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CLINICAL REVIEW

Vertebral Compression Fractures and Osteoporosis

Pre-test Quiz

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True or False

1. Osteoporosis is a purely radiological diagnosis made with the help of a bone mineral density scan such as dual-energy X-ray absorptiometry (DXA).

2. Vertebral compression fractures in the setting of osteoporosis may be provoked by very low-energy trauma from day-to-day activities.

3. Operative management of vertebral compression fractures, such as with vertebroplasty or kyphoplasty, should only be considered after 3-6 months of failed conservative management.

ABSTRACT

Osteoporosis and vertebral compression fractures are commonly encountered pathologies that can have a significant impact on mobility, quality of life, and overall morbidity. Here we review the diagnosis, epidemiology, and risk factors of osteoporosis, as well as the most recent recommendations for primary and secondary prevention. Additionally, the current treatment approaches of vertebral compression fractures are discussed, including the roles of non-operative and operative management, indications for surgical intervention, and the evidence available to support treatment decisions.

KEYWORDS: osteoporosis, VCF, vertebroplasty, kyphoplasty

INTRODUCTION

Osteoporosis has a very high disease burden with a prevalence of 11.9% in Canadians 40 years or older, amounting to 1.8 million women and 400,000 men, with the total prevalence increasing to 31% in those aged 80 to 84 years old.[1] Consequently, vertebral compression fractures (VCFs), one of the most common complications of osteoporosis, have an annual incidence of 10.7 per 1000 women and 5.7 per 1000 men in the United States, with a lifetime prevalence of 25% in postmenopausal women.[2]

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VCFs are associated with chronic pain, impaired mobility, and kyphosis, leading to a reduced quality of life and increased risk of mortality.[3] As such, an understanding of the risk factors of osteoporosis, primary and secondary prevention of VCFs, as well as appropriate treatment modalities is essential given the societal and healthcare impacts of osteoporosis and VCFs.

Overview of Osteoporosis

The World Health Organization (WHO) defines osteoporosis as a bone mineral density (BMD) level below 2.5 standard deviations of the young adult reference mean.[4] Alternatively, low-level trauma leading to a fracture associated with osteoporosis (i.e., hip, vertebral, humerus, pelvis) in individuals 50 years or older, or a fracture risk of at least 20% using the Fracture Risk Assessment Tool (FRAX) can be used to establish an osteoporosis diagnosis clinically.[5] FRAX calculates the ten-year probability of fractures using a combination of demographic information (age, sex, weight, height), BMD, and risk factors associated with osteoporosis (Table 1).[5] Etiologies of secondary osteoporosis commonly include endocrine disorders of the thyroid and parathyroid glands, malabsorption syndromes, and systemic glucocorticoid therapy (Table 2).[4]

Primary Prevention of Osteoporosis

The 2023 clinical practice guidelines for management of osteoporosis make the following three broad recommendations for all postmenopausal females and males aged 50 years or older:

1. Balance and muscle strengthening exercises at least twice weekly,
2. Foods rich in calcium and protein,
3. Vitamin D supplementation of 400 IU daily.[5]

The decision to start pharmacotherapy is made by assessing the 10-year fracture risk using FRAX, or based on previous history of fractures, where pharmacotherapy is suggested at a 10-year risk of at least 15%.[5] Options include anabolic therapy (teriparatide, romosozumab) in cases of recent or multiple vertebral fractures, bisphosphonates (alendronate, risedronate, zoledronic acid), or denosumab if bisphosphonates are contraindicated (Table 3).[5]

CLINICAL EVALUATION AND DIAGNOSIS

The clinical evaluation of osteoporosis and VCFs should include a thorough history to elicit any risk factors (Table 1) or possible secondary etiologies of osteoporosis (Table 2). VCFs can be provoked by low-energy trauma or exertional activity, and the classic presentation typically involves acute low back pain of variable intensity that is worsened on movement.[6,7]

Additionally, a functional history should also be obtained in order to determine the impact of the pain on the patient's instrumental activities of daily living (IADLs), which can help contextualize the severity of the disease.

While VCFs are most commonly attributed to osteoporosis, there are several red-flag etiologies which must be ruled out, including infection, trauma, and malignancy. In particular, a high index of clinical suspicion should be maintained in younger patients (less than 50 years old) presenting with VCFs for etiologies other than osteoporosis, given that the bone mass of the spine typically peaks around the 2nd decade of life.[8] Constitutional symptoms, intravenous drug use or immunosuppression, back pain associated with morning stiffness and palliated by physical activity are all red flag symptoms of back pain that must be explicitly ruled out.

