Vertebral fracture assessment: Current research status and application in patients with kyphoplasty

Efstathios Drampalos, Konstantinos Nikolopoulos, Christos Baltas, Alexia Balanika, Antonis Galanos, Nikolaos Papaioannou, Spyros Pneumaticos

Abstract
Imaging of the spine is of paramount importance for the recognition of osteoporotic vertebral fractures (VFs), and standard radiography (SR) of the spine is the suggested diagnostic method but is not routinely used because of the cost and radiation exposure considerations. VF assessment (VFA) is an efficient, low radiation method for identifying VFs at the time of bone mineral density (BMD) measurement. Prediction models used to indicate the need for VFA may have little predictive power in subspecialty referral populations such as rheumatologic patients or patients who underwent kyphoplasty. Rheumatologic patients are frequently at increased risk for VFs, and VFA should be performed on an individual basis, also taking into account the guidelines for the general population. Kyphoplasty is a new minimally invasive procedure for the treatment of VFs and is being performed with increasing frequency. Following kyphoplasty, there may be a risk of new VFs in adjacent vertebrae. The assessment and follow-up of patients who underwent kyphoplasty requires repetitive X-ray imaging with the known limitations of SR. Thus, VFA may facilitate the evaluation of VFs in these patients because most of the kyphoplasty patients would fulfill the criteria. In a pilot study, we measured the BMD and performed VFA in 28 patients treated with kyphoplasty. Ratios of anterior to posterior (A/P) and middle to posterior (M/P) height were measured, and Genant’s method was used to classify vertebrae accordingly. Intraobserver and interobserver reliability for A/P, M/P and the Genant’s method were determined. Only 1 patient did not meet the criteria for VFA. Of the 364 available vertebrae, 295 could be analyzed. Most missing data (concerning 69 vertebrae) occurred in the upper thoracic region. Three of the 69 non-eligible vertebrae were lumbar vertebrae with cement leakage from the kyphoplasty procedure. In our hands, VFA was highly reproducible, demonstrating very good agreement in terms of intraobserver and interobserver reliability. Agreement was very good on
Vertebral fracture assessment (VFA) is an umbrella term for the evaluation of patients with vertebral deformities (VDs) and distinguish them from vertebral fractures (VFs) by the application of Genant’s method to determine a VF based on reductions of anterior (A) and middle height (M) relative to the posterior height (P) of the vertebra. For the radiographic detection, use of ambiguous terminology in the radiology report, or both. 

Despite all of these facts, in a multicenter, multinational prospective study (the IMPACT trial), under-diagnosis of VFs was observed in all geographic regions (false-negative rates: North America, 45.2%; Latin America, 46.5%; and Europe/South Africa/Australia, 29.5%) with a global false-positive rate of 5%. According to the same study, under-diagnosis of VFs is a worldwide problem attributable, in part, to a lack of radiographic detection, use of ambiguous terminology in the radiology report, or both.

Imaging of the spine is of paramount importance for the recognition of VFs. Standard radiography (SR) of the spine is the reference method for identifying VFs but is not used routinely because of the cost and radiation exposure considerations. Dual-energy X-ray absorptiometry (DXA) systems equipped with special software can be used for the detection of VFs obtaining lateral views of the thoracic and lumbar spine (Figure 1). Densitometric imaging of the spine allows VF analysis to be efficiently performed simultaneously, improving the overall assessment of an individual’s future fracture risk with a very low radiation dose (10 microsieverts vs 800 microsieverts for standard anteroposterior and lateral radiographs of the thoracic and lumbar spine). Although lateral imaging of the spine with the use of X-ray absorptiometry has been previously described with different terms from the manufacturers (lateral vertebral assessment, dual vertebral assessment and instant vertebral assessment), the ISCD 2005 Official Positions replaced these terms with the label "Vertebral Fracture Assessment" or VF assessment (VFA).

Furthermore, vertebrae with an appearance consistent with a prevalent fracture on VFA images or radiographs are often characterized as deformities, implying that some of the "deformities" identified may not really be VFs.

**METHODS FOR VFA**

There are several methods available to determine vertebral deformities (VDs) and distinguish them from vertebrae with a normal shape. The semi-quantitative technique developed by Genant et al. is one of the most common approaches. The qualitative feature of the vertebrae shape is considered together with the approximate loss of vertebral height. This method uses fixed values of loss of height (0.60, 0.75 and 0.80).

A plethora of quantitative morphometric methods of detecting VFs has also been described. That study determined a VF based on reductions of anterior (A) and middle height (M) relative to the posterior height (P) within the vertebra and/or on reductions of these heights relative to corresponding heights of adjacent vertebrae. Most studies also used appropriate population-based samples of men and women. McCloskey et al. developed a quantitative technique that takes into account the vertebral level, "vertebrae with kyphoplasty" level and "2 above and 1 below the kyphoplasty vertebrae" level. The application of Genant’s method to these patients also resulted in perfect agreement. We believe that the potential value of VFA in patients treated with kyphoplasty requires further evaluation, particularly comparing VFA with SR and performing a longitudinal follow-up. More research will help to adopt care processes that determine which patients require VFA and how often VFA should be performed, while also considering the impact of this technique on the cost of healthcare organizations.

