Abstract: Vertebral fractures (VF) are common and can result in acute and chronic pain, decreases in quality of life and diminished lifespan. The identification of VF are important as they are robust predictors of future fractures. The majority of VF do not come to clinical attention. Numerous modalities exist for visualizing suspected VF. While differing definitions of VF may present challenges in comparing data between different investigations, at least one in five men and women over 50 years of age have one or more VF. There is clinical guidance to target spine imaging to individuals with a high probability of VF. Radiology reports of VF need to clearly state that the patient has a "fracture" with further pertinent details such as the number, recency and severity of VF, each of which is associated with risk of future fractures. Patients with VF should be considered for anti-fracture therapy. Physical and pharmacological modalities of pain control and exercises or physiotherapy to maintain spinal movement and strength are important components in the care of VF patients.
Clinical significance:

- Vertebral fractures are common in people over 50 years of age
- Approximately two-thirds of vertebral fractures do not come to clinical attention
- A prevalent vertebral fracture is a significant risk factor for future fracture
- Risk of future vertebral fracture increases with increasing number and severity of prevalent vertebral
- A recent vertebral fracture confers a much greater risk of future fracture risk than a remote vertebral fracture
- Most patients with vertebral fracture should be provided options for decreasing fracture risk
- Treatments options are available for both acute and chronic pain associated with vertebral fractures
March 9, 2014

Joseph S. Alpert, MD, Editor-in-Chief,
The American Journal of Medicine,
3615 N. Prince Village Place, Suite 181,
Tucson, Arizona 85719

Dear Dr. Alpert;

Please accept the enclosed review article entitled “Vertebral fractures: clinical importance and management” for consideration in an upcoming issue of AJM.

This manuscript represents original work, and it is not under consideration for publication elsewhere. All authors meet criteria for authorship and all authors will sign a statement attesting authorship, disclosing all potential conflicts of interest, and releasing the copyright should the manuscript be acceptable for publication.

Should you require any further information, please feel free to contact me via my contact information above.

On behalf of the authors, I thank you for your consideration of this manuscript.

Sincerely,

David L. Kendler
Title: Vertebral fractures: clinical importance and management


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All authors had access to the data and a role in writing this manuscript.

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Abstract:

Vertebral fractures (VF) are common and can result in acute and chronic pain, decreases in quality of life and diminished lifespan. The identification of VF are important as they are robust predictors of future fractures. The majority of VF do not come to clinical attention. Numerous modalities exist for visualizing suspected VF. While differing definitions of VF may present challenges in comparing data between different investigations, at least one in five men and women over 50 years of age have one or more VF. There is clinical guidance to target spine imaging to individuals with a high probability of VF. Radiology reports of VF need to clearly state that the patient has a "fracture" with further pertinent details such as the number, recency and severity of VF, each of which is associated with risk of future fractures. Patients with VF should be considered for anti-fracture therapy. Physical and pharmacological modalities of pain control and exercises or physiotherapy to maintain spinal movement and strength are important components in the care of VF patients.

Abstract words (limit 175): 172
Introduction

Vertebral fractures (VF) are the most common type of osteoporotic fracture and are associated with substantial morbidity\textsuperscript{1,2} and decreased survival.\textsuperscript{3,4} In the US, annual direct management costs for VF are over $1 billion (USD in 2011).\textsuperscript{5}

VF, once suspected, can be confirmed by x-rays (XR), computerized tomography (CT), magnetic resonance imaging (MRI) or vertebral fracture assessment (VFA). VFA can be completed at the time of bone mineral density (BMD) assessment with dual-energy x-ray absorptiometry (DXA). Information on radiation dose, image resolution, and relative cost for these imaging modalities can be found in Table 1. Non-fracture causes of vertebral height loss and deformity need to be ruled out before confirming VF.

Table 1. Imaging modalities for assessment of vertebral fractures.

