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CLINICAL REVIEW

Risk Assessment, Prevention, and Treatment in Osteoporosis-Related Fractures

Pre-test Quiz

1. The Fracture Risk Assessment Tool (FRAX) can be used with or without bone mineral density (BMD) measurements to estimate a patient's 10-year probability of major osteoporotic and hip fractures.
2. Long-term use of denosumab is associated with a durable reduction in vertebral fracture risk, but discontinuation without sequential therapy can result in rapid bone loss and rebound vertebral fractures.
3. Vertebroplasty and kyphoplasty are considered first-line treatments for all osteoporotic vertebral fractures due to their ability to restore bone strength and prevent future fractures in high-risk patients.

ABSTRACT

Osteoporosis-related fractures represent a growing global health burden, requiring comprehensive strategies that span risk assessment, prevention, pharmacologic therapy, and surgical care. Dual-energy X-ray absorptiometry (DEXA) remains the diagnostic standard. However, fracture prediction improves when combined with clinical risk models, such as the Fracture Risk Assessment Tool (FRAX), QFracture, Garvan Risk Calculator, or a simplified assessment created by the Canadian Association of Radiologists and Osteoporosis Canada (CAROC). Effective prevention should be approached across the lifespan, maximizing peak bone mass in youth and attenuating later loss through lifestyle modifications. Pharmacologic therapy remains central to proper management while the treatment sequence, duration, and adverse effects necessitate individualized decision-making. In primary care, targeted screening of at-risk populations, systematic use of fracture risk calculators, prompt initiation of secondary prevention after sentinel fractures, and integration of multidisciplinary models are paramount.

KEYWORDS: Osteoporosis, fragility fractures, DEXA, fracture risk calculators, pharmacologic therapy.

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Introduction

Osteoporosis is characterized by low bone mass and microarchitectural deterioration of bone tissue, resulting in increased bone fragility and susceptibility to fracture.[1] It primarily affects the elderly and results from a combination of hormonal factors, lifestyle choices, and external mechanical loads. Changes in the internal scaffolding of the vertebral bodies with greater loss of horizontal trabeculae compared to vertical trabeculae contributes to the increased vertebral fracture rate.[2]

In patients over 65 years, the prevalence of osteoporotic vertebral fractures (OVF) is 39%.[3] As life expectancy globally is projected to reach approximately 76 years by 2045, the expected number of centenarians worldwide, 3.2 million, will be significantly higher than the estimated 180,000 alive in 2000.[3]

In Canada, in 2021 there were over 861,000 people aged 85 and older, more than double the number recorded in 2001.[4] By 2050, this segment of the population is expected to surpass 2.7 million. It is estimated that 2 million people in Canada live with osteoporosis.

In 2004, Papaioannou et al. highlighted a care gap in Canadian osteoporosis management.[5] The situation is similar in the United States where a strikingly low number of patients received treatment for osteoporosis in the two years before an OVF, while after the event, only 7% of patients had pharmacologic therapy.[6]

Pathogenesis and clinical presentation

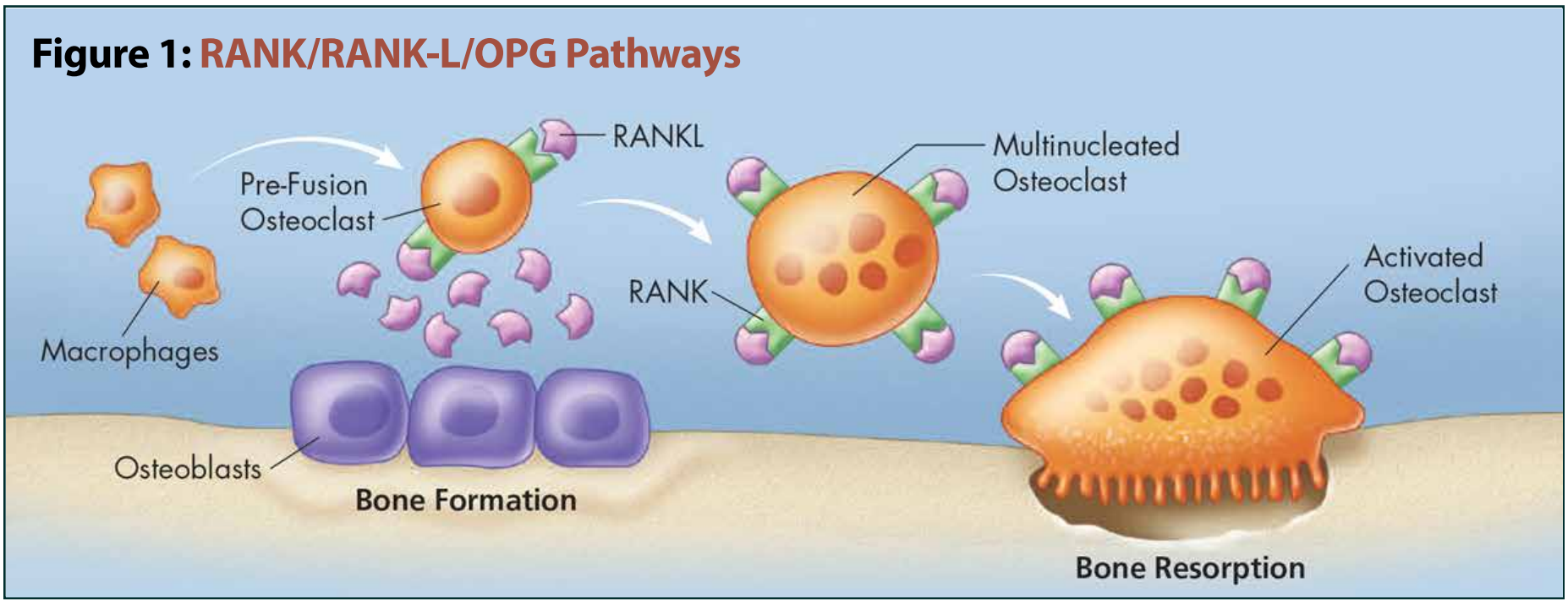
The osteoporotic disruption of bone remodeling homeostasis, favoring increased osteoclastic resorption over osteoblastic formation, is caused by a combination of intrinsic and extrinsic factors.[7] These include estrogen deficiency, aging, genetic predisposition, and modifiable lifestyle choices such as physical inactivity and inadequate intake of calcium and vitamin D.[8] Some evidence suggests that additional mechanisms, such as increased oxidative stress, impaired gastrointestinal calcium absorption, and changes in collagen composition and cross-linking may further compromise the bone's biomechanical competence.[8,9]

