REVIEW

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Vertebral Fractures: Clinical Importance and Management

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ABSTRACT

Vertebral fractures are common and can result in acute and chronic pain, decreases in quality of life, and diminished lifespan. The identification of vertebral fractures is important because they are robust predictors of future fractures. The majority of vertebral fractures do not come to clinical attention. Numerous modalities exist for visualizing suspected vertebral fracture. Although differing definitions of vertebral fracture may present challenges in comparing data between different investigations, at least 1 in 5 men and women aged >50 years have one or more vertebral fractures. There is clinical guidance to target spine imaging to individuals with a high probability of vertebral fracture. Radiology reports of vertebral fracture need to clearly state that the patient has a "fracture," with further pertinent details such as the number, recency, and severity of vertebral fracture, each of which is associated with risk of future fractures. Patients with vertebral fracture should be considered for anti-fracture therapy. Physical and pharmacologic modalities of pain control and exercises or physiotherapy to maintain spinal movement and strength are important components in the care of vertebral fracture patients.
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Vertebral fractures are the most common type of osteoporotic fracture and are associated with substantial morbidity[1,2] and decreased survival.[3,4] In the United States, annual direct management costs for vertebral fractures are more than $1 billion (United States dollars in 2011).[5]

Vertebral fracture, once suspected, can be confirmed by X-rays, computerized tomography, magnetic resonance imaging, or vertebral fracture assessment. Vertebral fracture assessment can be completed at the time of bone mineral density assessment with dual-energy X-ray absorptiometry.

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Information on radiation dose, image resolution, and relative cost for these imaging modalities can be found in **Table 1**. Nonfracture causes of vertebral height loss and deformity need to be ruled out before confirming vertebral fracture.

Asymptomatic (morphometric) and symptomatic vertebral fracture can be diagnosed using the Genant semi-quantitative method (Figure), which requires a ≥20% decrease in vertebral height (anterior, mid, or posterior dimensions), estimated visually, to diagnose a vertebral fracture.[9] In intervention and epidemiologic studies, a *prevalent* vertebral fracture is a fracture identified at the baseline of the study; *incident* vertebral fractures are those occurring after the baseline.

Vertebral fractures can also be diagnosed by standard quantitative morphometry or by comparing a vertebral body with adjacent vertebrae. By vertebral comparison, a vertebral fracture can be diagnosed if there is a greater than 3 standard deviation difference in vertebral heights between adjacent vertebral levels.[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 methodology relies on recognition of vertebral endplate deformity to identify vertebral fracture.[11] When comparing clinical trials or epidemiology studies, it is important to understand how vertebral fractures were defined, because this can have important implications on interpretation of the findings. **Tables 2** and **3** illustrate the diversity in study criteria for vertebral fracture.

Epidemiologic investigations provide incidence and prevalence of vertebral fractures, although their estimates are dependent on the underlying populations and definitions of vertebral fracture (**Table 3**). The Canadian Multicentre Osteoporosis Study reported that 21.5% of men and 23.5% of women aged >50 years have at least 1 vertebral compression deformity,[21] whereas the Norwegian population-based Tromso study found that 20.3% of men and 19.2% of women aged >70 years had at least 1 vertebral fracture.[30] A quarter of women aged >50 years in Rochester, Minnesota, had 1 or more vertebral fractures, as did more than one-third of women by age 70 years.[27] In the Study of Osteoporotic Fractures, 18% of postmenopausal women aged >65 years suffered an incident vertebral fracture over a 15-year follow-up.[31] Between 10% and 28% of vertebral fracture are found in postmenopausal women whose bone mineral density T-score is >−2.5.[32,33]

CLINICAL SIGNIFICANCE

- Approximately two-thirds of vertebral fractures do not come to clinical attention.
- Risk of future vertebral fracture increases with increasing number and severity of prevalent vertebral fractures.
- A recent vertebral fracture confers a much greater risk of future fracture risk than a remote vertebral fracture.
- Treatments options are available for both acute and chronic pain associated with vertebral fractures.

Despite the high prevalence of vertebral fracture, more than two-thirds of vertebral fractures remain undiagnosed.[34,35] The recognition of vertebral fractures in imaging reports obtained for purposes other than the investigation for vertebral fracture in a hospital setting is generally poor (**Table 4**).[36-45]

Care gaps in vertebral fracture diagnosis may result from radiologists assuming that vertebral fractures 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 vertebral fractures. Often, radiographs are of insufficient technical quality to accurately identify vertebral fractures. Radiologists should consistently apply published criteria for diagnosing vertebral fractures, such as the Genant semi-quantitative methodology,[9] vertebral morphometry,[46] and signs of endplate disruption.[11] Consistent, clear terminology should be used to report vertebral abnormalities, with information provided as to the number of vertebral fractures, their location, and their grade/severity.

Both symptomatic and asymptomatic vertebral fractures strongly indicate increased fracture risk in untreated patients. In the Study of Osteoporotic Fractures cohort, women with a prevalent vertebral fracture had an approximate 3-fold greater risk of incident vertebral fracture than women without a prevalent vertebral fracture.[31] Patients taking placebo who experienced a new vertebral fracture during an osteoporosis clinical trial had a 20% incidence of another new vertebral fracture within 1 year.[29] There is also a significantly elevated risk of any type of fracture soon after suffering a clinical vertebral fracture.[47,48] The risk of future vertebral fracture increases with the number and severity of prevalent vertebral fractures,[49,50] with a recent vertebral fracture imparting a greater risk of future vertebral fracture