Table 1: Risk factors of osteoporosis used in the FRAX score.

History of previous fractures
History of hip fracture in parents
Currently smoking
Glucocorticoid therapy
History of rheumatoid arthritis
Diseases associated with secondary osteoporosis (Table 2)
Alcohol use of ≥ 3 standard units per day

Specific physical exam findings that may point to a VCF include:

- Height loss,
- Rib-pelvis distance ≤ 2 cm at the midaxillary line, or
- Occiput-to-wall distance < 5 cm.[5]

Focal tenderness over the region of a suspected fracture is often present, and any mechanical nature of this pain should be elucidated, i.e. relief with recumbency and provocation with sitting/standing, suggestive of a more acute/subacute fracture. Additionally, a thorough neurological exam should be conducted in order to assess for motor or sensory loss, as well as for signs of upper or lower motor neuron disease. Special attention should be paid to saddle anesthesia, which may be associated with fecal or urinary incontinence and is worrying for cauda equina syndrome.

The low back pain and decreased mobility caused by VCFs are also known to be associated with several complications, including constipation, dyspnea, deep vein thrombosis, as well as chronic pain.[6,7]

Investigation

The 2023 clinical practice guidelines suggest BMD estimation with dual-energy X-ray absorptiometry (DXA) in order to stratify the risk of fractures for those aged 50 to 64 with either at least 2 risk factors (Table 1) or previous osteoporotic fractures, those aged 65-59 with

Table 2: Etiologies of secondary osteoporosis, reprinted from source.[4]

Endocrine or Metabolic Causes Hyperparathyroidism Hypophosphatasia Hypercortisolism Diabetes Adrenal insufficiency Hypogonadism Hyperthyroidism Growth hormone deficiency Acromegaly Pregnancy	**Medications** Glucocorticoids Aromatase inhibitors Gonadotropin-releasing hormone agonists Lithium Medroxyprogesterone acetate Chemotherapy and immunosuppressants Antiepileptics (phenobarbital, phenytoin, carbamazepine, valproate) Anticoagulants (heparin and coumadin) Thiazolidinediones Proton pump inhibitors Thyroid hormone (in supraphysiologic doses) Antiretrovirals (tenofovir, adefovir) Sodium-glucose co-transporter-2 inhibitors
Gastrointestinal Disorders Vitamin D deficiency Calcium deficiency High caffeine intake Anorexia nervosa Alcoholism Chronic liver disease Malabsorption (inflammatory bowel diseases, celiac sprue, pancreatic disease, gastric resection or bypass)	**Connective Tissue Disorders** Osteogenesis imperfecta Marfan syndrome Ehlers-Danlos syndrome Homocystinuria
Hematologic Disorders Multiple myeloma Leukemia and lymphoma Hemophilia Sickle cell disease Thalassemia Systemic mastocytosis	**Other** Idiopathic hypercalciuria Immobilization Low physical activity Rheumatoid arthritis Chronic obstructive pulmonary disease Chronic kidney disease Congestive heart failure Human immunodeficiency virus and acquired immunodeficiency syndrome

Table 3: Available pharmacological options for the treatment of osteoporosis.[5]

Class	Drug	Dosing Options	Treatment Duration
Bisphosphonates • Reassessment after initial 3 years recommended • Avoid in hypocalcemia • Avoid in decreased renal function (CrCl < 30–35 mL/min)	Alendronate	70 mg PO weekly 10 mg PO daily	3 years initially
	Risedronate	150 mg PO monthly 35 mg PO weekly 5 mg PO daily	
	Zoledronic Acid	5 mg IV yearly	
RANK-L Inhibitors • Uninterrupted treatment recommended • Delayed/missed injections may lead to rapid bone loss; bridging with bisphosphonates recommended if discontinuing after ≤ 4 doses	Denosumab	60 mg SQ every 6 months	Long-term
PTH Analogs • Avoid in decreased renal function (CrCl < 30mL/min) • Contraindicated if previous history of skeletal malignancy or radiotherapy • Consider using an anti-resorptive agent (bisphosphates, RANK-L inhibitors) after therapy	Teriparatide	20 mcg SQ daily	2 years
Sclerostin Inhibitors • Contraindicated if previous history of myocardial infarction or stroke • Consider using an anti-resorptive agent (bisphosphates, RANK-L inhibitors) after therapy	Romosozumab	210 mg SQ monthly	1 year

Abbreviations: CrCl = creatinine clearance, RANK-L = receptor activator of nuclear factor κ-B ligand, PTH = parathyroid hormone

one risk factor, and in those aged 70 and above with no risk factors.[5] In symptomatic patients, the diagnosis of VCFs can be confirmed with radiological imaging of the thoracic and lumbar spine.