<table>
<thead>
<tr>
<th>Modality</th>
<th>Average effective dose\textsuperscript{6}</th>
<th>Image resolution</th>
<th>Relative cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Radiography (AP and lateral)</td>
<td>2.5 mSv</td>
<td>0.1 mm\textsuperscript{7}</td>
<td>$$</td>
</tr>
<tr>
<td>Computerized tomography (spine)</td>
<td>6.0 mSv</td>
<td>250-300 µm\textsuperscript{8}</td>
<td>$$$$$</td>
</tr>
<tr>
<td>Magnetic resonance imaging (spine)</td>
<td>0 mSv</td>
<td>150-200 µm\textsuperscript{8}</td>
<td>$$$$$</td>
</tr>
<tr>
<td>Vertebral fracture assessment by DXA (VFA)</td>
<td>0.001 mSv</td>
<td>0.5 mm\textsuperscript{7}</td>
<td>$</td>
</tr>
</tbody>
</table>

Asymptomatic (morphometric) and symptomatic VF can be diagnosed using the Genant semi-quantitative method (Figure 1), which requires ≥20% decrease in vertebral height (anterior, mid or posterior dimensions), estimated visually, to diagnose a VF.\textsuperscript{9}

Figure 1. Classification of vertebral fractures by the Genant semi-quantitative method

(Reproduced from Genant et al. 1993, by permission of John Wiley and Sons)
VF can also be diagnosed by standard quantitative morphometry or by comparing a vertebral body with adjacent vertebrae. By vertebral comparison, a VF can be diagnosed if there is a greater than three standard deviation (SD) difference in vertebral heights between adjacent vertebral levels.\textsuperscript{10}

Endplate depression, discontinuity of the endplate or anterior cortex disruption is expected when fracture is the cause of the vertebral deformity. The Algorithm-Based Qualitative (ABQ) methodology relies on recognition of vertebral endplate deformity to identify VF.\textsuperscript{11} When comparing clinical trials or epidemiology studies, it is important to understand how VF were defined, as this can have important implications on interpretation of the findings. Table 2 illustrates the diversity in study criteria for VF.
Table 2. Radiographic vertebral fracture assessment methods from osteoporosis Phase III clinical trials and epidemiological studies.