Bone strength depends on bone mineral density (BMD) but also on the microarchitecture, material properties, and geometry. Bone remodeling, which maintains skeletal integrity, is a balance between osteoclastic bone resorption and osteoblastic bone formation regulated by pathways such as the RANK/RANKL/OPG system and WNT–Sclerostin signaling. RANK/RANKL/OPG is a pathway crucial for bone remodeling. RANKL (ligand) binds to its receptor, RANK, on osteoclast precursors to trigger differentiation and

activation, which leads to bone resorption. OPG (osteoprotegerin) acts as a decoy receptor, binding to RANKL and blocking the RANK-RANKL interaction, thereby inhibiting osteoclast formation and protecting bone from excessive resorption. The balance between RANKL and OPG determines overall bone mass.[10] Sclerostin is a protein produced by osteocytes that acts as a potent inhibitor of a crucial pathway for bone formation. This inhibition ultimately leads to reduced bone formation and increased bone resorption.[11] (Figure 1) Osteocytes play a central role as mechanosensors, detecting microdamage and initiating targeted remodeling.[12] With aging, there is an increase in cortical porosity and trabecular thinning, resulting in structural weakness. Failure to achieve optimal bone mass during early adulthood, combined with accelerated bone loss in later life, particularly after menopause, substantially increases the risk of fractures. Genetic variants, hormonal changes, chronic inflammation, and medications such as glucocorticoids contribute to this dysregulation.[13]

Because approximately two-thirds of vertebral fractures are clinically silent, producing chronic back pain, progressive height loss, and kyphotic deformity, they are often underrecognized.[14,15] In contrast, osteoporotic hip fractures, especially among the elderly, lead to immediate functional decline, high morbidity, and increased risk of death.[16] A recent study reported one-year mortality rates after hip fractures in older patients ranging from 17% to 22%, with some groups showing rates as high as 30%.[17,18] Other common fracture sites include the forearm, shoulder, and pelvis, while fractures of the skull, hands, or feet are rarely associated with osteoporosis.[6,19]

Figure 1: RANK/RANK-L/OPG Pathways



Preventive strategies, risk assessment tools, and guidelines for primary care providers

Preventive Strategies

Osteoporotic fractures may be avoided with structured, evidence-based preventive strategies.[18] Two objectives guide management: attenuation of disease severity and reduction in the incidence of events that precipitate low-energy injuries.[20]

Ideally prevention begins early in life allowing the benefits to be sustained across the years ahead. The primary goal in childhood and adolescence is to optimize bone mass and achieve the highest possible peak. In adulthood, particularly after menopause and in older age, the focus shifts toward slowing bone loss through lifestyle modifications and, when indicated, pharmacological therapy.[20] Prevention should target individuals with established osteoporosis or a history of fragility fractures and aim to prevent skeletal trauma.[21] The coexistence of risk factors (Table 1) substantially increases fracture probability.[22]

Vitamin D supplementation remains an area of ongoing debate.[23,24] The Endocrine Society advises against routine screening for vitamin D deficiency but recommends testing only in high-risk groups, such as individuals with chronic kidney or liver disease, malabsorption syndromes, or those taking medications that increase vitamin D catabolism. In children and adolescents aged 1–18 years, giving vitamin D is recommended to prevent nutritional rickets and potentially reduce respiratory tract infections. Doses in clinical trials range from 300 to 2,000 IU/day. (Table 2)

Calcium is a fundamental component of the inorganic bone matrix and a critical nutrient in the prevention of osteoporosis.[26] Intake recom-

