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Vertebral Compression Fractures Among Older Adults

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Vertebral compression fractures (VCF) are the hallmark of osteoporosis, yet two-thirds of all VCF remain undiagnosed and untreated. Both symptomatic and occult VCF are associated with considerable increases in morbidity and mortality, hospitalization rates, admissions to long-term care, and health care–related costs. These fractures increase the risk of future osteoporotic fractures, both vertebral and nonvertebral, independent of bone mineral density. Older adults have lower rates of diagnosis and treatment compared with younger patients, although clinical studies have shown the efficacy and safety of currently available therapies for osteoporosis in older adults are comparable with those in younger individuals.

Key words: *vertebral compression fractures, osteoporosis, bone mineral density, antiresorptive therapy, anabolic agents*

Epidemiology

Vertebral compression fractures (VCF) are a silent epidemic, representing 40% of all osteoporotic fractures and surpassing hip and wrist fractures. The prevalence of VCF among people over 50 years old is 10–26%, depending on the diagnostic criteria used.[1,2] The prevalence of VCF increases with age (Table 1), and[2–4] the risk of sustaining a new vertebral fracture at age 75 compared to age 55 doubles in men and triples in women.[5,6] Only about one-third of all VCF are diagnosed clinically.[7] Compared with younger adults, the older adults are under-diagnosed and under-treated (Figure 1).[8] Worldwide, there were 1.4 million new vertebral fractures in the year 2000,[9] and the fracture burden is expected to rise due to the increase in life expectancy, leading to escalating social and health care–associated costs.

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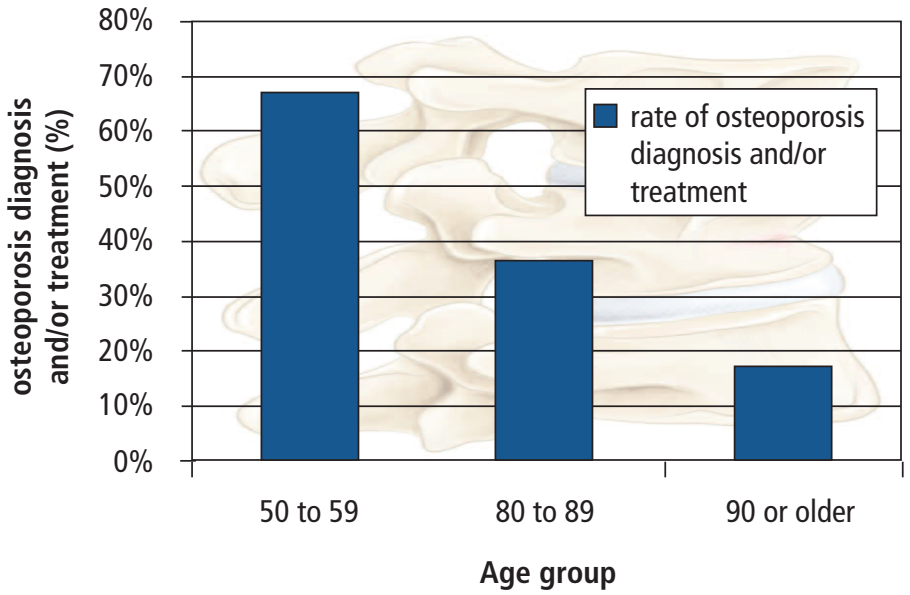
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Adverse Outcomes of Vertebral Compression Fractures

Vertebral compression fractures cause back pain in about 50% of cases,[10] either without a history of preceding trauma, or following low-exertion activity such as bending forward, standing from a seated position, or coughing. The pain is usually aggravated by standing, sitting, or movement and may radiate bilaterally to the anterior abdominal wall in a dermatomal distribution. The acute pain can last 6 weeks to 2 months,[10,11] but mechanical changes resulting from the fracture may lead to chronic back pain, particularly with multiple severe VCF.[12] Older adults have significantly more chronic pain and disability from VCF, even after adjusting for comorbid conditions.[10,13]