Radiologically, VCFs are most commonly categorized by the Genant classification, which groups the fractures into both severity (grade 1 to 3 or mild, moderate, and severe) and morphology based on the loss of anterior height (wedge deformity), posterior height (crush deformity), or middle height (biconcave deformity) of the vertebral body.[7] Additionally, while CT scans of the spine can be used for surgical planning, they are also associated with a higher cost and radiation dosage than plain radiographs.[9]

In addition to better delineating anatomy, MRI sequences can be used to determine chronicity of fractures and for prognostications, with STIR hyperintensities being associated with acute fractures (< 3 months) possibly amenable to vertebral augmentation, T1 hypointensities associated with back pain, and T2 vertebral body hyperintensities associated with a higher likelihood of residual back pain up to 6 months post-fracture.[9,10] Moreover, radionuclide bone scans such as positron emission tomography (PET) or bone scintigraphy can be used to investigate for features suggestive of malignant fractures based on radionuclide uptake patterns.[9]

Importantly, regardless of imaging modality, the fracture should be correlated to the location of the pain that the patient is experiencing, as many patients will often present with associated or comorbid musculoskeletal or degenerative pain that would not be relieved with vertebroplasty.

MANAGEMENT

Conservative Management

Treatment of VCFs should centre on a patient's goals of care, aiming to relieve pain, restore function, and prevent future fractures, while also considering the risks and benefits of conservative versus operative management. For those opting for conservative care, there is a greater than 50% likelihood of achieving significant pain relief, with most improvement occurring within three months.[11] A study involving 259 patients with VCFs found that those who experienced pain relief and reduced disability after three weeks of conservative therapy had a 95% probability of maintaining these benefits for up to 12 months.[11] The conservative treatment of VCFs consists of multiple approaches with varying degrees of supporting evidence. While some interventions, such as early mobility and pain management, have well-established benefits, others, including bracing, have limited or inconclusive evidence regarding their effectiveness.

Early mobility should be encouraged as soon as tolerated, as prolonged bed rest, while sometimes necessary for severe pain, can lead to complications such as bone mass loss, muscle weakness, pressure sores, and deep venous thrombosis.[12] Effective pain management during activity, primarily achieved through medication, is crucial for facilitating early mobilization and is therefore essential for improving patient outcomes. A systematic review of conservative treatment for VCFs identified calcitonin, followed by NSAIDs, as the most effective for short-term pain relief during activity, significantly reducing pain compared to placebo.[13] The same study also identified teriparatide, an osteoanabolic agent, as more beneficial for long-term pain relief compared to bisphosphonates, which showed limited effectiveness for both short-term and long-term pain relief.[13] Additionally, there is limited evidence supporting the use of opioids for pain management in VCF.[13,14] Bracing is frequently prescribed for six to eight weeks following a VCF, but studies on its effectiveness are inconclusive.[15–17] While some research suggests thoracolumbar bracing may improve posture, strength, and quality of life,[18] other studies have identified no long-term benefit when comparing no bracing to the use of rigid, soft or semirigid bracing.[13,17]