Table 1: Risk Factors for Osteoporosis

Non-modifiable	Modifiable
Advanced age	Tobacco use
Female sex	Alcohol intake
Postmenopausal status	Physical activity
Caucasian ethnicity	Inadequate Calcium, Vitamin D and Protein intake
Genetics	Glucocorticoid therapy
Family history of fragility fracture	Comorbidities (hypercalciuria, diabetes mellitus, Cushing's syndrome)

Table 2: Recommendations for Vitamin D supplementation

Age Group	Recommendation
1–18 y	300–2,000 IU/day*
≤50 y	Do not exceed 600 IU/day
50–74 y	Do not exceed 600 IU/day (≤70 y)/800 IU/day (>70y)
≥75 y	400–3,333 IU/day (daily low-dose preferred; avoid high-dose intermittent)

mendations vary worldwide, and supplementing with calcium alone has not been shown to consistently reduce fracture risk.[25] Combining calcium and vitamin D, however, has demonstrated a reduction in the overall fracture risk by 5–15% and in hip fractures by 13–30%. The most significant benefits were observed in elderly nursing homes residents.[25] Serum concentration of 25-hydroxyvitamin D should be between 20–50 ng/mL in the general population and between 30–50 ng/mL in individuals at high risk of fragility fractures.[26]

An essential component of preventing osteoporotic vertebral fractures is reducing the incidence of spinal trauma. Prevention encompasses comprehensive fall-prevention strategies including balance and gait training, targeted muscle strengthening—particularly of the ankle and foot to enhance postural stability—and resistance or impact-loading exercises to preserve bone mass and maintain functional mobility.[21] Optimizing sensory functions, vision and hearing, is critical as is a judicious reduction of medications that may cause sedation or orthostatic hypotension. Cervical myelopathy is a significant concern; 18% of patients with hip fractures were found to have upper neuron signs.[27] Additional measures include managing urinary incontinence to prevent urgency-related falls, proper foot care with well-fitted footwear, and environmental modifications such as improved lighting, the installation of handrails, provision of toilet supports, and use of appropriate walking aids like canes or walkers.[14,30]

Risk Assessment Tools

Osteoporosis is defined by the WHO as a T score of –2.5 or lower on dual-energy X-ray absorptiometry (DEXA), reflecting a bone mineral density 2.5 standard deviations below the mean of young adults. A T score between –1 and –2.5 indicates osteopenia, whereas a T score –1 or higher is considered normal.[28] While bone turnover markers, such as serum C-terminal telopeptide or procollagen type I N-terminal

propeptide, are increasingly used in specialized care to monitor therapy, their role in primary care remains limited. DEXA remains the gold standard for assessing BMD in the spine and hip, providing a standardized tool for predicting osteoporotic fractures.[29,32]

In recent years, it has been recognized that clinical risk factors, beyond BMD values, significantly contribute to fracture risk.[30] The use of a variety of tools developed to calculate a patient's fracture risk has been associated with an increased prediction of osteoporotic fractures.[31,32]

Most used is the Fracture Risk Assessment Tool (FRAX), which has been employed in several population-based cohort studies worldwide.[33] FRAX, developed by the WHO Collaborating Centre for Metabolic Bone Diseases, calculates the 10-year probability of hip and major osteoporotic fractures for patients aged 40–90 based on clinical risk factors, with or without the input of femoral neck BMD value. This computer-based algorithm is freely available online.[34] Two other calculators based on data from single countries are also commonly employed, the QFracture in the United Kingdom, which estimates 1 to 10-year fracture risk in people aged 30–99 without BMD measurement, and the Australian Garvan Fracture Risk Calculator, which provides osteoporotic or hip fracture risk percentage over 5 or 10 years based on age, sex, prior fracture, falls, and BMD.[35,36]

In 2005, Osteoporosis Canada, in partnership with the Canadian Association of Radiologists, created the Canadian Association of Radiologists and Osteoporosis Canada (CAROC) tool. CAROC stratifies 10-year fracture risk into low (<10%), moderate (10–20%), or high (>20%) categories based on age, sex, femoral neck T-score, and the presence of a prior fragility fracture or prolonged glucocorticoid therapy. The CAROC system aligns well with the Canadian population datasets and is a valuable tool when it is not feasible to use the full FRAX model.[37]

Computed tomography Hounsfield unit (HU) measurements of vertebral trabecular bone provide an opportunity for BMD estimation from routine chest, abdominal, or lumbar CT scans without additional radiation or cost. HU thresholds correlate strongly with DEXA T-scores and fracture risk, allowing for the early detection of osteoporosis in patients undergoing CT for other reasons.[38] HU values can differ depending on the anatomical location, even between vertebrae in the same patient. The range for diagnosing osteoporosis extends from 99 to 136 HU.[39]

Magnetic resonance imaging is a promising tool for evaluating bone quality. The Vertebral Bone Quality (VBQ) score utilizes T1-weighted images of the L1–L4

vertebral bodies and has shown good correlation with BMD values and T-scores.[40] MRI-based VBQ scores may help identify patients with low bone mass but prospective studies are still necessary.[41]