Table 1 Imaging Modalities for Assessment of Vertebral Fractures

Modality	Average Effective Dose[6] (mSv)	Image Resolution	Relative Cost
Radiography (anteroposterior and lateral)	2.5	0.1 mm[7]	$$
Computerized tomography (spine)	6.0	250-300 μm[8]	$$$$
Magnetic resonance imaging (spine)	0	150-200 μm[8]	$$$$
Vertebral fracture assessment by dual energy X-ray absorptiometry	0.001	0.5 mm[7]	$

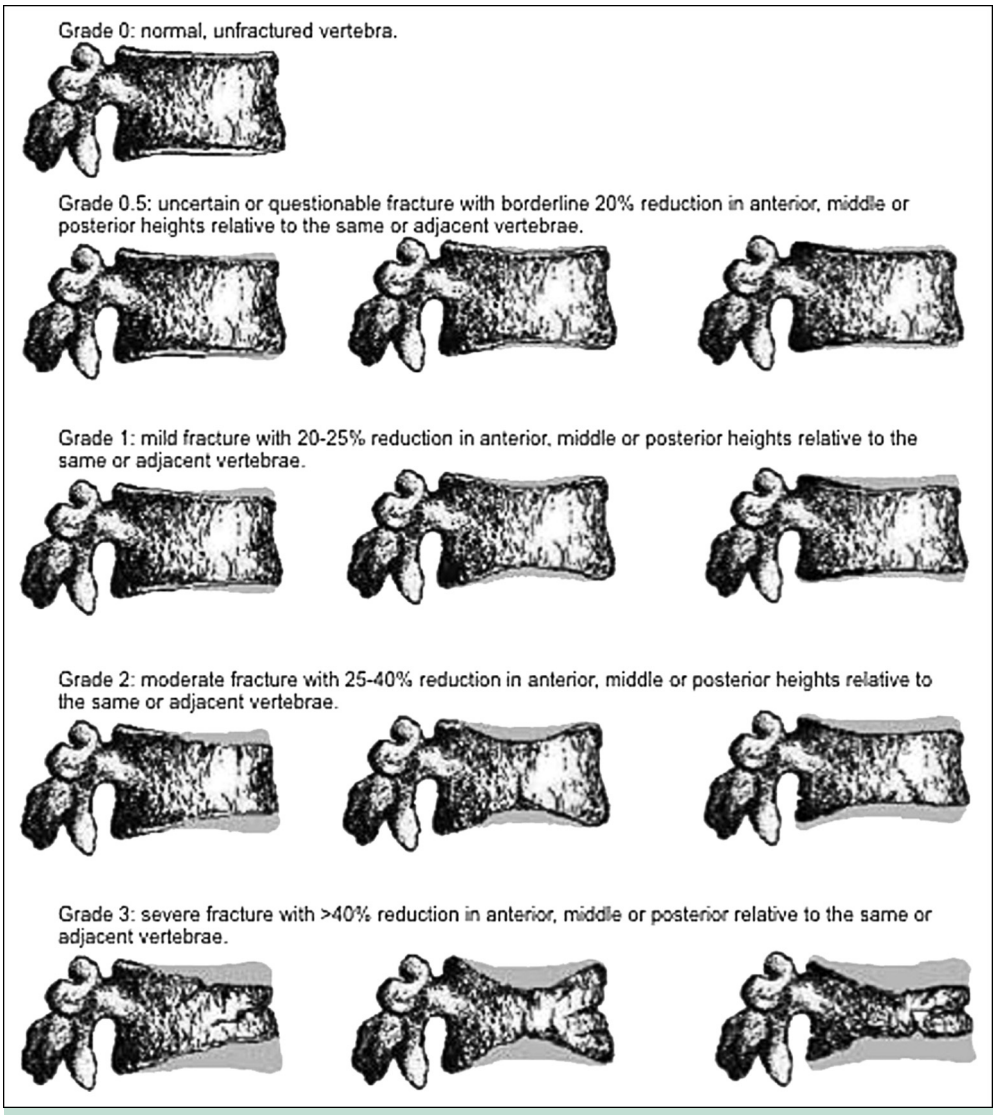

Figure Classification of vertebral fractures by the Genant semiquantitative method. Reproduced from Genant et al,[9] by permission of John Wiley & Sons.

than one that has occurred remotely.[51-53] Patients with multiple, more severe, and more recent vertebral fractures are also more likely to be symptomatic and have fractures recognized clinically.[35,54]

SCREENING/CASE FINDING IN THE CLINIC

It is important to develop improved strategies for the rapid, pragmatic, and reliable identification of vertebral fractures. Many osteoporosis guidelines emphasize the importance of identifying vertebral fractures 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, because the presence of a vertebral fracture would elevate the patient to a high (>20%) risk category.[55]

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

Similarly, the International Society for Clinical Densitometry Official Positions recommend lateral spine imaging, for individuals with a bone mineral density T-score of

Table 2 Radiographic Vertebral Fracture Assessment Methods From Osteoporosis Phase 3 Clinical Trials