Height loss and kyphosis are common consequences of VCF, which affect physical function.[14] Kyphosis is also a risk factor for falls and subsequent fractures, independent of bone mineral density (BMD).[15,16] Lumbar spine fractures may result in a protruding abdomen, early satiety, and decreased appetite, while multiple thoracic fractures can be associated with restrictive lung disease. Multiple vertebral fractures can lead to the costoiliac impingement syndrome, causing postural pain from prolonged sitting.[17] Psychosocial outcomes associated with VCF include anxiety related to fear of falls, and depression.[10] Both clinically and radiographically detected VCF are associated with increased back pain, functional limitation,[20] and reduced quality of life.[21,22] Functional decline after vertebral fracture is comparable to that of

Figure 1: Rate of Osteoporosis Diagnosis and Treatment by Age Group



Source: Adapted from Neuner JM, et al., 2003.[8]

hip fracture,[18,19] while the decrement in health utility scores in osteoporosis is comparable to that observed in other chronic medical conditions, such as arthritis, chronic obstructive pulmonary disease, diabetes mellitus, or heart disease.[23]

Increased morbidity, disability, and mortality is well documented for both symptomatic and asymptomatic VCF,[20,24–27] with an excess mortality as high as 23% in one study, compared with women without spinal fractures.[28] Mortality risk and hospitalization rates increase with age and number of VCF.[29]

The presence of VCF increase the risk of future fragility fractures, independent of age, weight, and BMD. One in five women will have another fragility fracture within 12 months.[3] Older women with more than three vertebral deformities have a 2.8-fold increase in the risk of subsequent hip fracture, and a tenfold risk increase for future vertebral fractures within three years.[31,32]

The health care costs associated with VCF are significant (Table 2).[33] More than 40% of women over 50 admitted to hospital with a primary diagnosis of vertebral fracture in 1997 were discharged to long-term care (LTC), while another 24.3% required other follow-up care.[34] Although admissions to hospital for VCF remain less frequent than for hip fractures, the average length of stay are comparable,[35] and costs attributable to the vertebral fracture continue after discharge in over 50% of cases.[33]

Table 1: Comparison of VCF Prevalence Data in Men and Women

	Men	Women
Overall prevalence (Canadian data[3])	21.5%	23.5%
Age-related prevalence[2–4]		
Age 50–59	16–29%	10%
Age 80–89	39%	45%

Sources: Davies KM, et al., 1996[2]; Jackson SA, et al., 2000[3]; O'Neill TW, et al., 1996.[4]

Table 2: Increased Health Care-Related Costs Associated with VCF

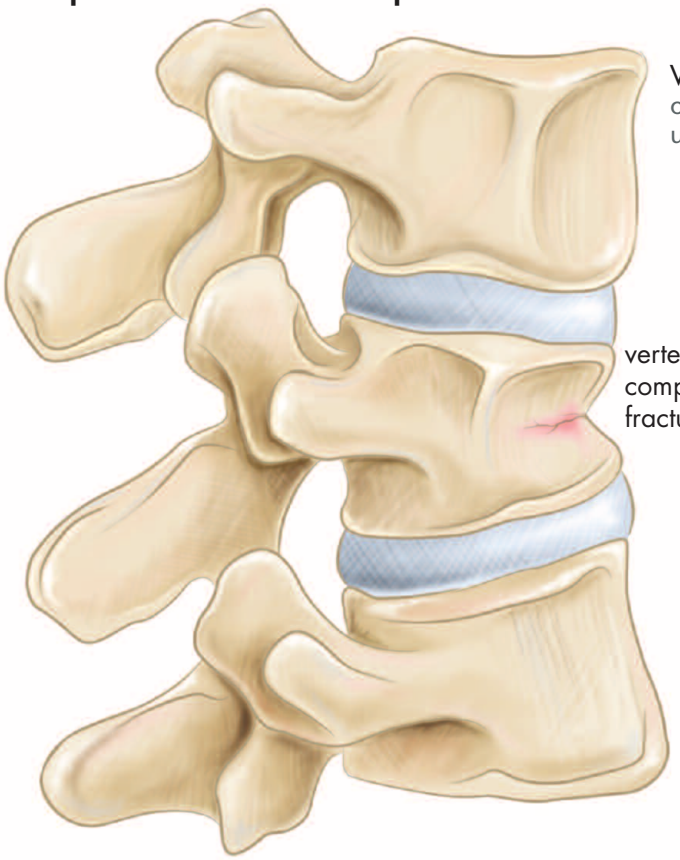
Hospital-related costs	Over 400,000 total hospital days, and over $500 million US (1997)
	Length of stay (LOS) increased by 2.1 days
Post-hospital Costs	Increased rate of discharge to LTC
	Increased need for follow-up care

