Alberta Doctors' Digest

Acute care for hip fractures will cost Alberta over $62 million in 2020

Care gap

Osteoporosis is exceedingly costly, both for the patient and the health care system. Osteoporosis Canada estimates, based on CIHI data, that acute care for patients with hip fractures will cost Alberta over $62 million in 2020. This does not include increased costs of care post-discharge. Roughly a quarter of patients with hip fractures will require institutional care post-discharge. Mortality is increased post-vertebral and post-hip fracture approximately three-fold. One-year post-op mortality for hip fracture patients is 25-30%.

Despite the fact that we have validated tools for calculating fracture risk and decades of experience using medications to lower that risk, many patients are not on treatment. Patients who have experienced a fragility fracture are often not screened for osteoporosis or offered appropriate therapy and rates are worsening over time.

In an effort to increase the number of patients appropriately treated for osteoporosis after an initial fragility fracture, the Alberta Health Services Bone and Joint Health Strategic Clinical Network has implemented a variety of fracture liaison services (FLS). This includes Catch A Break, which alerts patients with a wrist, humerus, pelvis or lower leg fracture to an increased risk of future fracture and encourages them to contact their physician for further evaluation. FLS are now embedded in a number of hospitals across most zones to evaluate, initiate therapy and follow patients for one year after hip fracture.

Patients who have experienced a fragility fracture are often not screened for osteoporosis or offered appropriate therapy and rates are worsening over time (Photo credit: freepix.com)

Case

Ms Y is a 72-year-old woman with a history of hypertension, osteoarthritis and well-controlled gastroesophageal reflux disease (GERD). She presents for a periodic health maintenance visit and seems generally well. Her current medications are ramipril, hydrochlorothiazide and pantoprazole. Your electronic medical record (EMR) reminds you that she has not been screened for osteoporosis.

Osteoporosis is a disease of compromised bone strength which can lead to increased risk of fracture. Bone strength reflects a combination of bone density and bone quality. Osteoporosis leads to an increased incidence of fractures resulting from low-impact trauma, or no trauma in the case of numerous vertebral fractures. In patients over the age of 50, 80% of all fractures are thought to be related to osteoporosis.

Objectives

- Be comfortable using established tools to estimate fracture risk and utilize that risk, not bone mineral density alone, to counsel patients regarding medications for osteoporosis.
- Be aware of the large gap in care for patients with osteoporosis.
- Understand benefits and risks of first-line medications for osteoporosis.

This article focuses on post-menopausal osteoporosis and follows the Toward Optimized Practice (TOP) guidelines on the topic.

Screening

To identify those at high risk, individuals over the age of 50 should be assessed periodically with focused history and physical exam for risk factors for osteoporosis and fracture. This assessment includes a review of or for the following:

- previous fragility fracture (a fracture resulting from a fall from standing height or less)
- parental hip fracture
- current smoking
- consumption of >3 units alcohol/day
- history of use of corticosteroids
- past medical history
- history of falls within the past year
- history of problems with gait and balance

Low weight (<60kg in men, <50kg in women), significant weight loss (>10%), and loss of height (potentially indicative of vertebral compression fractures) increase the risk of fracture. Patients with endocrine disease (hyperparathyroidism, hyperthyroidism, hypogonadism, diabetes), malabsorption (celiac disease, inflammatory bowel disease, cystic fibrosis), and rheumatologic illness are at higher risk of osteoporosis. Glucocorticoids, anticonvulsants, proton-pump inhibitors and numerous other medications can also contribute to fracture risk through a variety of mechanisms.

Estimating risk

Bone mineral density (BMD) as measured by dual energy X-ray absorptiometry (DEXA) is commonly used to diagnose low bone density. It also indicates a measurement for individuals > 65 years or those with increased risk of osteoporosis. BMD is generally reported as an exact density as well as a T score (the number of standard deviations away from the density of a healthy 20-year-old female). Bone density, however, may misrepresent a person's true probability of fracture. Bone quality, the other major component of bone strength, cannot yet be clinically measured.

A number of tools exist to help clinicians estimate fracture risk. CAROC is one recommended by Osteoporosis Canada. It uses age, gender, BMD at femoral neck, and presence/absence of previous fragility fracture to estimate fracture risk. The Fracture Risk Assessment Tool (FRAX) was developed and validated by the World Health Organization and can be done with or without a BMD measurement. Patients with a 20% probability of fracture within the next 10 years are considered high risk. Neither CAROC or FRAX takes into account a patient's risk of falling.

A previous fragility fracture is a strong indicator of poor bone quality and future fracture risk. It is generally agreed that patients experiencing a vertebral or hip fracture have established osteoporosis. In the absence of BMD, a wrist fracture portends a 14.2% 10-year probability of second fracture. A vertebral fracture has a 25.7% probability, a hip fracture has 24.9%, and humerus fracture has 23.7%. Perhaps most importantly, up to half of patients with hip fractures have previously sustained fractures, indicating a missed opportunity to initiate secondary prevention.