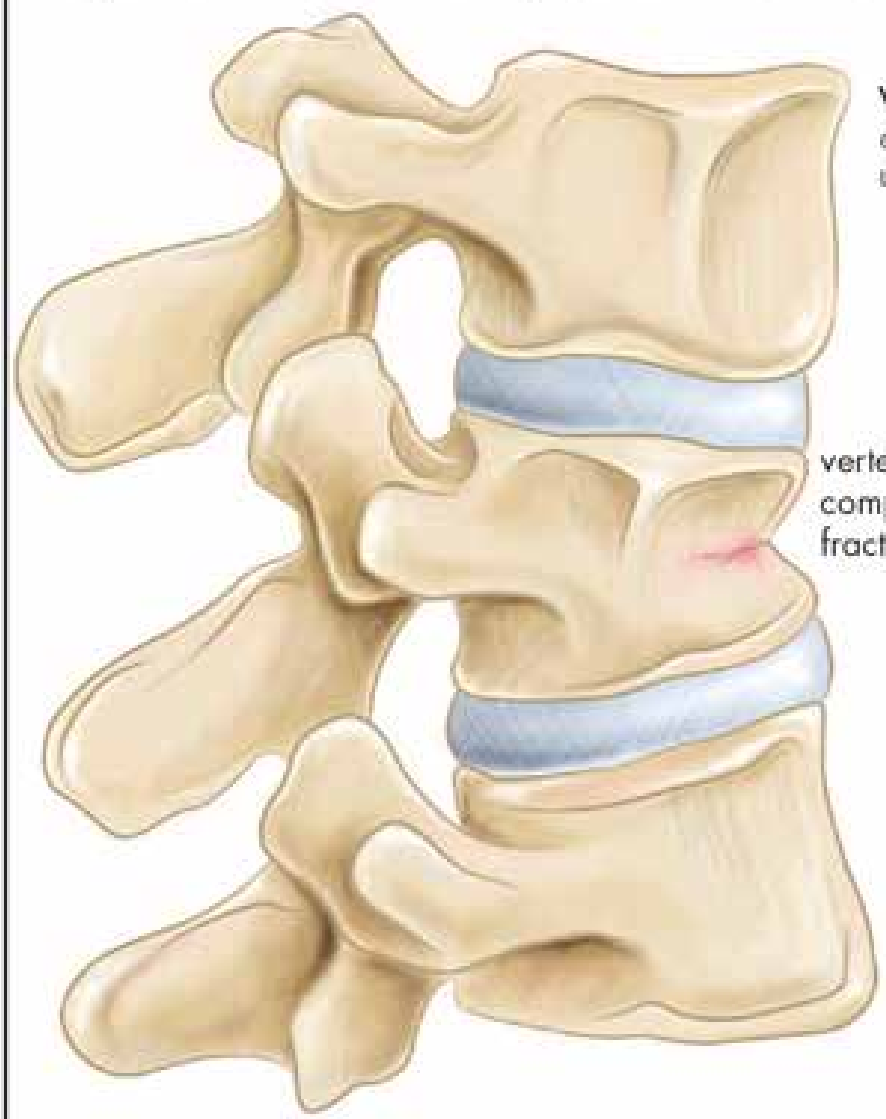
Operative Management

The most recent consensus statement by multiple neurosurgical and interventional radiology societies strongly recommend operative intervention in the case of failed conservative management, which is defined as severe pain refractory to analgesia that prevents ambulation or physical therapy, or failure of analgesia due to adverse side effects.[12] Additionally, opinions have also began to shift regarding the timing of operative management; previously, nonoperative management would be trialled for a period of 6-8 weeks, with operative management considered if symptoms persist.[2,19] However, a recent systematic review demonstrated that early surgical treatment of VCFs with kyphoplasty showed no significant difference in terms of clinical outcomes, with earlier intervention associated with decreased adjacent vertebral fractures compared to delayed intevention.[19]