Sources: Gehlbach SH, et al., 2003[33]; Burge R, et al., 2002[34]; Papaioannou A, et al., 2001.[35]

Evaluation

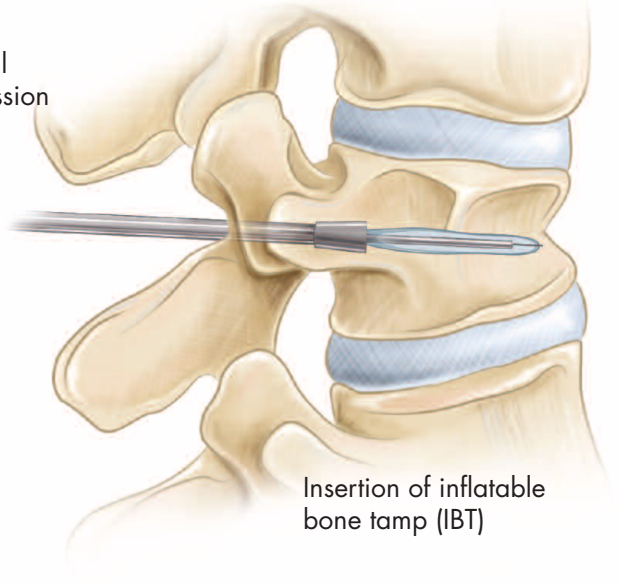
Clinical evaluation of patients with VCF begins with a detailed history and physical examination, looking for evidence of fragility fractures and for secondary causes of bone loss (Table 3). Patients should have their height measured at baseline and at serial assessments. Patients with symptomatic VCF typically have spinal tenderness on palpation and spinal deformity, while asymptomatic patients may present with height loss, kyphosis, and decreased rib-pelvis distance (Table 4).[36,37] All patients with back pain, height loss, or kyphosis should have lateral spinal radiographs, looking for vertebral compression fractures.[38] Severe chronic pain, symptoms related to nerve impingement or bladder and bowel changes, and neurologic deficits are not characteristic of VCF. If the initial evaluation suggests a possible underlying malignancy, further tests may include bone marrow biopsy, isotope bone scan, MRI, etc. As two-thirds of VCF are incidental findings on radiographs ordered for other reasons, guidelines for recognizing and reporting VCF apparent on routine imaging studies have recently been published.[39]