Phase 3 Trial, Therapy	N	Mean Age (y)	Baseline Prevalence of Vertebral Fractures (%)	Definition of Prevalent Vertebral Fracture
VERT-NA,[12] risedronate	2458	I: 69 P: 68	100	Ratio of the anterior or middle vertebral body height to the posterior vertebral body height $\leq$0.8 (both QM and SQ)
VERT-MN,[13] risedronate	1226	I: 71 P: 71	100	Diagnosed by QM and SQ
FIT I,[14] alendronate	2027	I: 71 P: 71	100	Any ratio of vertebral heights more than 3 SDs below the mean population norm for that vertebral level
FIT II,[15] alendronate	4272	I: 67.6 P: 67.7	0	NA
Alendronate Phase 3 Osteoporosis Treatment Study Group,[16] alendronate	881	I: 64 P: 64	20	Any vertebral height ratio more than 3 SDs below the corresponding reference ratio (from reference population)
Neer,[17] teriparatide	1637	I: 69-71 P: 69	8	Graded as normal or as mildly, moderately, or severely deformed (a decrease in height of approximately 20%-25%, 26%-40%, or >40%, respectively)
FREEDOM,[18] denosumab	7868	I: 72 P: 72	23-24	Vertebral body with a SQ Grade of 1 or more (Genant SQ method)
HORIZON-PFT,[19] zoledronic acid	3889	I: 73 P: 73	62-64	Vertebral height ratio of at least 3 SD below the vertebra-specific mean height ratio on QM reading with SQ confirmation
Clodronate phase 3 trial,[20] clodronate	593	I: 66-68 P: 68	46-67	Vertebral morphometry using SQ method

FIT I = Fracture Intervention Trial I; FREEDOM = Fracture Reduction Evaluation of Denosumab in Osteoporosis Every 6 Months; HORIZON-PFT = Health Outcomes and Reduced Incidence with Zoledronic Acid Once Yearly Pivotal Fracture Trial; I = intervention arm; P = placebo arm; QM = quantitative method: ratios from direct vertebral body height measurements define fractures; SD = standard deviation; SQ = semiquantitative method: visual grading of height and area reduction used to define fracture; VERT-MN = Vertebral Efficacy With Risedronate Therapy Multi-National; VERT-NA = Vertebral Efficacy With Risedronate Therapy-North America.

<-1.0 and 1 or more of the following: age $\geq$70 years (women) or $\geq$80 years (men), historical height loss >4 cm, glucocorticoid therapy equivalent to $\geq$5 mg of prednisone or equivalent per day for $\geq$3 months, and/or self-reported (but undocumented) vertebral fracture.[57] The International Society for Clinical Densitometry further recommends that vertebral fracture screening should be considered for women aged $\geq$70 years with normal bone mineral density with other fracture risk factors and signs that a vertebral fracture may have been recent.

Simple strategies, such as monitoring a patient's height over time with a wall-mounted stadiometer, can be powerful indicators of an incident vertebral fracture. Siminoski et al[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 vertebral fracture.

Vertebral fracture assessment by dual energy X-ray absorptiometry is an attractive option for identifying vertebral fractures, because it can be completed at the same time as dual energy X-ray absorptiometry assessment of bone mineral density. A performance algorithm that is invoked by the densitometrist has been implemented in some centers to direct cost-effective utilization of vertebral fracture assessment.[60]

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 vertebral fractures are common, such as glucocorticoid-treated patients, routine spinal imaging should be considered.

Indications for follow-up imaging after vertebral fracture assessment by dual energy X-ray absorptiometry include equivocal vertebral fracture seen on vertebral fracture assessment by dual energy X-ray absorptiometry spine image; possible abdominal aortic aneurysm on vertebral fracture assessment or lateral spine radiographs; and features on vertebral fracture assessment 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.[61]

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 vertebral fracture, or taking pharmacologic therapy, consider repeat imaging when contemplating stopping therapy and if there is a reasonable chance that a new vertebral fracture has occurred. The identification of a vertebral

Table 3 Radiographic Vertebral Fracture Assessment Methods From Epidemiologic Studies

Study Name	N	Age Range (y)	Prevalence: Definition of Prevalent Vertebral Fracture	Incidence: Definition of Incident Vertebral Fracture
CaMOS[21]	4613	≥50	Men = 21.5%, women = 23.5%: >3 SD below mean vertebral height of population	NA
The Rotterdam Study[22]	3469	≥55	NA	7.8/1000 p-y at 55-65 y; 19.6 and 5.2-9.3/1000 p-y at >75 y for women and men, respectively: QM by McCloskey-Kanis assessment method*
European Vertebral Osteoporosis Study[23]	15,570	50-79	Mean 12% (8%-20% over age) in men and mean 12% (6%-21% over age) in women: McCloskey method: vertebral height of <3 SD below adjacent vertebrae	NA
European Prospective Osteoporosis Study[24]	6788	≥50	NA	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
Study of Osteoporotic Fractues[25]	5166	≥68	21.8%: Black morphometric definition: ≥3 SD height loss	NA
Latin American Vertebral Osteoporosis Study[26]	1922	≥50	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	NA
Rochester, Minn[27]	762	≥50	25.3% in women: >3 SD below any mean vertebral height	17.8/1000 p-y in women: >3 SD below any mean vertebral height.
Mr. OS (Hong Kong) and Ms. OS (Hong Kong)[28]	4000	≥65	14.9% in men and 16.5% in women: Genant's SQ method	NA
Osteoporosis and Ultrasound Study[29]	674	39-80	6.2%: ABQ method with Vertebral Fracture Assessment	4.45/1000 p-y: ABQ with Vertebral Fracture Assessment

ABQ = Algorithm-Based Qualitative method; CaMOS = Canadian Multicentre Osteoporosis Study; Mr. OS = The Osteoporotic Fractures in Men Study; NA = not provided; p-y = person-years; QM = quantitative method: ratios from direct vertebral body height measurements define fractures; SD = standard deviation; SQ = semiquantitative method: visual grading of height and area reduction used to define fracture.

*McCloskey-Kanis assessment method: QM that defines fracture as either anterior or posterior wedge, biconcavity, or compression.

†Eastell criteria: QM that defines fracture as either wedge, biconcavity, or compression.