<table>
<thead>
<tr>
<th>Phase III clinical trials</th>
<th>N</th>
<th>Mean age (years)</th>
<th>Baseline prevalence of VFs</th>
<th>Definition of prevalent VF</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Phase III trial, Therapy</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VERT-NA, risedronate</td>
<td>2458</td>
<td>I: 69 P: 68</td>
<td>100%</td>
<td>Ratio of the anterior or middle vertebral body height to the posterior vertebral body height ≤0.8 (both QM and SQ)</td>
</tr>
<tr>
<td>VERT-MN, risedronate</td>
<td>1226</td>
<td>I: 71 P: 71</td>
<td>100%</td>
<td>Diagnosed by QM and SQ</td>
</tr>
<tr>
<td>FIT I, alendronate</td>
<td>2027</td>
<td>I: 71 P: 71</td>
<td>100%</td>
<td>Any ratio of vertebral heights more than 3 SDs below the mean population norm for that vertebral level</td>
</tr>
<tr>
<td>FIT II, alendronate</td>
<td>4272</td>
<td>I: 67.6 P: 67.7</td>
<td>0%</td>
<td>NA</td>
</tr>
<tr>
<td>Alendronate phase III Osteoporosis Treatment Study Group, alendronate</td>
<td>881</td>
<td>I: 64 P: 64</td>
<td>20%</td>
<td>Any vertebral-height ratio more than 3 SDs below the corresponding reference Ratio (from reference population)</td>
</tr>
<tr>
<td>Neer, teriparatide</td>
<td>1637</td>
<td>I: 69-71 P: 69</td>
<td>8%</td>
<td>Graded as normal or as mildly, moderately, or severely deformed (a decrease in height of approximately 20 to 25 percent, 26 to 40 percent, or more than 40 percent, respectively)</td>
</tr>
<tr>
<td>FREEDOM, denosumab</td>
<td>7868</td>
<td>I: 72 P: 72</td>
<td>23-24%</td>
<td>Vertebral body with a SQ Grade of 1 or more (Genant SQ method)</td>
</tr>
<tr>
<td>HORIZON-PFT, zoledronic acid</td>
<td>3889</td>
<td>I: 73 P: 73</td>
<td>62-64%</td>
<td>Vertebral height ratio of at least 3 SD below the vertebra-specific mean height ratio on QM reading with SQ confirmation</td>
</tr>
<tr>
<td>Clodronate Phase III trial, clodronate</td>
<td>593</td>
<td>I: 66-68 P: 68</td>
<td>46-67%</td>
<td>Vertebral morphometry using SQ method</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Epidemiologic studies</th>
<th>N</th>
<th>Age range (years)</th>
<th>Prevalence: Definition of prevalent VF</th>
<th>Incidence: Definition of incident VF</th>
</tr>
</thead>
<tbody>
<tr>
<td>CaMOS</td>
<td>4613</td>
<td>≥50 y</td>
<td>Men = 21.5%, women = 23.5%: &gt;3 SD below mean vertebral height of population</td>
<td>NA</td>
</tr>
<tr>
<td>The Rotterdam Study</td>
<td>3469</td>
<td>≥55 y</td>
<td>NA</td>
<td>7.8/1000 p-y at 55-65 y; 19.6 and 5.2-9.3/1000 p-y at &gt;75 y for women and men, respectively: QM by</td>
</tr>
<tr>
<td>Study</td>
<td>Sample Size</td>
<td>Age</td>
<td>Fracture Assessment Method</td>
<td>Notes</td>
</tr>
<tr>
<td>----------------------------------------------------------------------</td>
<td>-------------</td>
<td>-----------</td>
<td>---------------------------</td>
<td>----------------------------------------------------------------------</td>
</tr>
<tr>
<td>European Vertebral Osteoporosis Study&lt;sup&gt;23&lt;/sup&gt;</td>
<td>15570</td>
<td>50-79 y</td>
<td>Mean 12% (8-20% over age) in men and mean 12% (6-21% over age) in women: McCloskey method – vertebral height of &lt;3 SD below adjacent vertebrae.</td>
<td>NA</td>
</tr>
<tr>
<td>European Prospective Osteoporosis Study&lt;sup&gt;24&lt;/sup&gt;</td>
<td>6788</td>
<td>≥50 y</td>
<td>NA</td>
<td>Age-standardized incidence was 10.7/1000 p-y in women and 5.7/1000 p-y in men via morphometric analysis; incidence increased with age: ≥20% loss in any vertebral height.</td>
</tr>
<tr>
<td>Study of Osteoporotic Fractures&lt;sup&gt;25&lt;/sup&gt;</td>
<td>5166</td>
<td>≥68 y</td>
<td>21.8%: Black morphometric definition – ≥3 SD height loss.</td>
<td>NA</td>
</tr>
<tr>
<td>Latin American Vertebral Osteoporosis Study&lt;sup&gt;26&lt;/sup&gt;</td>
<td>1922</td>
<td>≥50 y</td>
<td>6.9-27.8% from 50→80 y of age: QM by modified Eastell criteria** – reduction in any vertebral height ≥ 3 SD for normal mean or from adjacent vertebrae.</td>
<td>NA</td>
</tr>
<tr>
<td>Rochester MN USA&lt;sup&gt;27&lt;/sup&gt;</td>
<td>762</td>
<td>≥50 y</td>
<td>25.3% in women: &gt;3 SD below any mean vertebral height.</td>
<td>17.8/1000 p-y in women: &gt;3 SD below any mean vertebral height.</td>
</tr>
<tr>
<td>Mr. OS (Hong Kong) and Ms. OS (Hong Kong)&lt;sup&gt;28&lt;/sup&gt;</td>
<td>4000</td>
<td>≥65 y</td>
<td>14.9% in men and 16.5% in women: Genant’s SQ method.</td>
<td>NA</td>
</tr>
<tr>
<td>Osteoporosis and Ultrasound Study&lt;sup&gt;29&lt;/sup&gt;</td>
<td>674</td>
<td>39-80 y</td>
<td>6.2%: ABQ method with VFA.</td>
<td>4.45/1000 p-y: ABQ method with VFA.</td>
</tr>
</tbody>
</table>