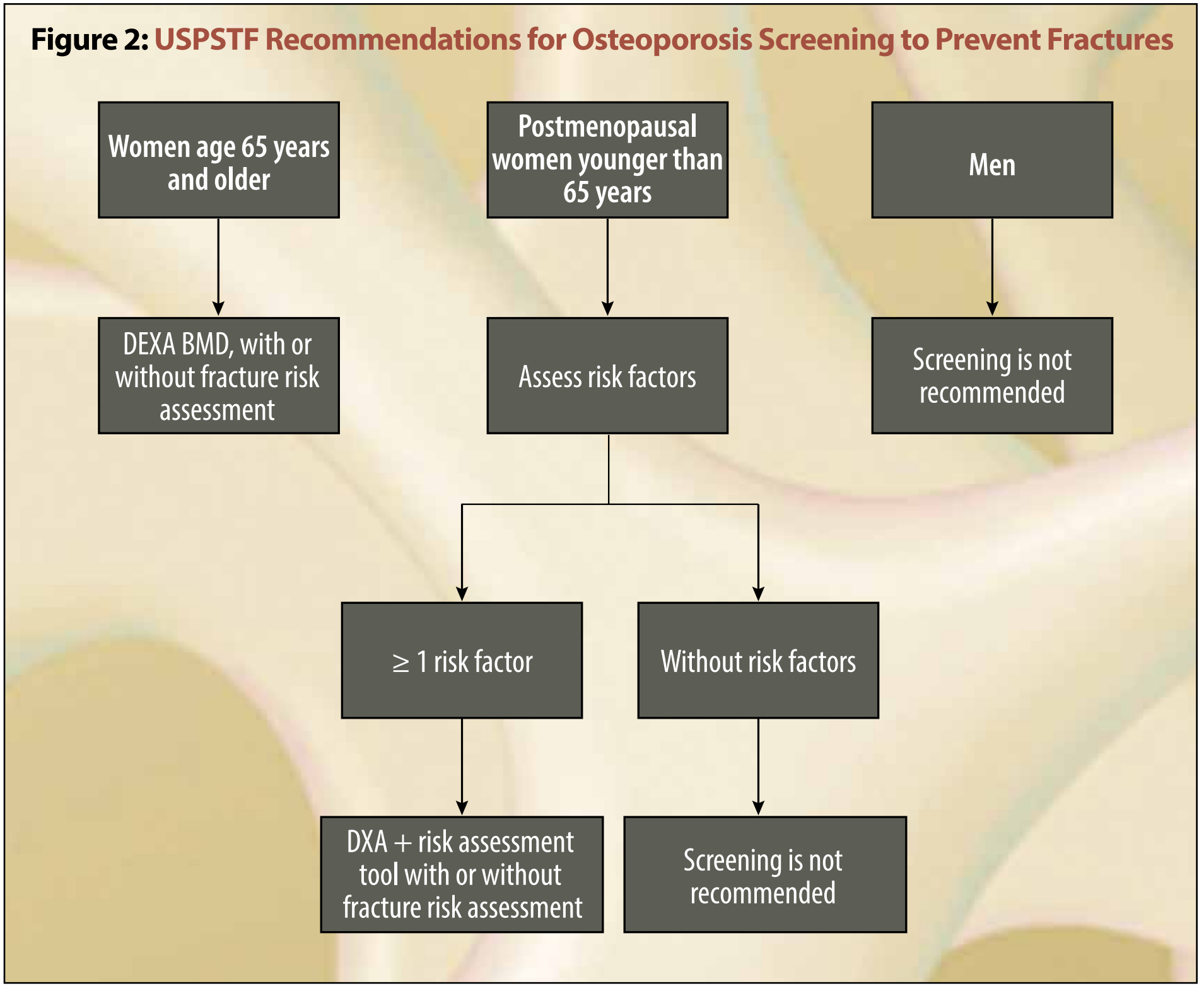
Guidelines for Primary Care Providers

Primary care providers are central to the promotion of lifestyle modifications that address modifiable risk factors. Evidence-based guidelines emphasize the importance of a systematic and proactive approach incorporating risk assessment, pharmacological interventions, and prevention programs.[15,42] To optimize health system resource allocation, osteoporosis screening should be selective.[42] Major guidelines, including those from the Endocrine Society, the National Institute for Health and Care Excellence (NICE), and the Canadian Osteoporosis Guidelines, recommend targeted screening in populations at increased risk—postmenopausal women, men aged 70 years or older, and younger individuals with clinical risk factors. The integration of DEXA with validated fracture risk algorithms provides the most accurate stratification.[43] The most recent statement from the US Preventive Services Task Force (USPSTF) introduced updated recommendations derived from a comprehensive evidence synthesis.[44] (Figure 2)

The 2023 Canadian clinical practice guideline emphasizes the critical role of exercise in preventing and managing osteoporosis. Balance and functional training, performed at least twice weekly, is strongly recommended to reduce fall risk and improve physical function. Progressive resistance training, recommended at a minimum of two sessions per week, should target key muscle groups, including the spinal extensors and abdominals, to reinforce postural control and bone strength. Additional activities, such as walking, impact exercise, yoga, and Pilates, may be encouraged for enjoyment and overall well-being, but should complement, rather than replace, structured balance and resistance programs. Good practice statements recommend modifying activities in high-risk individuals that involve rapid twisting or sustained spinal flexion and encourage referral to exercise professionals trained in osteoporosis management when available.[42]

The occurrence of a fragility fracture should trigger immediate secondary prevention measures. That first fracture should initiate a prompt response, ensuring appropriate referrals, and integrating multidisciplinary support.[18] Evidence suggests that fewer than one-third of patients receive adequate pharmacological treatment following a sentinel fracture.

