcitonin had a low, but observable, increased rate of malignancy compared to placebo. The subcutaneous form of calcitonin is still available on the Canadian market. Calcitonin is not a first-line treatment medication for osteoporosis, and does not decrease the risk of hip or nonvertebral fractures.

ANABOLIC (BONE FORMATION) AGENTS

Teriparatide is a recombinant parathyroid hormone amino acid 1 to 34 and is effective at increasing bone mineral density and decreasing vertebral and non-vertebral fractures in post-menopausal women.[45,46] Therapy may be inconvenient because teriparatide has to be injected subcutaneously daily.

WHEN TO REPEAT BMD

The response to therapy with any osteoporosis medication is often examined by repeating bone mineral density tests, although the bone density response may vary with different therapies. The optimal time to repeat bone density tests is one to three years initially. Ideally, testing should be performed at the same laboratory for each visit, to decrease variability between machines.

Once bone mineral density is stable, the testing interval can lengthen, allowing for five to ten years for those who are low-risk and do not have a reason for potential fast bone loss.

REFERRAL TO OSTEOPOROSIS SPECIALIST

The decision for a primary-care physician to refer a patient with osteoporosis should be made on a case-by-case basis. Certain patients would likely benefit from referral. These include patients with continuing bone loss or fracture despite taking first-line therapy, intolerance to medication, secondary causes of osteoporosis, and extremely low bone mineral density values.

CONCLUSION

This article touches on the workup and treatment of elderly patients with osteoporosis. It is aimed at Canadian primary-care providers, and uses the CAROC guidelines (as opposed to US or UK guidelines) to assess ten-year fracture risk.

This was not meant to be an in-depth review of the mechanisms of bone loss in the elderly. The desire is to provide an easy-to-follow practical guide to the office-based treatment of osteoporosis. The expectation is to decrease the risk of fragility fractures and its consequences in the frail, elderly population.

CONFLICT OF INTEREST DISCLOSURES

The authors declare that no conflicts of interest exist.

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