N: sample size; I: intervention arm; P: placebo arm; QM: quantitative method, ratios from direct vertebral body height measurements define fractures; SQ: semi-quantitative method, visual grading of height and area reduction used to define fracture; SD: standard deviation; VERT-NA: Vertebral Efficacy With Risedronate Therapy- North America; VERT-MN: Vertebral Efficacy With Risedronate Therapy Multinational; FIT I: Fracture Intervention Trial I; HORIZON-PFT: Health Outcomes and Reduced Incidence with Zoledronic Acid Once Yearly Pivotal Fracture Trial; FREEDOM: Fracture Reduction Evaluation of Denosumab in Osteoporosis Every 6 Months; CaMOS: Canadian Multicentre Osteoporosis Study; Mr. OS: The Osteoporotic Fractures in Men Study; *McCloskey-Kanis assessment method: QM method that defines fracture as either anterior or posterior wedge, biconcavity or compression; **Eastell criteria: QM method that defines fracture as either wedge, biconcavity or compression.
Epidemiological investigations provide incidence and prevalence of VF, although their estimates are dependent on the underlying populations and definitions of VF (Table 2.). The Canadian Multicentre Osteoporosis Study reported that 21.5% of men and 23.5% of women over 50 years of age have at least one vertebral compression deformity, while the Norwegian population-based Tromso study found that 20.3% of men and 19.2% of women over 70 years of age had at least one VF. A quarter of women over the age of 50 years in Rochester, MN, had one or more VF, as did more than a third of women by age 70 years. In the Study of Osteoporotic Fractures (SOF), 18% of postmenopausal women over age 65 years suffered an incident VF over a 15-year follow-up. Between 10% and 28% of VF are found in postmenopausal women whose BMD T-score > -2.5.

Despite the high prevalence of VF, more than two-thirds of VF remain undiagnosed. The recognition of VF in imaging reports obtained for purposes other than the investigation for VF in a hospital setting is generally poor (Table 3).

<table>
<thead>
<tr>
<th>Lead Author, year of publication</th>
<th>Device</th>
<th>Patient mean age year (range)</th>
<th>N</th>
<th>% of VF recognized</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bartalena, 2009</td>
<td>CT</td>
<td>63 (20-88)</td>
<td>323</td>
<td>15%</td>
</tr>
<tr>
<td>Chan, 2012</td>
<td>CT</td>
<td>NA (≥65)</td>
<td>175</td>
<td>14%</td>
</tr>
<tr>
<td>Obaid, 2008</td>
<td>CT</td>
<td>65 Md (18-90)</td>
<td>307</td>
<td>5%</td>
</tr>
<tr>
<td>Williams, 2009</td>
<td>CT</td>
<td>70 (55-89)</td>
<td>192</td>
<td>13%</td>
</tr>
<tr>
<td>Woo, 2008</td>
<td>CT</td>
<td>61 (18-92)</td>
<td>200</td>
<td>9%</td>
</tr>
<tr>
<td>Cataldi, 2008</td>
<td>XR</td>
<td>67.5 (50-86)</td>
<td>145</td>
<td>11%</td>
</tr>
<tr>
<td>Kim, 2004</td>
<td>XR</td>
<td>75 (≥60)</td>
<td>100</td>
<td>55%</td>
</tr>
</tbody>
</table>
VF: vertebral fractures; Md: median; NA: not provided; CT: computed tomography; XR: radiograph.

Care gaps in VF diagnosis may result from radiologists assuming that VFs are normal in older individuals, treating physicians focusing on acute aspects of a patient’s illness rather than skeletal comorbidities, or a lack of understanding of the clinical significance of VF. Often, radiographs are of insufficient technical quality to accurately identify VF. Radiologists should consistently apply published criteria for diagnosing VF, such as the Genant semiquantitative methodology, vertebral morphometry, and signs of endplate disruption. Consistent, clear terminology should be used to report vertebral abnormalities with information provided as to the number of VF, their location, and their grade/severity.

Both symptomatic and asymptomatic VF strongly indicate increased fracture risk in untreated patients. In the SOF cohort, women with a prevalent VF had an approximate three-fold greater risk of incident VF than women without a prevalent VF. Patients on placebo who experienced a new VF during an osteoporosis clinical trial had a 20% incidence of another new VF within one year. There is also a significantly elevated risk of any type of fracture soon after suffering a clinical VF. The risk of future VF increases with the number and severity of prevalent VF, with a recent VF imparting a greater risk of future VF than one that has occurred remotely. Patients with multiple, more severe and more recent VF are also more likely to be symptomatic and have fractures recognized clinically.