Table 4 Recognition of Vertebral Fractures in Hospital Setting

Lead Author, Year of Publication	Device	Patient Mean Age (y), (range)	N	% Vertebral Fractures Recognized
Bartalena, 2009[37]	CT	63 (20-88)	323	15
Chan, 2012[38]	CT	NA (≥65)	175	14
Obaid, 2008[36]	CT	65 Md (18-90)	307	5
Williams, 2009[39]	CT	70 (55-89)	192	13
Woo, 2008[40]	CT	61 (18-92)	200	9
Cataldi, 2008[41]	XR	67.5 (50-86)	145	11
Kim, 2004[42]	XR	75 (≥60)	100	55
Majumdar, 2005[43]	XR	75 (≥60)	459	60
Mui, 2003[44]	XR	65 (55-89)	106	15
Santamaria Fernandez, 2012[45]	XR	66 (NA)	254	8

CT = computed tomography; Md = median; NA = not provided; XR = radiograph.

fracture in a patient contemplating stopping therapy may alter their decision.

CASE FINDING DURING ACUTE CARE

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

RADIOGRAPHIC INTERPRETATION

Conventional radiography and vertebral fracture assessment are currently the most economical options for vertebral fracture identification. Advantages of vertebral fracture assessment, if performed concomitantly with bone mineral density assessment, are its lower cost, lower radiation, and less obliquity compared with lateral spine radiographs. Advantages of radiographs are superior spatial resolution with cortical edges and endplates, and comparatively sharper and improved visualization of upper thoracic vertebrae, allowing for a greater number of evaluable vertebrae. However, the majority of significant vertebral fractures are at T10-L2 and are relatively easily visualized by vertebral fracture assessment.[62] If vertebral fracture assessment results are uncertain, radiographs should be obtained. Magnetic resonance imaging may be appropriate to evaluate vertebral fracture when there is clinical or radiographic concern for malignancy or infection, or if there is spinal cord compromise. Further, bone edema seen on magnetic resonance imaging 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 vertebral fracture 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 vertebral fractures, and their recency (if possible); a recent vertebral fracture may be present if bone edema is seen with magnetic resonance imaging or when there is localized increase of a radionucleotide with a bone scan. Pathologic fractures (eg, those due to multiple myeloma, metastatic cancer, or infection) should be excluded, and the clinical context of the vertebral fracture 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 pharmacologic therapies significantly reduce the risk of vertebral fracture.[18,19,63] Individuals diagnosed with vertebral fracture should be offered appropriate therapy as soon as practical.

The identification of vertebral fractures play an important part in fracture liaison services, such as the International Osteoporosis Foundation's "Capture the Fracture,"[64] the American Orthopedic Association's "Own the Bone,"[65] and National Bone Health Alliance's "Strong Bones America"[66] fracture liaison services programs, which seek to link patients with a fragility fracture to medical care targeted to reduce future fracture risk. Such care may include fracture risk assessment (with tools to estimate 10-year fracture risk such as 10-year fracture risk assessment [FRAX]), bone densitometry, chemistries to rule out secondary causes of bone loss, nutrition interventions, falls prevention programs, gait and balance training, and pharmacotherapy. The most effective fracture liaison services programs involve a fracture liaison services nurse to identify patients and direct them to the appropriate services to meet their needs. Such programs have been demonstrated to be highly cost-effective.[67-70]

HOW DO THERAPY DECISIONS CHANGE WITH NUMBER AND SEVERITY OF VERTEBRAL FRACTURES?

Osteoporosis pharmacotherapy should be strongly considered for patients with an osteoporotic vertebral fracture, especially those with more recent, higher grade, or multiple fractures. In clinical trials, the patient subgroups who achieve the greatest absolute risk reduction for future fracture are those with a prevalent vertebral fracture. The presence of vertebral fracture may direct therapy toward agents with greater proven and more rapid efficacy, and/or agents that promote more assured adherence to therapy. Anabolic

therapy with subcutaneous teriparatide or parenteral antiresorptive therapy with intravenous zoledronic acid or subcutaneous denosumab are highly effective at reducing risk of vertebral fracture. 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 vertebral fracture, most clinical practice guidelines emphasize the importance of pharmacotherapy to reduce the risk of future fractures regardless of FRAX result or bone mineral density.[55,71] 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 vertebral fracture. 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 vertebral fracture can be problematic; often there are differences in interpretation between radiologists. A grade 1 vertebral fracture does not predict future fracture to the same degree as a higher grade vertebral fracture. Because of this and the difficulty in diagnosis, often a grade 1 vertebral fracture 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 vertebral fractures, bone mineral density, and other clinical risk factors. In this instance, FRAX may be particularly relevant for informing whether to suggest pharmacologic treatment (select negative for personal history of fracture if the grade 1 vertebral fracture is the only fracture). A grade 1, solitary, asymptomatic, incidentally discovered vertebral fracture is of questionable clinical significance.

In the Multiple Outcomes of Raloxifene Evaluation phase 3 clinical trial, nonvertebral fractures were not reduced by therapy. However, in a post hoc analysis, nonvertebral fractures were reduced by raloxifene in patients with a grade 3 vertebral fracture, suggesting that a high grade vertebral fracture is more important in predicting future nonvertebral fracture events than a grade 1 or 2 vertebral fracture.[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 vertebral fracture. 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 2 years) is teriparatide, subsequent to which another osteoporosis therapy should be initiated. With the bisphosphonates, stabilization of bone mineral density 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 3-6 years may be limited to those with a prevalent vertebral fracture and/or a femoral neck bone mineral density T-score of ≤ -2.5.[72,73] if therapy is interrupted, a re-evaluation of the patient's fracture risk after 2 years off therapy is warranted. Although there are few data to guide when and for how long bisphosphonate "drug holidays/interruptions" can be taken, published expert opinion may provide guidance.[74] 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 vertebral fracture may be accompanied by bone pain and muscle spasm. Disabling pain can persist for several months.[3] 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 6-12 weeks.[75] 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,[17] and in a meta-analysis, teriparatide-treated patients reported less back pain than comparator in multiple active and placebo-controlled trials.[76] There is no evidence that other anti-remodeling agents reduce the severity of acute or chronic pain due to vertebral fracture.