Medications

Patients with moderate probability (10%-19.9%) of fracture should consider pharmacologic treatment and patients with high probability (>20%) should strongly

consider therapy in the absence of contraindications. All treatment should be accompanied by Vitamin D supplementation (800-2,000 IU daily) and 1,200 mg/day of (preferably dietary) calcium.

Oral and IV bisphosphonates and denosumab have all demonstrated efficacy at reducing vertebral, non-vertebral and hip fractures, and are recommended first-line therapy. Teriparitide (an anabolic agent) is also first-line but is not reviewed here due to high cost. Recent meta-analysis suggests that denosumab improves bone density measurements but there is not enough data to claim that it is superior at preventing clinical fractures. Note that etidronate (Didrocal) is not effective at reducing non-vertebral fractures.

Bisphosphonates work by inhibiting osteoclasts, decreasing their ability to resorb bone and helping to restore the disrupted balance between bone resorption and bone building that occurs post-menopause in women and with aging in some men. Once-weekly oral bisphosphonates (alendronate and risedronate) are first-line treatment for osteoporosis. They are generally well tolerated, although they do have specific instructions such as take on an empty stomach with a full glass of water and remain upright and fasting for 30-60 minutes afterwards. Zoledronic acid is a parenteral alternative, infused annually. Bisphosphonates are renally cleared and are contraindicated in CrCl <35 mL/min (30 mL/min in risedronate).

Denosumab is a human monoclonal antibody that binds to cytokine RANKL, inhibiting osteoclast maturity and function. By blocking osteoclast action, it is also an anti-resorptive agent. Denosumab is administered every six months via subcutaneous injection.

Adverse events

Common side effects to oral bisphosphonates include reflux, esophagitis and gastrointestinal ulcers. IV zoledronic acid can cause flu-like illness within one to three days of infusion. There is some suggestion of increased atrial fibrillation with IV bisphosphonates, but the data remains mixed at this point.

Rare but serious side effects associated with anti-resorptives – bisphosphonate-related osteonecrosis of the jaw (ONJ) and atypical femoral fractures (AFF) – have been well publicized and have likely led to a decreased uptake. The risk of these are low; NNH in the case of AFF is estimated as 2,000 and for ONJ is between 10,000-100,000 (the NNH is smaller in doses of anti-resorptives used for treatment of malignancy). Similar adverse events have been found for denosumab. It is key to understand that the number of osteoporotic fractures that are prevented by these treatments far exceeds the incidence of these adverse events.

Patients taking these medications should be counselled appropriately about how to monitor and prevent these side effects: maintaining good oral hygiene and anticipating invasive dental procedures prior to starting bisphosphonate therapy may help prevent bisphosphonate-related ONJ. Patients should notify their health care provider if they develop new thigh or groin pain while on bisphosphonates, and providers should strongly consider bilateral full femoral X-rays +/- bone scan, to look for cortical thickening or incomplete fractures.

Because denosumab is not renally cleared it, has been considered an attractive option for treating osteoporosis in patients with chronic kidney disease (CKD). Unfortunately, in patients with CrCl <30 mL/min, there is an increased risk of clinically significant

hypocalcemia post-injection. Overall, fracture risk in patients with CKD is complex, and likely best managed by nephrology.

Duration of therapy

Because the risk of AFF may increase with longer duration of bisphosphonate use, and because bisphosphonates accumulate in bone, the American Society of Bone Mineral Research algorithm recommends that patients who are initially at high risk and remain at high risk receive an oral bisphosphonate for 10 years and six years of IV zolendronic acid. The risk/benefit ratio beyond these times is currently unknown. For lower-risk patients, consider a drug holiday after five years of clinical stability (no fractures, stable BMD) or three years of zoledronic acid..

There appears to be a short-term increase in the number of vertebral compression fractures after stopping denosumab, so the current pattern of practice is to continue it indefinitely or change to a bisphosphonate to avoid this. This becomes a challenge if denosumab is stopped due to worsening kidney function where bisphosphonates are contraindicated.

Back to the case

On further history, you note that Ms Y had a wrist fracture at the age of 62. Her mother had a hip fracture which precipitated a move to long-term care. She had one fall in the past year and is “not as quick as she used to be.” On exam she is 58 kg and 162 cm. She is not a smoker and does not drink regularly. She has no illnesses that predispose her to osteoporosis. Her estimated glomerular filtration rate is 52 mL/min. She has never had a BMD. You calculate her FRAX score in the absence of a BMD as a 34% chance of a major osteoporotic fracture and 18% chance of hip fracture within the next 10 years.

You counsel her regarding the risks and benefits of the medication, and she agrees to take alendronate once weekly in addition to dietary calcium and Vitamin D 1,000-2,000 U daily. In the event that her GERD significantly worsens with alendronate, you can trial risedronate once weekly. If both agents are intolerable, the Alberta Blue Cross Coverage for Seniors benefit has special authorization for annual IV zoledronic acid which can be administered at local infusion centres or in the person’s home, or semi-annual denosumab injections which can be provided by physicians, nurses and many pharmacists.

Together you agree to bring her in shortly to review balance and falls risk.

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References available upon request.