Figure 2: USPSTF Recommendations for Osteoporosis Screening to Prevent Fractures



Pharmacologic therapies

Pharmacological intervention is indicated in patients with a prior fragility fracture, a DEXA T-score at or below −2.5, or high fracture risk as determined by clinical algorithms. Because of their efficacy, cost-effectiveness, and robust safety profile, antiresorptive medications—usually bisphosphonates (alendronate, risedronate, ibandronate, zoledronic acid) or raloxifene, and menopausal hormone therapy remain the first-line agents.[18] Denosumab represents a potent antiresorptive alternative, especially in patients with renal impairment. Anabolic agents such as teriparatide, abaloparatide, and romosozumab should be reserved for high-risk individuals or those with multiple fractures. The choice of therapy should take into account the fracture risk profile, comorbidi-

ties, renal function, and patient adherence.[42] (Figure 3) Moderate to high-certainty evidence supports the effectiveness of pharmacotherapy in females with less certainty in men.

Research validates the use of bisphosphonates in reducing the frequency of vertebral and hip fractures. Ibandronate is effective only for treating vertebral fractures, while there is high quality evidence that denosumab reduces vertebral, hip, and peripheral fractures. Both ibandronate and denosumab rarely cause jaw osteonecrosis (0.2–10 per 10,000 patient-years) and atypical femur fractures especially in Asian women. Stopping them leads to rapid bone loss and a bisphosphonate should be given to prevent rebound fractures (Table 3).

Raloxifene, an estrogen receptor agonist, modestly reduces vertebral fracture risk in postmenopausal women but has no effect on nonvertebral fractures. It increases the risk of venous thromboembolism and may elevate the risk of stroke.