Vertebral Augmentation Techniques

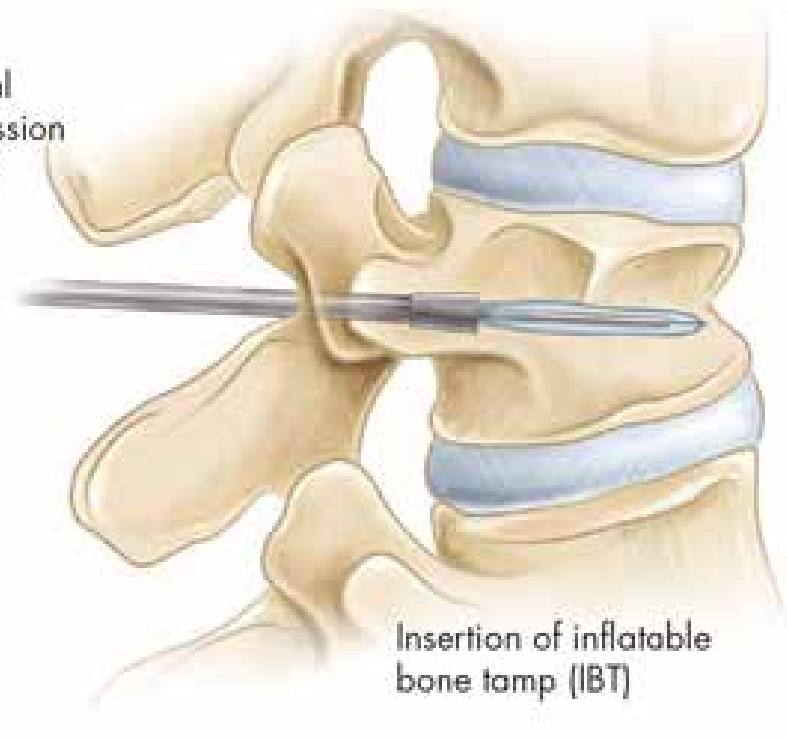
Operative management of VCFs with vertebral augmentation is comprised of two main techniques: percutaneous vertebroplasty and balloon kyphoplasty.[2] In vertebroplasty, polymethyl methacrylate bone cement is injected into the vertebral body under fluoroscopic guidance, providing increased strength within the ver-

Repair of Vertebral Compression Fractures

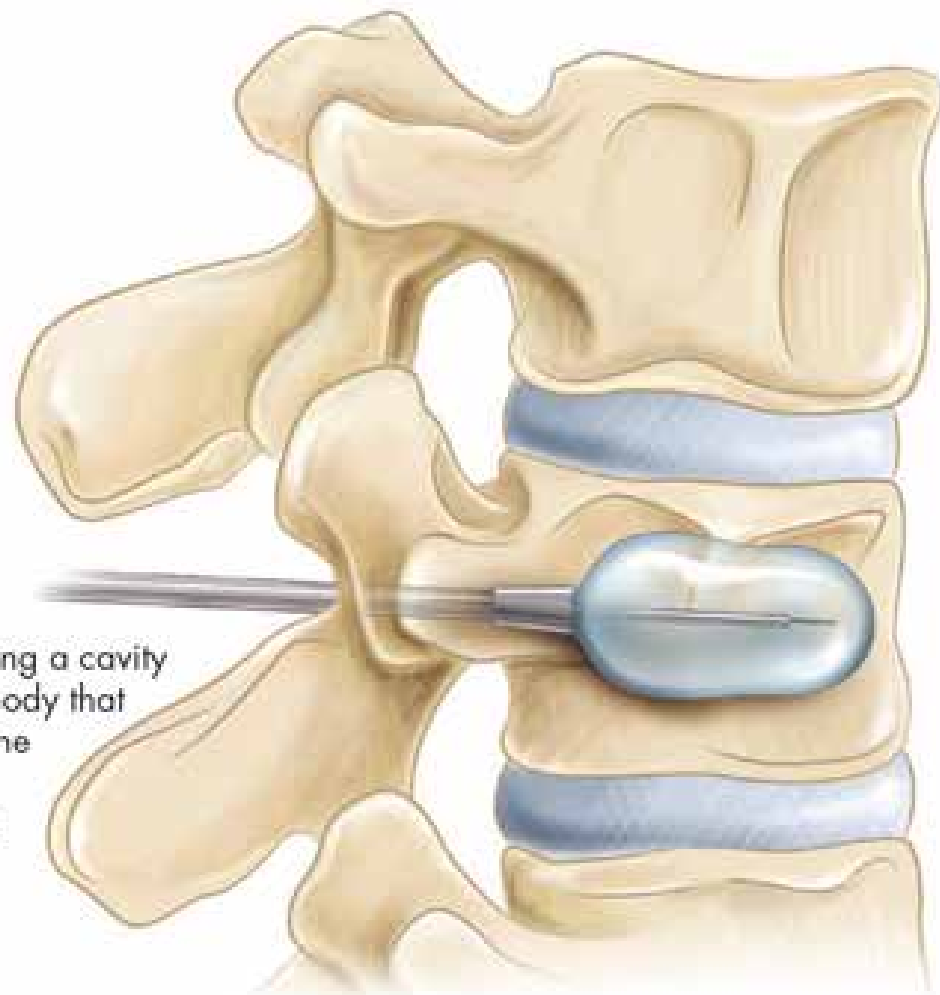


Vertebral compression fractures (VCF) are the hallmark of osteoporosis, yet two-thirds of all VCF remain undiagnosed and untreated.

vertebral compression fracture



Insertion of inflatable bone tamp (IBT)



kyphoplasty is a minimally invasive surgical procedure used for treating vertebral fractures resulting from osteoporosis. It is designed to strengthen the spine and relieve back pain.