**Screening/case finding in the clinic**

<table>
<thead>
<tr>
<th>Authors, Year</th>
<th>XR</th>
<th>Vertebral Scores</th>
<th>Total</th>
<th>Grade</th>
<th>Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Majumdar, 2005</td>
<td>XR</td>
<td>75 (≥60)</td>
<td>459</td>
<td>60%</td>
<td></td>
</tr>
<tr>
<td>Mui, 2003</td>
<td>XR</td>
<td>65 (55-89)</td>
<td>106</td>
<td>15%</td>
<td></td>
</tr>
<tr>
<td>Santamaria Fernandez, 2012</td>
<td>XR</td>
<td>66 (NA)</td>
<td>254</td>
<td>8%</td>
<td></td>
</tr>
</tbody>
</table>
It is important to develop improved strategies for the rapid, pragmatic and reliable identification of VF. Many osteoporosis guidelines emphasize the importance of identifying VF and promote more frequent use of vertebral imaging for fracture risk assessment and determining the need for pharmacotherapy. Osteoporosis Canada’s 2010 guidelines recommend consideration of spine imaging for anyone found at moderate (10-20%) 10-year probability of major osteoporotic fracture, as the presence of a VF would elevate the patient to a high (>20%) risk category.\textsuperscript{55}

In their 2014 guidelines, the US National Osteoporosis Foundation suggests that spine imaging should be considered for women age 70 years and older and men age 80 years and older if their BMD T-score at the lumbar spine, femoral neck or total hip is ≤-1.0; for women age 65-69 years or men age 70-79 years of age with a BMD T-score of ≤-1.5 at the lumbar spine, femoral neck or total hip; and for postmenopausal women and men age 50 years and older with a low trauma fracture during adulthood (age ≥40 years), a historical height loss of 4 cm or more, prospective (incident) measured height loss of 2 cm or more and/or recent or ongoing long-term glucocorticoid treatment.\textsuperscript{56}

Similarly, the International Society for Clinical Densitometry (ISCD) Official Positions recommend lateral spine imaging, for individuals with a BMD T-score of < -1.0 and one or more of the following: age ≥70 (women) or ≥ 80 (men), historical height loss >4 cm, glucocorticoid therapy equivalent to ≥5 mg of prednisone or equivalent per day for ≥3 months and/or self-reported (but undocumented) VF.\textsuperscript{57} The ISCD further recommends that VF screening should be considered for women 70 years of age and older with normal BMD with other fracture risk factors and signs that a VF may have been recent.

Simple strategies, such as monitoring a patient’s height over time with a wall-mounted stadiometer, can be a powerful indicator of an incident VF. Siminoski et al.\textsuperscript{58,59} have shown that a historical height loss of >6 cm or a measured height loss of >2 cm when followed over 1-3 years is highly predictive of an underlying VF.
VFA is an attractive option for VF assessment, since it can be completed at the same time as DXA. A performance algorithm that is invoked by the densitometrist has been implemented in some centres to direct cost effective utilization of VFA.  

Other indications for spine imaging include new fixed kyphosis and unexplained persistent back pain, with appropriate caution to avoid over-use of spine imaging for chronic low back pain. In patient populations where VF are common, such as glucocorticoid-treated patients, routine spinal imaging should be considered.

Indications for follow-up imaging after VFA by DXA include equivocal VF seen on VFA by DXA spine image, possible abdominal aortic aneurysm on VFA or lateral spine radiographs, features on VFA or lateral spine radiographs that suggest malignancy, lytic or sclerotic lesions of the vertebral body or expansion or erosion of the vertebra or pedicles. Caution is advised among those with a history of malignancy with potential for bone metastases.

If spine imaging is indicated, there should be clear instructions to the radiologist to specifically state “fracture” or “no fracture”. For those patients with a VF, or on pharmacologic therapy, consider repeat imaging when contemplating stopping therapy and if there is a reasonable chance that a new VF has occurred. The identification of a VF in a patient contemplating stopping therapy may alter their decision.

Case finding during acute care

There are frequent opportunities to identify VF during imaging for other purposes. Radiologists should be made aware of the valuable additional clinical information afforded by identification and clear reporting of VF.
Radiographic interpretation

Conventional radiography and VFA are currently the most economical options for VF identification. Advantages of VFA, if performed concomitantly with BMD, are lower cost, lower radiation and less obliquity than lateral spine radiographs. Advantages of XR are superior spatial resolution with cortical edges and endplates, comparatively sharper and improved visualization of upper thoracic vertebrae, allowing for a greater number of evaluable vertebrae. However, the majority of significant VF are at T10-L2 and are relatively easily visualized by VFA.\textsuperscript{62} If VFA results are uncertain, XR should be obtained. MRI may be appropriate to evaluate VF when there is clinical or XR concern for malignancy or infection, or if there is spinal cord compromise. Further, bone edema seen on MRI may indicate fracture acuity; this may be helpful if vertebroplasty or kyphoplasty is being considered. A radioisotope bone scan may identify metastases and help determine fracture acuity.