Figure 2:
Repair of Vertebral Compression Fractures

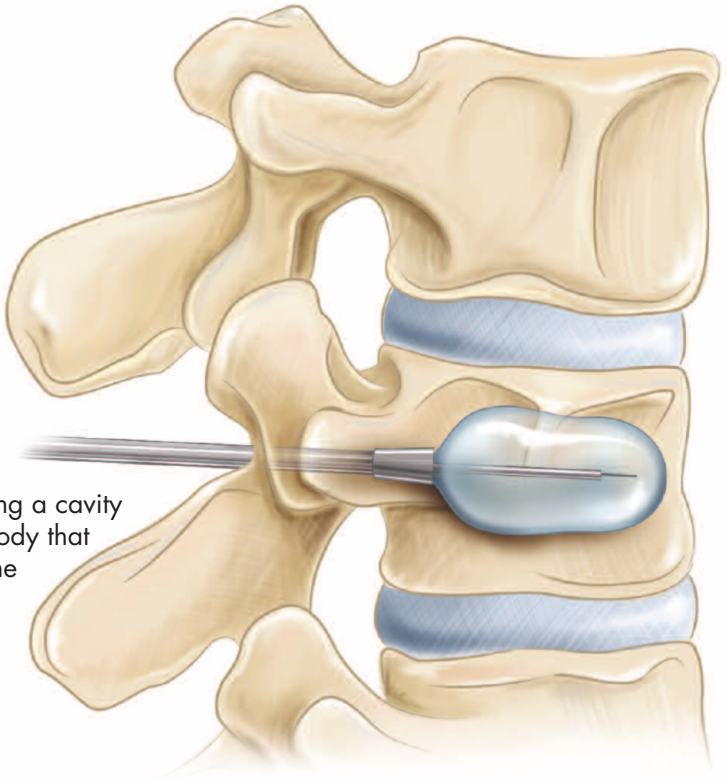


Vertebral compression fractures (VCF) are the hallmark of osteoporosis, yet two-thirds of all VCF remain undiagnosed and untreated.

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

Table 3: Workup for Secondary Causes of Osteoporosis

Calcium (total and ionized)
Phosphate level
Alkaline phosphatase (total or bone alkaline phosphatase)
Kidney function tests
Liver enzymes
Complete blood count and differential
Serum thyroid stimulating hormone (TSH)
Additional investigations as indicated:
25-hydroxy vitamin D level
Serum parathyroid hormone
Serum testosterone level in men
Serum immune electrophoresis, urine protein
Electrophoresis and Bence Jones protein
24-hour urinary calcium and creatinine
24-hour urinary free cortisol
Celiac disease screening (anti-tissue transglutaminase, anti-gliadin, and anti endomysial antibody titers

Imaging Studies

Most commonly, compression fractures involve the T8–T12, L1, and L4–5 vertebral bodies. It is important to image the entire thoraco-lumbar spine, because 20–30% of vertebral compression fractures are multiple.[40] Isolated fractures above T7 level are rare in osteoporosis and should alert clinicians to another underlying destructive process.[41] The most common types of vertebral deformities are wedge fractures, biconcave or "codfish" deformities, and compression (crush) fractures. Posterior wedging is not typical of osteoporotic vertebral fractures, and may signal pathologic fractures. Spinal radiographs cannot differentiate between recent or old fractures, while bone scans may not become positive for up to 10 days following a fracture. In such situations, special MRI protocols including short tau inversion recovery (STIR) sequence may be useful by imaging bone marrow edema in recent (under 2 months old) vertebral fractures.

Table 4: Three Physical Signs Suggesting Possible VCF

Prospective height loss of 2 cm or more
Wall to occiput distance of 6 cm or more (suggests VCF in the thoracic spine)
Rib to pelvis distance of less than 2 finger breadths, or less than 3.5. cm (suggests VCF in the lumbar spine)

Table 5: Less Common Causes of Secondary Osteoporosis

Trauma
Paget's disease
Eosinophilic granulomas
Pott's disease (tuberculosis of the spine)
Malignancy: primary bone tumours, multiple myeloma, lymphoma or leukemia, or metastases

Sources: Dass B, et al., 2002[43] and Lecouvert FE, et al., 1997.[44]