Physical therapy is beneficial to patients recovering from acute vertebral fracture to reduce pain and improve mobility. The use of pain management techniques in the acute phase after vertebral fracture is beneficial—ultrasound, hydrotherapy, ice, heat, early mobilization, stretching exercises to decrease muscle spasm, and a gentle strengthening exercise program. Evidence that muscle strengthening, gait training, or flexibility exercises can reduce the risk for future vertebral fracture is not available. Many exercise programs for patients at risk of vertebral fracture focus on maintaining patients safe from falling. Spine extension rather than flexion exercises may lead to better pain relief and place less load on the anterior aspect of the vertebral body, possible resulting in less exercise-related fracture.

Back bracing (ie, spinal orthoses, corset) may be considered in the acute treatment phase after vertebral fracture to help immobilize the fracture site, reducing loads on fractured vertebrae and improving spinal alignment to allow for healing and pain management.[77,78] 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 vertebral fracture when there is persistent pain despite medical therapy or when neurologic deficits are present. Vertebroplasty and kyphoplasty may reduce short-term vertebral fracture pain, but have disadvantages of procedural complications and may increase the risk of fracture of adjacent vertebrae.[79,80] Vertebroplasty or kyphoplasty are typically considered in patients who have intractable pain from vertebral fracture despite at least 6 weeks of conservative medical therapy; recent vertebral fractures are more likely to benefit from vertebroplasty.[81]

MANAGEMENT OF CHRONIC PAIN WITH OLD VERTEBRAL FRACTURES

Patients with a remote vertebral fracture may experience chronic back pain related to degenerative changes adjacent to the vertebral fracture. Additionally, the biomechanics of the spine are disrupted because of 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 vertebral fracture, 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 vertebral fracture.[82-86] On the basis of 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 that may put them at risk for more vertebral fractures, which include forward bending, exercising with trunk in flexion, twisting, sudden, abrupt movements, jumping, and jarring movements, high-intensity exercise, and heavy weight-lifting.[87,88] The degree of activity restriction should be tempered by clinical judgment.

SUMMARY

Vertebral fractures are common, increase in prevalence with age, and are often asymptomatic, under-diagnosed, and under-treated. Physicians should be vigilant in the identification and follow-up of patients with vertebral fracture. Recognition of a vertebral fracture may dramatically alter the risk categorization of a patient and the management required to prevent future fractures. Once a vertebral fracture has been diagnosed, the clinician should seek secondary causes of osteoporosis before initiating therapy. Vertebral fracture 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.

References

1. Ettinger B, Black DM, Nevitt MC, et al. Contribution of vertebral deformities to chronic back pain and disability. The Study of Osteoporotic Fractures Research Group. *J Bone Miner Res*. 1992;7(4):449-456.
2. Nevitt MC, Ettinger B, Black DM, et al. The association of radiographically detected vertebral fractures with back pain and function: a prospective study. *Ann Intern Med*. 1998;128(10):793-800.
3. Fink HA, Ensrud KE, Nelson DB, et al. Disability after clinical fracture in postmenopausal women with low bone density: the fracture intervention trial (FIT). *Osteoporos Int*. 2003;14(1):69-76.
4. Cooper C, Atkinson EJ, Jacobsen SJ, O'Fallon WM, Melton LJ III. Population-based study of survival after osteoporotic fractures. *Am J Epidemiol*. 1993;137(9):1001-1005.
5. Baaj AA, Downes K, Vaccaro AR, Uribe JS, Vale FL. Trends in the treatment of lumbar spine fractures in the United States: a socioeconomics perspective: clinical article. *J Neurosurg Spine*. 2011;15(4):367-370.
6. Mettler FA Jr, Huda W, Yoshizumi TT, Mahesh M. Effective doses in radiology and diagnostic nuclear medicine: a catalog. *Radiology*. 2008;248(1):254-263.
7. Guermazi A, Mohr A, Grigorian M, Taouli B, Genant HK. Identification of vertebral fractures in osteoporosis. *Semin Musculoskelet Radiol*. 2002;6(3):241-252.
8. Link TM. Osteoporosis imaging: state of the art and advanced imaging. *Radiology*. 2012;263(1):3-17.
9. Genant HK, Wu CY, van Kiujk C, Nevitt MC. Vertebral fracture assessment using a semiquantitative technique. *J Bone Miner Res*. 1993;8(9):1137-1148.
10. McCloskey EV, Spector TD, Eyres KS, et al. The assessment of vertebral deformity: a method for use in population studies and clinical trials. *Osteoporos Int*. 1993;3(3):138-147.
11. Ferrar L, Jiang G, Adams J, Eastell R. Identification of vertebral fractures: an update. *Osteoporos Int*. 2005;16(7):717-728.
12. Harris ST, Watts NB, Genant HK, et al. Effects of risedronate treatment on vertebral and nonvertebral fractures in women with postmenopausal osteoporosis: a randomized controlled trial. Vertebral Efficacy With Risedronate Therapy (VERT) Study Group. *JAMA*. 1999;282(14):1344-1352.
13. Reginster J, Minne HW, Sorensen OH, et al. Randomized trial of the effects of risedronate on vertebral fractures in women with established postmenopausal osteoporosis. Vertebral Efficacy with Risedronate Therapy (VERT) Study Group. *Osteoporos Int*. 2000;11(1):83-91.
14. Black DM, Cummings SR, Karpf DB, et al. Randomised trial of effect of alendronate on risk of fracture in women with existing vertebral fractures. Fracture Intervention Trial Research Group. *Lancet*. 1996;348(9041):1535-1541.
15. Cummings SR, Black DM, Thompson DE, et al. Effect of alendronate on risk of fracture in women with low bone density but without vertebral fractures: results from the Fracture Intervention Trial. *JAMA*. 1998;280(24):2077-2082.
16. Liberman UA, Weiss SR, Broll J, et al. Effect of oral alendronate on bone mineral density and the incidence of fractures in postmenopausal osteoporosis. The Alendronate Phase III Osteoporosis Treatment Study Group. *N Engl J Med*. 1995;333(22):1437-1443.