Clinical interpretation of spine imaging

Reports of spine imaging should be clear and decisive whenever possible, with comments on radiograph quality, which vertebral bodies are evaluable and on other clinically-important radiographic features, such as signs of malignancy. The severity of each VF should be reported using standardized methodology, reported as mild (Grade 1), moderate (Grade 2) or severe (Grade 3) and information provided as to the location, number of VFs and their recency (if possible); a recent VF may be present if bone edema is seen with MRI or when there is localized increase of a radionucleotide with a bone scan. Pathologic fractures (e.g., those due to multiple myeloma, metastatic cancer, or infection) should be excluded and the clinical context of the VF should be provided. If there are signs that the fracture may
have occurred with major trauma, these findings should be mentioned. Congenital and developmental abnormalities in vertebral anatomy should be identified and reported appropriately.

**Prevention of subsequent vertebral fractures**

Numerous pharmacological therapies significantly reduce the risk of VF.\textsuperscript{18,19,63} Individuals diagnosed with VF should be offered appropriate therapy as soon as practical.

VF play an important part in fracture liaison services (FLS) such as the IOF “Capture the Fracture” campaign.\textsuperscript{64} FLS programs are involved in case identification, investigation, and intervention to optimize secondary fracture prevention. FLS has been shown to be effective in preventing future fractures and reducing healthcare costs.\textsuperscript{65-68}

*How do therapy decisions change with number and severity of vertebral fractures?*

Osteoporosis pharmacotherapy should be strongly considered for patients with an osteoporotic VF, especially those with more recent, higher grade or multiple fractures. The presence of VF may direct therapy toward agents with greater proven and more rapid efficacy, and/or agents which promote more assured adherence to therapy. Secondary causes of bone loss and fracture should be evaluated and addressed before therapy initiation.

Because of the marked increase in future fracture risk after VF, most clinical practice guidelines emphasize the importance of pharmacotherapy to reduce the risk of future fractures regardless of 10-year fracture risk assessment (FRAX) or BMD.\textsuperscript{55,69} It is important to note that the FRAX algorithm allows for a “yes” response for previous adult low-trauma fracture, but does not account for different locations of fracture being more predictive of future fracture. It also does not account for the presence of multiple
fractures, recent fractures or more severe VF. These nuances should be considered when using FRAX in clinical decision making.

**Do Grade 1 vertebral fractures warrant osteoporosis pharmacotherapy?**

A secure diagnosis of Grade 1 VF can be problematic; often there are differences in interpretation between radiologists. A Grade 1 VF does not predict future fracture to the same degree as a higher grade VF. Because of this and the difficulty in diagnosis, often a Grade 1 VF without other risk factors does not warrant osteoporosis pharmacotherapy. However, clinical judgement needs to be exercised with respect to the recency of the fracture, the number of VF, BMD, and other clinical risk factors. In this instance, a FRAX assessment may be particularly relevant for informing whether to suggest pharmacological treatment (select negative for personal history of fracture if the Grade 1 VF is the only fracture). A Grade 1, solitary, asymptomatic, incidentally discovered VF is of questionable clinical significance.

In the MORE (Multiple Outcomes of Raloxifene Evaluation) Phase III clinical trial, non-vertebral fractures were not reduced by therapy. However, in a post-hoc analysis, non-vertebral fractures were reduced by raloxifene in patients with a Grade 3 VF, suggesting that a high grade VF is more important in predicting future non-vertebral fracture events than a Grade 1 or 2 VF.51

**Do Grade 2 and 3 vertebral fractures warrant lifelong osteoporosis pharmacotherapy?**

The length of time a patient remains on osteoporosis therapy depends on clinical risk factors for fracture, which include number, severity and recency of VF. There are patients who likely should not
interrupt treatment and others who may be candidates for at least a temporary bisphosphonate treatment interruption.