Inflation of IBT, creating a cavity inside the vertebral body that can be filled with bone cement in order to stabilize the fracture

tebral body once the cement hardens.[20] In comparison, kyphoplasty is a second generation technique that first involves the inflation of a bone tamp within the vertebral body before injection of bone cement, theoretically providing more vertebral body reduction and also decreasing the risk of cement extravasation.[20] While vertebroplasty and kyphoplasty are currently the most widely-adopted and studied techniques, third generation approaches which involve mechanical expansion of the vertebral body as opposed to using bone cement for reduction are available, but their relative utility and cost profile in comparison to older generation approaches remains under investigation.[20]

There have been several studies and meta analyses comparing the efficacy of the surgical techniques available with non-operative management, with some presenting conflicting results. A pair of studies published in 2009 investigating the efficacy of vertebroplasty in osteoporotic VCFs and painful VCFs, respectively, showed no benefits of vertebroplasty compared to sham procedure.[21,22] Since then, several other studies have compared the safety and efficacy of operative management with either vertebroplasty or kyphoplasty to medical management alone. In a meta analysis of 27 studies, Papanastassiou et al. (2012) showed that both vertebroplasty and kyphoplasty were superior to nonsurgical management in pain reduction and preventing future VCF.[23]

Additionally, there have been several studies comparing vertebroplasty to kyphoplasty in terms of safety and efficacy. The previously discussed meta analysis of Papanastassiou et al. (2012) also showed

KEY POINTS

1. Osteoporosis has a very large disease burden in Canada, and vertebral compression fractures are one of its most common complications.
2. The Fracture Risk Assessment Tool (FRAX) should be used to calculate a 10-year risk of fractures in order to guide the management of osteoporosis.
3. A vertebral compression fracture should be suspected in patients with a history of osteoporosis presenting with acute low back pain.
4. Operative treatment options of vertebral compression fractures include vertebroplasty and kyphoplasty, both of which have been shown to be safe and efficacious in clinical trials.

similar outcomes in both surgical techniques, albeit with decreased risk of cement extravasation in balloon kyphoplasty.[23] A recent study comparing the two techniques for patients with osteoporotic VCFs also showed a similar result, with no significant difference in postoperative visual analog pain score or fracture reduction among vertebroplasty and kyphoplasty.[24] With regards to cement extravasation, the EVOLVE trial in 2018 showed that balloon kyphoplasty, compared to nonsurgical care, resulted in a significant improvement in pain and quality of life through multiple rating scales, but also demonstrated a 21.4% cement extravasation rate, all cases of which were asymptomatic.[25]

Lastly, as with all procedures, there are risks present which should be clearly discussed before proceeding with the operation, with the patient involved through shared decision making. In addition to the risks typically associated with surgeries such as bleeding, infection, injury to adjacent structures (e.g., spinal cord leading to new deficits) and the risks of anesthesia, there is also a risk of cement extravasation as noted previously, with 1% of cement extravasation cases leading to pulmonary embolisms, and 3% having nerve root involvement.[9]

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CLINICAL PEARLS

- Physical activity as tolerated should be encouraged as part of a conservative approach to managing a vertebral compression fracture.
- Plain radiographs can be used to assess for the presence of vertebral compression fractures, while MRI sequences can be used in determining the acuity of vertebral compression fractures.
- Vertebral augmentation is indicated in vertebral compression fractures if the pain is intractable and limits ambulation despite appropriate analgesic therapy.

Post-test Quiz

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Multiple Choice

1. All of the following are risk factors for 10-year fracture risk, as calculated by the FRAX score, EXCEPT:

2. Which of the following is true regarding the pharmacotherapy of osteoporosis?

3. Which of the following signs and symptoms are associated with a vertebral compression fracture?

4. Which of the following is a reasonable initial conservative management strategy for a vertebral compression fracture?

5. Which of the following is true regarding surgical management of vertebral compression fractures?:

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