17. Neer RM, Arnaud CD, Zanchetta JR, et al. Effect of parathyroid hormone (1-34) on fractures and bone mineral density in postmenopausal women with osteoporosis. *N Engl J Med*. 2001;344(19):1434-1441.
18. Cummings SR, San Martin JA, McClung MR, et al. Denosumab for prevention of fractures in postmenopausal women with osteoporosis. *N Engl J Med*. 2009;361(8):756-765.
19. Black DM, Delmas PD, Eastell R, et al. Once-yearly zoledronic acid for treatment of postmenopausal osteoporosis. *N Engl J Med*. 2007;356(18):1809-1822.
20. McCloskey E, Selby P, Davies M, et al. Clodronate reduces vertebral fracture risk in women with postmenopausal or secondary osteoporosis: results of a double-blind, placebo-controlled 3-year study. *J Bone Miner Res*. 2004;19(5):728-736.
21. Jackson SA, Tenenhouse A, Robertson L. Vertebral fracture definition from population-based data: preliminary results from the Canadian Multicenter Osteoporosis Study (CaMos). *Osteoporos Int*. 2000;11(8):680-687.
22. van der Klift M, de Laet CE, McCloskey EV, Hofman A, Pols HA. The incidence of vertebral fractures in men and women: the Rotterdam Study. *J Bone Miner Res*. 2002;17(6):1051-1056.
23. O'Neill TW, Felsenberg D, Varlow J, Cooper C, Kanis JA, Silman AJ. The prevalence of vertebral deformity in european men and women: the European Vertebral Osteoporosis Study. *J Bone Miner Res*. 1996;11(7):1010-1018.
24. Felsenberg D, Silman AJ, Lunt M, et al. Incidence of vertebral fracture in europe: results from the European Prospective Osteoporosis Study (EPOS). *J Bone Miner Res*. 2002;17(4):716-724.
25. Schousboe JT, Rosen HR, Vokes TJ, et al. Prediction models of prevalent radiographic vertebral fractures among older women. *J Clin Densitom*. 2014;17(3):378-385.
26. Clark P, Cons-Molina F, Deleze M, et al. The prevalence of radiographic vertebral fractures in Latin American countries: the Latin American Vertebral Osteoporosis Study (LAVOS). *Osteoporos Int*. 2009;20(2):275-282.
27. Melton LJ III, Lane AW, Cooper C, Eastell R, O'Fallon WM, Riggs BL. Prevalence and incidence of vertebral deformities. *Osteoporos Int*. 1993;3(3):113-119.
28. Kwok AW, Gong JS, Wang YX, et al. Prevalence and risk factors of radiographic vertebral fractures in elderly Chinese men and women: results of Mr. OS (Hong Kong) and Ms. OS (Hong Kong) studies. *Osteoporos Int*. 2013;24(3):877-885.
29. Ferrar L, Roux C, Felsenberg D, Gluer CC, Eastell R. Association between incident and baseline vertebral fractures in European women: vertebral fracture assessment in the Osteoporosis and Ultrasound Study (OPUS). *Osteoporos Int*. 2012;23(1):59-65.
30. Waterloo S, Ahmed LA, Center JR, et al. Prevalence of vertebral fractures in women and men in the population-based Tromso Study. *BMC Musculoskelet Disord*. 2012;13:3.
31. Cauley JA, Hochberg MC, Lui LY, et al. Long-term risk of incident vertebral fractures. *JAMA*. 2007;298(23):2761-2767.
32. Greenspan SL, von Stetten E, Emond SK, Jones L, Parker RA. Instant vertebral assessment: a noninvasive dual X-ray absorptiometry technique to avoid misclassification and clinical mismanagement of osteoporosis. *J Clin Densitom*. 2001;4(4):373-380.
33. Schousboe JT, Ensrud KE, Nyman JA, Kane RL, Melton LJ III. Cost-effectiveness of vertebral fracture assessment to detect prevalent vertebral deformity and select postmenopausal women with a femoral neck T-score >-2.5 for alendronate therapy: a modeling study. *J Clin Densitom*. 2006;9(2):133-143.
34. Cooper C, O'Neill T, Silman A. The epidemiology of vertebral fractures. European Vertebral Osteoporosis Study Group. *Bone*. 1993;14(suppl 1):S89-S97.
35. Fink HA, Milavetz DL, Palermo L, et al. What proportion of incident radiographic vertebral deformities is clinically diagnosed and vice versa? *J Bone Miner Res*. 2005;20(7):1216-1222.
36. Obaid H, Husamaldin Z, Bhatt R. Underdiagnosis of vertebral collapse on routine multidetector computed tomography scan of the abdomen. *Acta Radiol*. 2008;49(7):795-800.