Figure 3: Overview of Treatment Approaches to Osteoporosis

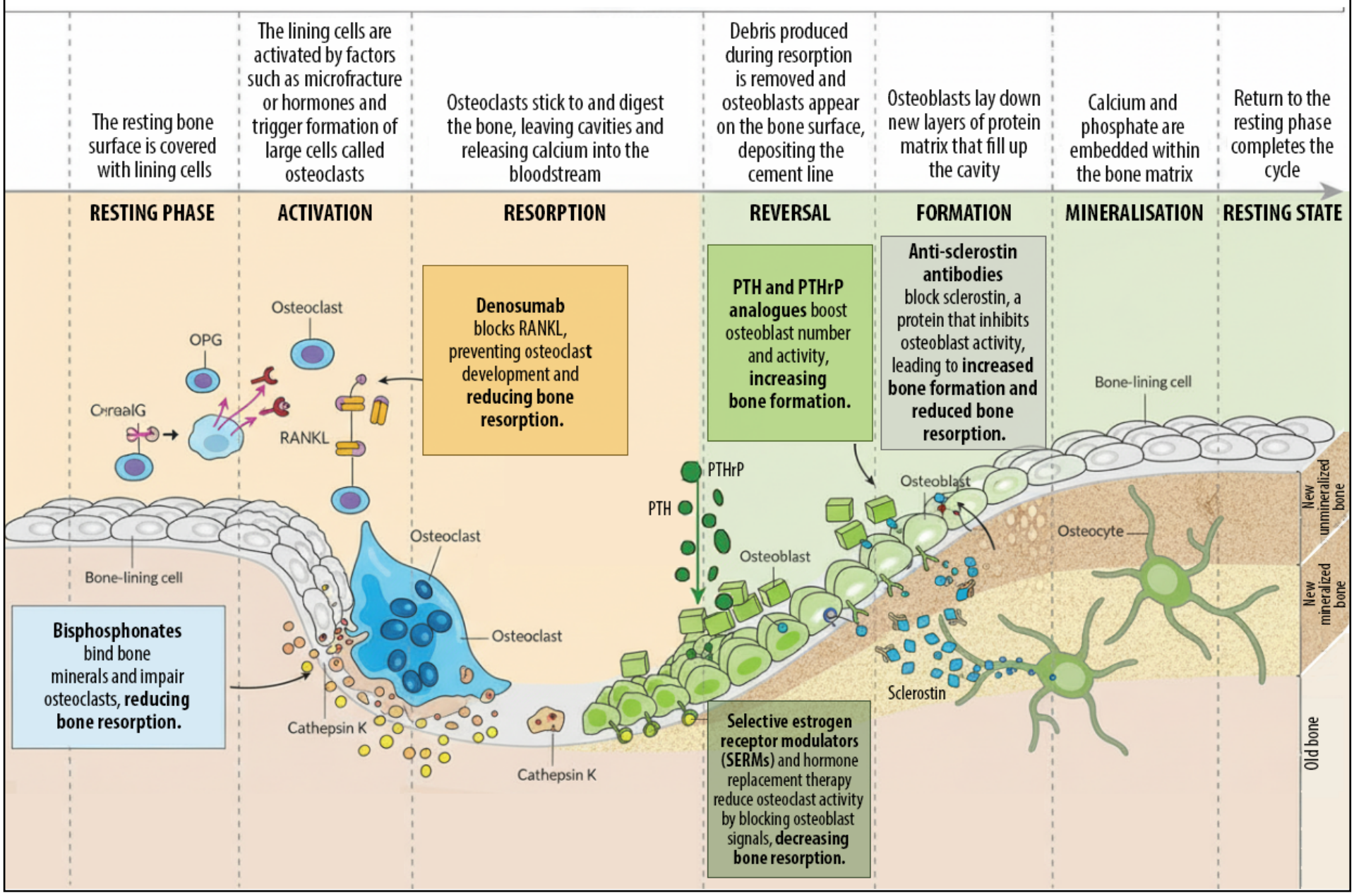


Table 3: Pharmacological Fracture Prevention Therapies

Class	Drug-brand name	Dosing	Contraindications
Antiresorptive Agents			
Oral Bisphosphonates	Alen/Iban Risedronate	70/35/150 mg per wk	Esophageal abnormalities; Creatinine clearance <30-35mL/min and hypocalcemia (both)
Intravenous Bisphosphonates	Ibandronate Zoledronic acid-Reclast®	3mg every 3 mo <30-35mL/min 5mg every 12-18 mo	Creatinine clearance and hypocalcemia (both)
RANKL inhibitor	Denosumab-Prolia™	Injection every 6 months	Hypocalcemia
Calcitonin Salmon	(Fortical®/Miacalcin®)	Nasal spray/ injection Daily/Schedule varies	Rhinitis, epistaxis, and allergic reactions. Cancer risk was higher
Estrogen-related therapies	Estrogen, Raloxifene-Evista®	Oral/transdermal Daily/weekly	Venous thromboembolism, stroke, or cardiovascular disease
Anabolic agents			
PTH analog	Teriparatide-Forteo® Abaloparatide-Tymlos®	Injection Daily <30mL/min;	Creatinine clearance Bone malignancy, increased risk for osteosarcoma; hypercalcemia
Sclerostin inhibitor	Romosozumab-Evenity™ (210mg mensal SC por 12 meses)	Injection monthly for 12 months	Myocardial infarction or stroke (within the past 12 months) or hypocalcemia

Teriparatide and abaloparatide are anabolic agents that stimulate bone formation and are used in patients at high risk of fractures. They are contraindicated in hyperparathyroidism, skeletal malignancy, or Paget's disease. Romosozumab increases bone formation and reduces vertebral and peripheral fractures but carries the FDA's highest-level safety warning for increased cardiovascular risk and is contraindicated in patients with a cardiovascular event within 12 months.

In women at very high fracture risk, anabolic therapies are more effective than bisphosphonates in lowering vertebral, nonvertebral, and hip fractures. Long-term use, greater than five years, of oral bisphosphonates offers modest reductions in the incidence of vertebral fractures. Extended use of zoledronic acid for six years may reduce the frequency of vertebral fractures, although the evidence remains uncertain. Denosumab maintains efficacy up to 10 years, with stable rates of atypical femoral fractures and osteonecrosis of the jaw.

For patients at low or moderate risk who remain fracture-free, a drug holiday may be appropriate. Fracture risk does not appear to increase in the first two years after stopping therapy but may rise after that.

Data are lacking on the outcomes of switching therapies after an inadequate bisphosphonate response, however in patients who remain at high fracture risk after three to five years of bisphosphonate therapy, a switch to denosumab may be appropriate.[42,45] Transitioning from denosumab to teriparatide may cause transient bone loss and should be avoided; changing to romosozumab may be a safer alternative.[1]

Pharmacologic therapy is indicated for postmenopausal women and men aged 50 years who have osteoporosis based on bone mineral density screening, high fracture risk, or a history of hip, vertebral, or multiple fragility fractures, even if their BMD is within the osteopenic or normal range. Bisphosphonates are considered appropriate first-line treatment. In cases where bisphosphonates are contraindicated or poorly tolerated, denosumab is a suitable alternative. Raloxifene may be considered for postmenopausal women who are not at elevated risk of thromboembolism and cannot take bisphosphonates.

Longitudinal follow-up addressing fall risk, comorbidities, and polypharmacy is crucial for maintaining adherence, monitoring therapeutic efficacy, and adjusting management strategies. DEXA should be repeated every one or two years in high-risk patients or after changes in therapy.[42]

Conservative and Surgical Treatments

Most osteoporotic fractures are treated conservatively. Reassurance, weight-bearing, and activity

restrictions, with or without external bracing, are encouraged.[46]

If nonoperative treatment fails some patients may be candidates for surgical intervention; the stability of the lesion and neurologic compromise are significant factors in decision-making.