Laboratory Evaluation

Secondary osteoporosis occurs in almost two-thirds of men, and one-fifth of postmenopausal women.[42] Evaluation should include secondary causes of osteoporosis such as vitamin D deficiency or renal failure (Table 3). Less common causes of vertebral deformities are presented in Table 5.[43,44] Differentiating between pathological and benign VCF can be difficult in older adults, especially in patients with a known malignancy elsewhere. Isotope bone scans are very sensitive but not specific. MRI is the imaging modality of choice, using diffusion-weighted images to differentiate between osteoporotic fractures (hypointense) and metastases (hyperintense),[45] although multiple myeloma can often mimic benign osteoporotic fractures on MRI.[44]

Bone mineral density testing should be performed for suspected osteoporosis to confirm the diagnosis and provide a baseline for assessing the response to therapy. Dual energy X-ray absorptiometry (DXA) is the gold standard for assessing bone mineral density (BMD) and should be performed at the hip (femoral neck or total hip) and spine (L1 to L4). Causes of falsely elevated vertebral BMD include VCF, aortic calcifications, degenerative disk disease, or apophyseal arthropathy, particularly in older males.[45] In such situations, hip BMD measurements may prove more useful. In patients over 65, interpretation

Table 6: Summary of Selected Studies of Current Antiresorptive and Anabolic Therapies for Osteoporosis (Hormone Replacement Therapy Studies Not Included)

Author, Year, Reference #	Study Type	Study Population	Intervention	Results Relative Risk (95% Confidence Interval)
Cranney, et al., 2001.[62]	Systematic Review	1,267 women in 13 RCTs (mean age 52–72)	Etidronate	Vertebral fractures 0.63 (0.44–0.92) Nonvertebral fractures NS
Cummings, et al., 1998.[63]	RCT	2,218 postmenopausal women (mean age 67.7) without VCF	Alendronate	Vertebral fractures primary prevention 0.56 (0.39–0.80)
Black, et al., 1996.[64]	RCT	2,027 postmenopausal women with VCF (mean age 71)	Alendronate	Vertebral fractures secondary prevention 0.59 (0.41–0.68)
Wells, et al., 2008.[65]	Systematic Review	12,068 women with low BMD (mean age 51 to 71)	Alendronate	Vertebral fractures 0.55 (0.45–0.67) (primary and secondary prevention) Nonvertebral fractures 0.55 (0.45– 0.67)
Reginster, et al., 2000.[68]	RCT	1,226 postmenopausal women with VCF (mean age 71)	Risedronate	Vertebral fractures 0.39 (0.22–0.68) at 1 year and 0.51 (0.36–0.73) at 3 years Nonvertebral fractures 0.67 (0.44–1.04)
Wells, et al., 2008.[71]	Systematic Review	14,049 women in 7 RCTs	Risedronate	Vertebral fractures secondary prevention 0.61 (0.50–0.76), primary prevention NS Nonvertebral fractures secondary prevention 0.80 (0.72–0.90), primary prevention NS
Black, et al., 2007.[73]	RCT	7,765 women with osteoporosis (mean age 73)	Zoledronic acid once yearly	Morphometric VCF risk 0.30 (0.24–0.38) Hip fractures 0.59 (0.42–0.83) All secondary end points significantly reduced: nonvertebral fractures 0.75, all clinical fractures 0.66, clinical VCF 0.23, multiple morphometric VCF 0.11
Lyles, et al., 2007.[74]	RCT	2,125 hip fracture patients (24% men) (mean age 74)	Zoledronic acid once yearly for 3 years	Vertebral fracture risk 0.54 (0.32– 0.92) Nonvertebral fractures 0.73 (0.55– 0.98) Hip fracture 0.70 (0.41–1.19) NS Any fracture 0.65 (0.50–0.84) Any cause of death 0.72 (0.56–0.93)
Ettinger, et al., 1999.[79]	RCT	Group 1 = 4,524 women with low hip BMD (mean age 65) Group 2 = 2,204 women with low BMD and VCF (mean age 69)	Raloxifene 60 mg daily	Group 1: Vertebral fracture risk 0.50 (0.30–0.70) with Raloxifene 60 mg daily and 0.60 (0.40–0.90) for Raloxifene 120 mg/day Group 2: Vertebral fracture reduction 0.70 (0.60–0.90) with Raloxifene 60 mg daily and 0.50 (0.40–0.60) for Raloxifene 120 mg/day Nonvertebral fracture risk was NS in both groups
Chesnut 3rd et al., 2000.[81]	RCT	1,255 postmenopausal women with VCF (mean age 69)	Salmon Calcitonin 200 IU daily	Vertebral fracture risk 0.67 (0.47–0.97) overall, 0.64 (0.43–0.96) for secondary prevention Nonvertebral fractures NS
Neer, et al., 2001.[84]	RCT	1,637 women with VCF (mean age 69)	Teriparatide (1-34 amino acid fragment)	Vertebral fracture risk 0.35 (0.22–0.55) Nonvertebral fractures risk 0.47 (0.25 to 0.88)
Greenspan, et al., 2007.[87]	RCT	2,532 women with low BMD (mean age 64) (30% in control arm and 36% in PTH arm withdrew from the study by 3 months)	Recombinant human parat-hormone(1-84 amino acid fragment)	Vertebral fracture risk variable: 0.42 (0.24–0.72) in patients who completed the study, to 0.60 (0.36–1.00) in intention-to-treat analysis. Nonvertebral fractures NS