37. Bartalena T, Giannelli G, Rinaldi MF, et al. Prevalence of thoracolumbar vertebral fractures on multidetector CT: underreporting by radiologists. *Eur J Radiol*. 2009;69(3):555-559.
38. Chan PL, Reddy T, Milne D, Bolland MJ. Incidental vertebral fractures on computed tomography. *N Z Med J*. 2012;125(1350):45-50.
39. Williams AL, Al-Busaidi A, Sparrow PJ, Adams JE, Whitehouse RW. Under-reporting of osteoporotic vertebral fractures on computed tomography. *Eur J Radiol*. 2009;69(1):179-183.
40. Woo EK, Mansoubi H, Alyas F. Incidental vertebral fractures on multidetector CT images of the chest: prevalence and recognition. *Clin Radiol*. 2008;63(2):160-164.
41. Cataldi V, Laporta T, Sverzellati N, De Filippo M, Zompatori M. Detection of incidental vertebral fractures on routine lateral chest radiographs. *Radiol Med*. 2008;113(7):968-977.
42. Kim N, Rowe BH, Raymond G, et al. Underreporting of vertebral fractures on routine chest radiography. *AJR Am J Roentgenol*. 2004;182(2):297-300.
43. Majumdar SR, Kim N, Colman I, et al. Incidental vertebral fractures discovered with chest radiography in the emergency department: prevalence, recognition, and osteoporosis management in a cohort of elderly patients. *Arch Intern Med*. 2005;165(8):905-909.
44. Mui LW, Haramati LB, Alterman DD, Haramati N, Zelefsky MN, Hamerman D. Evaluation of vertebral fractures on lateral chest radiographs of inner-city postmenopausal women. *Calcif Tissue Int*. 2003;73(6):550-554.
45. Santamaría Fernández S, Miralles F, Ruiz Serrato A, et al. Prevalence of thoracic vertebral fractures in Spanish patients hospitalized in Internal Medicine Departments. Assessment of the clinical inertia. (PREFRAMI study). *Eur J Intern Med*. 2012;23(2):e44-e47.
46. Jiang G, Ferrar L, Barrington NA, Eastell R. Standardised quantitative morphometry: a modified approach for quantitative identification of prevalent vertebral deformities. *Osteoporos Int*. 2007;18(10):1411-1419.
47. van Geel TA, Huntjens KM, van den Bergh JP, Dinant GJ, Geusens PP. Timing of subsequent fractures after an initial fracture. *Curr Osteoporos Rep*. 2010;8(3):118-122.
48. Johnell O, Kanis JA, Oden A, et al. Fracture risk following an osteoporotic fracture. *Osteoporos Int*. 2004;15(3):175-179.
49. Lindsay R, Silverman SL, Cooper C, et al. Risk of new vertebral fracture in the year following a fracture. *JAMA*. 2001;285(3):320-323.
50. Black DM, Arden NK, Palermo L, Pearson J, Cummings SR. Prevalent vertebral deformities predict hip fractures and new vertebral deformities but not wrist fractures. Study of Osteoporotic Fractures Research Group. *J Bone Miner Res*. 1999;14(5):821-828.
51. Delmas PD, Genant HK, Crans GG, et al. Severity of prevalent vertebral fractures and the risk of subsequent vertebral and nonvertebral fractures: results from the MORE trial. *Bone*. 2003;33(4):522-532.
52. Johnell O, Kanis J. Epidemiology of osteoporotic fractures. *Osteoporos Int*. 2005;16(suppl 2):S3-S7.
53. Schousboe JT, Fink HA, Taylor BC, et al. Association between self-reported prior wrist fractures and risk of subsequent hip and radiographic vertebral fractures in older women: a prospective study. *J Bone Miner Res*. 2005;20(1):100-106.
54. Black DM, Cummings SR, Genant HK, Nevitt MC, Palermo L, Browner W. Axial and appendicular bone density predict fractures in older women. *J Bone Miner Res*. 1992;7(6):633-638.
55. Papaioannou A, Morin S, Cheung AM, et al. 2010 clinical practice guidelines for the diagnosis and management of osteoporosis in Canada: summary. *CMAJ*. 2010;182(17):1864-1873.
56. Cosman F, de Beur SJ, LeBoff MS, et al. Clinician's guide to prevention and treatment of osteoporosis. *Osteoporos Int*. 2014;25(10):2359-2381.
57. The International Society For Clinical Densitometry. 2013 ISCD official positions—adult. Available at: www.iscd.org/official-positions/2013-iscd-official-positions-adult/. Accessed January 1, 2015.
58. Siminoski K, Warshawski RS, Jen H, Lee K. The accuracy of historical height loss for the detection of vertebral fractures in postmenopausal women. *Osteoporos Int*. 2006;17(2):290-296.