For the stable vertebral fractures, without neurological compromise but with persistent pain, a percutaneous cement augmentation technique, vertebroplasty or kyphoplasty, may be indicated. Vertebroplasty involves inserting a spinal needle through the pedicle into the vertebral body and injecting polymethylmethacrylate (PMMA) cement. Kyphoplasty involves inserting and inflating a balloon within the vertebral body to create a cavity which is then filled with PMMA. Using the balloon is intended to reduce the risk of cement leakage and allow for partial restoration of vertebral height and correction of kyphosis. Both procedures should decrease pain and improve function.

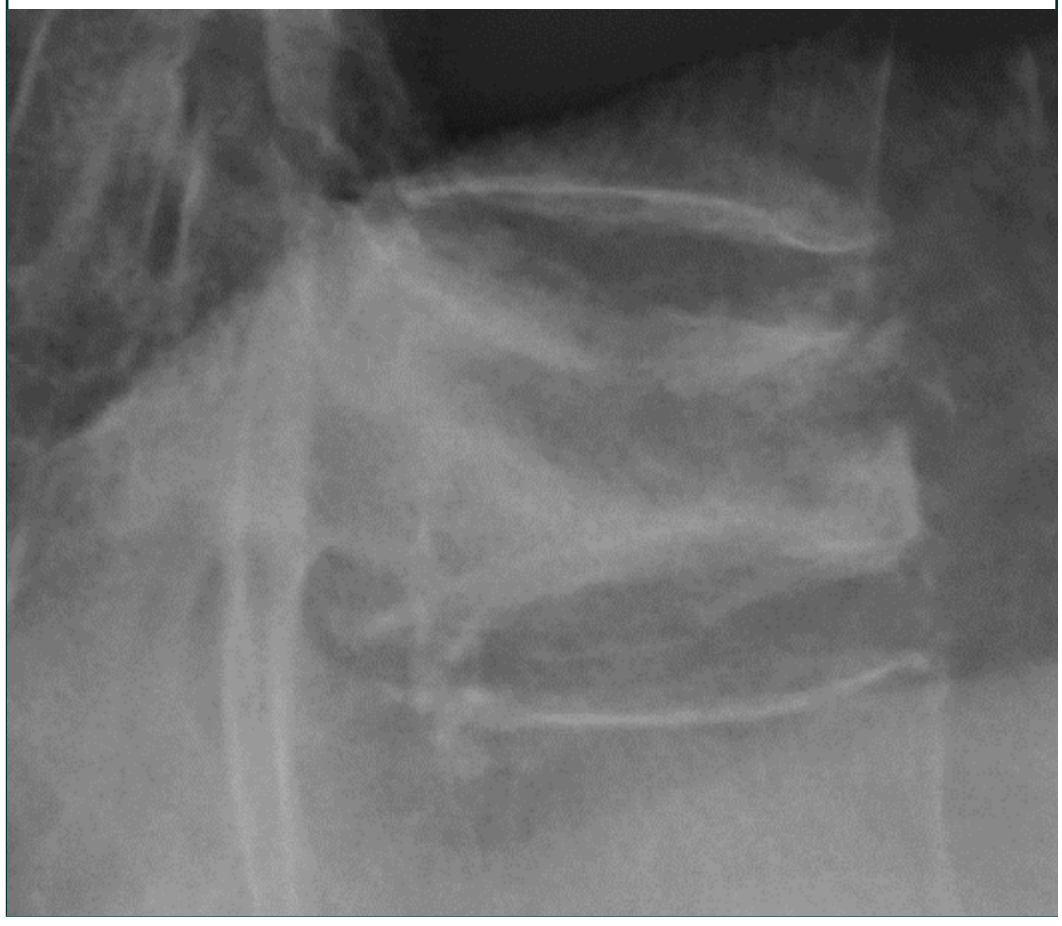
The optimal timing for such interventions is not clear. Early surgery may reduce the risk of complications such as urinary tract infection, pneumonia, and thrombophlebitis related to prolonged bed rest but may lead to unnecessary surgery in patients who could improve without an operation. A recent meta-analysis demonstrated advantages to performing surgery within four weeks of fracture.[47] Although cement augmentation is minimally invasive, it is not free from complications and, although they are rare, reported adverse events include infection, cement leakage, pulmonary embolism, neurological deficits, adjacent vertebral fractures, and death.[48,49] Attempting at least two to four weeks of optimized conservative management would determine whether symptoms improve without surgical intervention.

When treating these fractures conservatively, several prognostic

KEY POINTS

- Hip fractures in the elderly lead to a 17–30% one-year mortality.
- The DEXA scan is the gold standard for identifying osteoporosis but fracture risk tools assist management.
- Prevention includes early bone mass optimization; lifestyle measures and fall prevention in elderly.
- Bisphosphonates are the first-line pharmacologic treatment.
- Most vertebral fractures are treated conservatively; vertebroplasty/kyphoplasty should only be used for persistent pain.