RCT: randomized controlled trial; VCF: vertebral compression fractures; PTH: parathyroid hormone; BMD: bone mineral density; NS: not significant

Table 7: Summary of Antifracture Effects of Pharmacological Anti-osteoporosis Agents Currently Approved in Canada

Pharmacological Agent	Vertebral Fracture Risk	Nonvertebral Fracture Risk	Hip Fracture
Etidronate	↓	↔	↔
Alendronate	↓	↓	↓
Risedronate	↓	↓	↓
Zoledronic Acid	↓	↓	↓
Raloxifene	↓	↔	↔
Parathormone 1-34	↓	↓	↔
Parathormone 1-84	↓	↔	↔
Vitamin D and Calcium	↓ (Inconsistent effects)	↔	↔
Calcitonin	↓	↔	N/A

N/A ↓: decreases risk. ↔: no effect. N/A: not studied

of BMD results is based on T-score. The Osteoporosis Society of Canada and the Canadian Association of Radiologists recently published recommendations for bone mineral density reporting integrating clinical risk factors in a quantitative 10-year fracture risk assessment for both men and women.[46]

Management

Management goals for patients with VCF are to control pain when present, maintain function, exclude important or serious underlying conditions, and prevent fractures.

Strategies for pain control in patients with VCF include local physical modalities such as warm or cold compresses, gentle physical therapy, and an appropriate activity level, combined with analgesics. First line of therapy is acetaminophen administered regularly in therapeutic doses. Opioid analgesics and nonsteroidal anti-inflammatory drugs (NSAIDs) can be effective short term, but require careful monitoring for constipation and delirium (from narcotics) and gastric and renal side effects (from NSAIDs). Calcitonin in doses of 200 IU to 400 IU intranasally daily is useful for short-term relief of pain from acute VCF when started within 2 weeks from the onset of pain.[47]

In carefully selected patients with symptomatic acute and subacute VCF, percutaneous vertebroplasty and kyphoplasty can result in rapid and persistent pain reduction.[48–50] Vertebroplasty involves percutaneous injection of polymethylmetacrylate (PMMA) into the vertebral body, while in kyphoplasty the crushed vertebral body is first re-expanded using an inflatable balloon (Figure 1). Other benefits include decrease in analgesic use, and improvement in function and quality of life.[51] Possible complications include cement extravasation (higher rates with vertebroplasty compared with kyphoplasty[50]) and neurologic injuries short term, and an increase in subsequent adjacent fractures within two months of the procedure.[52] The two methods have not been studied in randomized trials against conventional care.