59. Siminoski K, Jiang G, Adachi JD, et al. Accuracy of height loss during prospective monitoring for detection of incident vertebral fractures. *Osteoporos Int*. 2005;16(4):403-410.
60. Schousboe J, McKiernan F, Fuehrer J, Binkley N. Use of a performance algorithm improves utilization of vertebral fracture assessment in clinical practice. *Osteoporos Int*. 2014;25(3):965-972.
61. Schousboe JT, Vokes T, Broy SB, et al. Vertebral fracture assessment: the 2007 ISCD official positions. *J Clin Densitom*. 2008;11(1):92-108.
62. Jager PL, Jonkman S, Koolhaas W, Stiekema A, Wolffenbuttel BH, Slart RH. Combined vertebral fracture assessment and bone mineral density measurement: a new standard in the diagnosis of osteoporosis in academic populations. *Osteoporos Int*. 2011;22(4):1059-1068.
63. MacLean C, Newberry S, Maglione M, et al. Systematic review: comparative effectiveness of treatments to prevent fractures in men and women with low bone density or osteoporosis. *Ann Intern Med*. 2008;148(3):197-213.
64. Akesson K, Marsh D, Mitchell PJ, et al. Capture the Fracture: a Best Practice Framework and global campaign to break the fragility fracture cycle. *Osteoporos Int*. 2013;24(8):2135-2152.
65. American Orthopaedic Association. Own the Bone. Avaiable at: www.ownthebone.org/. Accessed Ocbober 8, 2015.
66. National Bone Health Alliance. Strong Bones America. Available at: www.nbha.org/. Accessed October 8, 2015.
67. Huntjens KM, van Geel TA, Blonk MC, et al. Implementation of osteoporosis guidelines: a survey of five large fracture liaison services in the Netherlands. *Osteoporos Int*. 2011;22(7):2129-2135.
68. Cooper MS, Palmer AJ, Seibel MJ. Cost-effectiveness of the Concord Minimal Trauma Fracture Liaison service, a prospective, controlled fracture prevention study. *Osteoporos Int*. 2012;23(1):97-107.
69. Sander B, Elliot-Gibson V, Beaton DE, Bogoch ER, Maetzel A. A coordinator program in post-fracture osteoporosis management improves outcomes and saves costs. *J Bone Joint Surg Am*. 2008;90(6):1197-1205.
70. Greene D, Dell RM. Outcomes of an osteoporosis disease-management program managed by nurse practitioners. *J Am Acad Nurse Pract*. 2010;22(6):326-329.
71. Management of osteoporosis in postmenopausal women. 2010 position statement of The North American Menopause Society. *Menopause*. 2010;17(1):25-54.
72. Black DM, Reid IR, Boonen S, et al. The effect of 3 versus 6 years of zoledronic acid treatment of osteoporosis: a randomized extension to the HORIZON-Pivotal Fracture Trial (PFT). *J Bone Miner Res*. 2012;27(2):243-254.
73. Black DM, Schwartz AV, Ensrud KE, et al. Effects of continuing or stopping alendronate after 5 years of treatment: the Fracture Intervention Trial Long-term Extension (FLEX): a randomized trial. *JAMA*. 2006;296(24):2927-2938.
74. McClung M, Harris ST, Miller PD, et al. Bisphosphonate therapy for osteoporosis: benefits, risks, and drug holiday. *Am J Med*. 2013;126(1):13-20.
75. Knopp JA, Diner BM, Blitz M, Lyritis GP, Rowe BH. Calcitonin for treating acute pain of osteoporotic vertebral compression fractures: a systematic review of randomized, controlled trials. *Osteoporos Int*. 2005;16(10):1281-1290.
76. Nevitt MC, Chen P, Dore RK, et al. Reduced risk of back pain following teriparatide treatment: a meta-analysis. *Osteoporos Int*. 2006;17(2):273-280.
77. Stadhouder A, Buskens E, Vergroesen DA, Fidler MW, de Nies F, Oner FC. Nonoperative treatment of thoracic and lumbar spine fractures: a prospective randomized study of different treatment options. *J Orthop Trauma*. 2009;23(8):588-594.
78. Pfeifer M, Begerow B, Minne HW. Effects of a new spinal orthosis on posture, trunk strength, and quality of life in women with postmenopausal osteoporosis: a randomized trial. *Am J Phys Med Rehabil*. 2004;83(3):177-186.
79. Blasco J, Martinez-Ferrer A, Macho J, et al. Effect of vertebroplasty on pain relief, quality of life, and the incidence of new vertebral fractures: a 12-month randomized follow-up, controlled trial. *J Bone Miner Res*. 2012;27(5):1159-1166.
80. Mudano AS, Bian J, Cope JU, et al. Vertebroplasty and kyphoplasty are associated with an increased risk of secondary vertebral compression fractures: a population-based cohort study. *Osteoporos Int*. 2009;20(5):819-826.
81. National Institute for Health and Care Excellence. Percutaneous vertebroplasty and percutaneous balloon kyphoplasty for treating osteoporotic vertebral compression fractures. Available at: www.nice.org.uk/guidance/ta279. Accessed April 9, 2014.
82. Sinaki M, Itoi E, Wahner HW, et al. Stronger back muscles reduce the incidence of vertebral fractures: a prospective 10 year follow-up of postmenopausal women. *Bone*. 2002;30(6):836-841.
83. Harrison JE, Chow R, Dornan J, Goodwin S, Strauss A. Evaluation of a program for rehabilitation of osteoporotic patients (PRO): 4-year follow-up. The Bone and Mineral Group of the University of Toronto. *Osteoporos Int*. 1993;3(1):13-17.
84. Sinaki M. Exercise for patients with osteoporosis: management of vertebral compression fractures and trunk strengthening for fall prevention. *PM R*. 2012;4(11):882-888.
85. Sinaki M, Mikkelsen BA. Postmenopausal spinal osteoporosis: flexion versus extension exercises. *Arch Phys Med Rehabil*. 1984;65(10):593-596.
86. Chow R, Harrison J, Dornan J. Prevention and rehabilitation of osteoporosis program: exercise and osteoporosis. *Int J Rehabil Res*. 1989;12(1):49-56.
87. Sinaki M. Yoga spinal flexion positions and vertebral compression fracture in osteopenia or osteoporosis of spine: case series. *Pain Pract*. 2013;13(1):68-75.
88. Ekin JA, Sinaki M. Vertebral compression fractures sustained during golfing: report of three cases. *Mayo Clin Proc*. 1993;68(6):566-570.