At this time, the only therapy that is limited in its length of use (to two years) is teriparatide, subsequent to which another osteoporosis therapy should be initiated. With the bisphosphonates, persistence of BMD can often be seen in clinical trials of groups of patients, for months to years after discontinuing long-term use. Continued benefit of bisphosphonate therapy beyond three to six years may be limited to those with a prevalent VF and/or a femoral neck BMD T-score of ≤ -2.5 (FLEX and HORIZON extension trial). If therapy is interrupted, a re-evaluation of the patient's fracture risk after two years off therapy is warranted. While there are few data to guide when and for how long bisphosphonate “drug holidays/interruptions” can be taken, published expert opinion may provide guidance. All other non-bisphosphonate osteoporosis therapies have a more rapid resolution of effects and so should not be discontinued in patients at high risk of fracture.

Management of acute, symptomatic fractures

Acute VF may be accompanied by bone pain and muscle spasm. Disabling pain can persist for several months. General measures include short-term bed-rest and pain relief with acetaminophen, nonsteroidal anti-inflammatory drugs, and narcotics. If pain is not controlled by these general measures, calcitonin can be provided as an analgesic with discontinuation after six to 12 weeks. However, calcitonin is not recommended as a long-term therapy for osteoporosis and has no effect on chronic pain. Teriparatide treatment was associated with less back pain in the pivotal Fracture Protection Trial, and in a meta-analysis, teriparatide-treated patients reported less back pain than comparator in multiple active and placebo controlled trials. There is no evidence that other anti-remodeling agents reduce the severity of acute or chronic pain due to VF.
Physical therapy is beneficial to patients recovering from acute VF to reduce pain and improve mobility. The use of pain management techniques in the acute phase following VF is beneficial – ultrasound, hydrotherapy, ice, heat, early mobilization, stretching exercises to decrease muscle spasm and a gentle strengthening exercise program.

Back bracing (i.e. spinal orthoses, corset) may be considered in the acute treatment phase following VF to help immobilize the fracture site, reducing loads on fractured vertebrae and improving spinal alignment to allow for healing and pain management.\textsuperscript{75,76} Bracing is best considered as short-term management in special circumstances; strong back muscles are the best long-term brace.

Vertebral augmentation, such as vertebroplasty and kyphoplasty, remain controversial but might be considered in patients with documented VF when there is persistent pain despite medical therapy or when neurological deficits are present. Vertebroplasty and kyphoplasty may reduce short-term VF pain, but have disadvantages of procedural complications and may increase the risk of fracture of adjacent vertebrae.\textsuperscript{77,78} Vertebroplasty or kyphoplasty are typically considered in patients who have intractable pain from vertebral fracture despite at least six weeks of conservative medical therapy - recent vertebral fractures are more likely to benefit from vertebroplasty.\textsuperscript{79}

**The management of chronic pain with old vertebral fractures**

Patients with remote a VF may experience chronic back pain related to degenerative changes adjacent to the VF. Additionally, the biomechanics of the spine are disrupted due to kyphosis possibly resulting in chronic soft tissue or arthritic pain. Such pain syndromes can be difficult to manage and may require an integrated approach. Rarely, spine surgeons may be called upon to restore sagittal alignment
with spine fusion procedures. Pain specialists may provide multifaceted interventions including pharmacotherapy, transcutaneous electrical nerve stimulation and acupuncture.

For patients with chronic pain from VF, physical therapy may assist with general muscle strengthening, improve posture and balance and strengthen quadriceps muscles. Exercise decreases both pain and subsequent fracture risk in patients with VF.\(^{80-84}\) Based on the initial condition of the patient, the physiotherapist should provide an exercise recommendation that includes weight-bearing aerobic activities, postural training, progressive resistance training, stretching and balance training. Wheeled walkers provide support for the spine and may relieve pain. Gait stabilization and fall prevention can greatly benefit patients. An evaluation of the home environment for fall risk hazards may be appropriate.

Patients should be advised to avoid activities which may put them at risk for more VFs which include forward bending, exercising with trunk in flexion, twisting, sudden, abrupt movements, jumping, and jarring movements, high-intensity exercise and heavy weight-lifting.\(^{85,86}\) The degree of activity restriction should be tempered by clinical judgment.

**Summary**

VF are common, increase in prevalence with age, often asymptomatic, under-diagnosed and under-treated. Physicians should be vigilant in the identification and follow-up of patients with VF. Recognition of a VF may dramatically alter the risk categorization of a patient and the management required to prevent future fractures. Once a VF has been diagnosed, the clinician should seek secondary causes of osteoporosis prior to initiating therapy. VF patients should also receive effective management of acute and/or chronic pain through medications and physical therapy, including information on reducing fall risk through walking aids, gait and balance training.


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