Strategies for preventing future fractures include lifestyle modification and fall prevention measures, calcium and vitamin D supplementation, antiresorptive agents, and anabolic drugs. Lifestyle modifications should include weight-bearing exercise, avoidance of smoking and alcohol, and diet optimization with an adequate intake of calcium and vitamin D, and an appropriate caloric intake to avoid malnutrition and weight loss. Dietary calcium is the preferred source, while calcium carbonate or citrate are the preferred supplements when the dietary calcium is insufficient. Vitamin D deficiency is common[53] and supplementation with vitamin D and calcium can decrease falls and nonvertebral fractures in frail older people in the long-term care setting.[54,61] Exercise programs for persons with VCF can reduce pain and analgesics use, and can improve quality of life.[55,56] The presence of VCF signifies osteoporosis, and increase the risk of falls and fall-related injuries. Preventative measures for falls include multidisciplinary multifactorial programs (community-based or in residential care facilities), muscle strengthening and balance retraining programs, tai-chi exercises, home hazard assessment and modification, medication review with withdrawal of psychotropic medication, and cardiac pacing for selected patients.[57–60] Pharmacological intervention is recommended for patients at high risk of fragility fractures. Therapies shown to increase bone mass and decrease vertebral fracture risk in older adults include antiresorptive agents (bisphosphonates, selective estrogen receptor modulators [SERMs]), and anabolic agents such as teriparatide (Tables 6 and 7). Most of the evidence comes from trials in postmenopausal women under the age of 80.

Bisphospohonates

Bisphosphonates inhibit bone resorption by interfering with the activity of osteoclasts. Bisphosphonates currently approved in Canada include alendronate, risedronate, and zoledronate.

Etidronate is an older bisphosphonate with proven protective effects against vertebral compression fractures, but not against nonspine fractures.[62] Alendronate is equally effective in reducing the risk of symptomatic VCF in women aged 75 to 85 years, compared with women under 65 years of age,[63–67] and is well tolerated. Risedronate is effective for secondary prevention of both ver-

tebral and nonvertebral fractures, and is well-tolerated.[68,69,71] The effect is rapid, seen during the first year of the VERT trial, and maintained at 3 years[69] and 5 years.[70] The efficacy of risedronate in women aged 80 years or older was examined in a post-hoc analysis of three randomized trials, showing 81% decrease in vertebral fractures with risedronate by 1 year, and 44% after 3 years, but no protective effect for nonvertebral fractures.[72] Intravenous zoledronate given as an annual infusion significantly decreased vertebral and nonvertebral fractures (including hip fractures) in the 3-year HORIZON trial.[73] Another large zoledronic acid trial in hip fracture patients confirmed the reduction in spine and nonspine clinical fractures, and also showed significantly lowered all-cause mortality by 28% ($p = 0.01$), suggesting that reducing fracture risk in frail individuals may reduce mortality.[74] Bisphosphonates are currently regarded as first line of therapy for osteoporosis due to proven efficacy at all fracture sites (including the hip), safety profile, and cost-effectiveness.[75,76] Oral bisphosphonates are generally well tolerated, but individuals with gastrointestinal side effects or poor long-term compliance may be candidates for injectable bisphosphonates. Adherence to treatment tends to be generally poor with bisphosphonates,[77,80] and less frequent administration schedules appear to be preferred by patients.[78]

Raloxifene is a SERM with estrogen agonist effects on the bone and lipid metabolism, but estrogen antagonist effects on the breast and endometrium. It is effective in reducing new VCF, and can also protect against breast cancer (RR 24%).[79] In contrast, the Raloxifene Use for the Heart (RUTH) trial showed raloxifene is not safe for women at increased risk for cardiovascular disease, due to higher rates of venous thromboembolism (hazard ratio 1.44) and fatal stroke (hazard ratio 1.49) compared to placebo.[80]