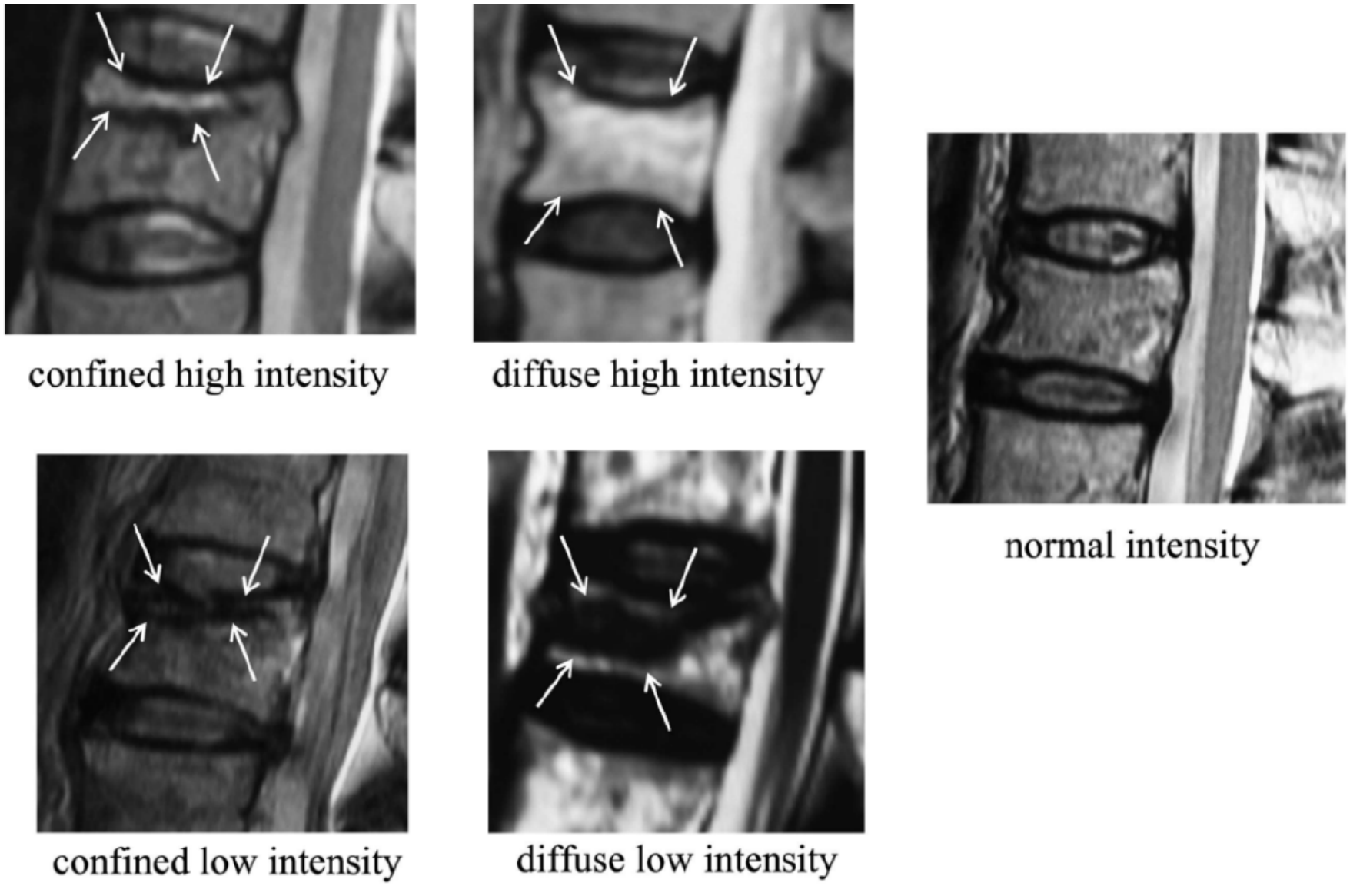
Figure 4



signs are of value. The presence of a vertebral cleft on X-ray (Figure 4) or MRI changes (Figure 5), characterized by high intensity confined to a partial zone within the fractured vertebra and a diffuse low intensity pattern within the vertebra, indicate an increased risk of pseudoarthrosis.[50]

Persistent pain or a neurological deficit, findings indicative of an unstable fractures, require specialist referral. In such cases, fusion with or without decompression may be necessary.

Figure 5



Clinical Pearls

About two thirds of vertebral fractures are silent so screening at-risk patients is important.

Calcium plus Vitamin D is more effective than calcium alone.

Fall-prevention strategies in the elderly such as balance, strength and environment modification reduce fracture risk more than drugs do.

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Post-test Quiz

1. Which of the following is considered the gold standard for diagnosing osteoporosis?
2. Which preventive strategy has shown the strongest evidence for reducing fall-related fracture risk in elderly patients?
3. What is the primary risk when discontinuing denosumab therapy without subsequent treatment?
4. In postmenopausal women at very high fracture risk, which therapy provides the greatest reduction in vertebral and nonvertebral fractures?
5. Which statement best reflects current recommendations for surgical management of osteoporotic vertebral fractures?

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