Calcitonin was shown effective for secondary prevention at dose of 100 IU intra-nasally daily.[81] A meta-analysis of 4 randomized studies (N=1404) found a reduction in the incidence of vertebral fractures with calcitonin (pooled relative risk of 0.46) compared with placebo or calcium and/or vitamin D.[82]

Hormone replacement therapy is no longer recommended as primary therapy for the sole indication of osteoporosis prevention due to the association with adverse cardiovascular events and increase in breast cancer risk.[83]

Anabolic Agents

The peptides from the parathyroid hormone family are potent stimulators of bone formation. Teriparatide reduces spine and nonspine fractures (but not hip fractures), with sustained effect up to 30 months after the withdrawal of treatment.[84,85] The safety profile and efficacy of teriparatide (TPTD) in women 75 years and older is comparable to that seen in younger women.[86] Possible side effects of TPTD are dizziness and leg cramps, injection sites reactions, headache, nausea, arthralgias, myalgias, lethargy and weakness. Parathormone (PTH), the intact hormone, showed similar reduction in vertebral fractures, but not in nonspine or hip fractures.[87] Although the combination of PTH and alendronate does not seem to be additive,[88] maintenance therapy with alendronate after PTH allows the benefits in BMD to be preserved, as seen in the PaTH study.[88] Teriparatide and PTH are generally well tolerated, although patients should be monitored for hypercalcemia. Teriparatide is usually reserved for severe osteoporosis, and the treatment period is limited to two years, because of an increase in the risk of osteosarcoma in rodents with teriparatide (although not reported in humans), but also due to the cost and requirements for daily self-injection. A recent systematic review also found beneficial effects of teriparatide in reducing back pain.[90]

Key Points

- The majority of VCF are asymptomatic, and only two-thirds are recognized clinically.
- Both symptomatic and asymptomatic VCF are associated with increased morbidity, disability, and mortality.
- The most common types of vertebral deformities are wedge fractures, biconcave or "codfish" deformities, and compression (crush) fractures. Posterior wedging is not typical of osteoporotic vertebral fractures and may signal pathologic fractures.
- The risk of future fragility fractures (including hip fracture) is significantly increased in patients with VCF, independent of age, weight, and BMD.
- Common consequences of VCF include height loss, kyphosis, limitation in mobility, functional decline, and decrease in quality of life. Psychosocial outcomes include depression, anxiety, loss of self-esteem, anger, and fear of falling.
- Strategies for pain control include local physical modalities, gentle physical therapy, judicious bed rest, and adequate analgesia.

Clinical Pearls

- Calcitonin 200 IU to 400 IU intranasally daily can be effective in controlling pain.
- Vertebroplasty and kyphoplasty can provide rapid and persistent pain reduction in carefully selected patients with symptomatic acute and subacute vertebral compression fractures.

Conclusion

As the most common manifestation of osteoporosis, vertebral compression fractures represent a serious public health issue. They are associated with significant morbidity and mortality and an increased risk of future fragility fractures, including hip fractures, within 1 year. Two-thirds of VCF are not recognized and therefore not treated, missing an important preventive opportunity for patients at high risk for future fractures.

Strategies to increase clinical diagnosis of VCF include assessment of clinical risk factors and screening patients at risk with DXA. A case-finding strategy can identify high-risk patients, using clinical risk factors and BMD measurements to estimate 10-year fracture risk and guide choice of therapy. Optimal care includes identifying and treating possible causes of secondary osteoporosis. Patients with low-trauma VCF should be considered for treatment regardless of BMD results. Although not required prior to initiating treatment, BMD measurement may help choose the most appropriate therapeutic agent and monitor response to treatment. Osteoporosis remains underdiagnosed and undertreated in the very old. Age alone should not be a contraindication to therapy.

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