**Key words:** Vertebral fracture assessment; Current research; Kyphoplasty; Guideline

© The Author(s) 2015. Published by Baishideng Publishing Group Inc. All rights reserved.

**Core tip:** Vertebral fracture assessment (VFA) is an efficient, low radiation method of identifying vertebral fractures at the time of bone mineral density measurement. Models used to indicate the need for VFA may have little predictive power in subgroups of the general population such as patients with kyphoplasty. In our hands, VFA applied in patients with kyphoplasty was highly reproducible, demonstrating very good agreement in terms of intraobserver and interobserver reliability. More research will help the adoption of care processes to determine when and how often VFA should be performed, considering also the impact of such cost on healthcare organizations.

Drampalos E, Nikolopoulos K, Baltas C, Balanika A, Galanos A, Papaioannou N, Pneumaticos S. Vertebral fracture assessment: Current research status and application in patients with kyphoplasty. World J Orthop 2015; 6(9): 680-687 Available from: URL: http://www.wjgnet.com/2218-5836/full/v6/i9/680.htm DOI: http://dx.doi.org/10.5312/wjo.v6.i9.680

**INTRODUCTION**

Vertebral fracture (VF) is the emblem of osteoporosis and is associated with increased mortality and morbidity. The clinical symptoms include pain (acute and chronic), impaired pulmonary function, thoracic kyphosis, height loss, depression and deterioration of quality of life. Thoracic and lumbar fractures are unique because most of the fractures do not present clinical symptoms at the time of their occurrence.

VFs commonly occur in postmenopausal women and older men, with an estimated prevalence of 10%-26% in both men and women age 50 and older, depending on the population and definition of VF utilized. Prevalent VFs anticipate new fractures independently of bone mineral density (BMD), as patients with one or more fractures have a 4-fold increased risk of subsequent hip fractures and a 5-fold increased risk of further VFs. Furthermore, VFs that do not come to medical attention seem to be associated with increased back pain and functional limitation.

Drampalos E et al. Current research in vertebral fracture assessment

Drampalos E, Nikolopoulos K, Baltas C, Balanika A, Galanos A, Papaioannou N, Pneumaticos S. Vertebral fracture assessment: Current research status and application in patients with kyphoplasty. World J Orthop 2015; 6(9): 680-687 Available from: URL: http://www.wjgnet.com/2218-5836/full/v6/i9/680.htm DOI: http://dx.doi.org/10.5312/wjo.v6.i9.680

**METHODS FOR VFA**

There are several methods available to determine vertebral deformities (VDs) and distinguish them from vertebrae with a normal shape. The semi-quantitative technique developed by Genant et al. is one of the most common approaches. The qualitative feature of the vertebrae shape is considered together with the approximate loss of vertebral height. This method uses fixed values of loss of height (0.60, 0.75 and 0.80).

A plethora of quantitative morphometric methods of detecting VFs has also been described. That study determined a VF based on reductions of anterior (A) and middle height (M) relative to the posterior height (P) within the vertebra and/or on reductions of these heights relative to corresponding heights of adjacent vertebrae. Most studies also used appropriate population-based samples of men and women. McCloskey et al. developed a quantitative technique that takes into account the vertebral level, "vertebrae with kyphoplasty" level and "2 above and 1 below the kyphoplasty vertebrae" level. The application of Genant’s method to these patients also resulted in perfect agreement. We believe that the potential value of VFA in patients treated with kyphoplasty requires further evaluation, particularly comparing VFA with SR and performing a longitudinal follow-up. More research will help to adopt care processes that determine when and how often VFA should be performed, while also considering the impact of this technique on the cost of healthcare organizations.
account the size of adjacent vertebrae into assessing VFs. Eastell et al.\textsuperscript{[14]} defined a fracture based on the deviation of the vertebral height of > 3 SD compared with a population-based sample. Melton et al.\textsuperscript{[15]} used the ratio of 0.85 for the definition of VFs, with the vertebral dimensions being adjusted for the specific level. Ross et al.\textsuperscript{[16]} developed a method that uses Z-scores to identify VFs. A modified approach to visual diagnosis of VFs, known as the algorithm-based qualitative method (ABQ), was proposed by Jiang et al.\textsuperscript{[17]}. This technique focuses on the appearance of the central vertebral endplate to identify VFs without a minimum threshold of vertebral height reduction.

When used for VFA images, the Genant's method, quantitative morphometry and the most recent ABQ method result in good intraobserver and interobserver reliability, approximating that of SR.\textsuperscript{[18-20]} In a multicenter study, including 203 postmenopausal women with imaging of their spine by both DXA and SR that were independently evaluated by three experienced radiologists on two different occasions, there was good agreement with kappa values ranging from 0.64 to 0.77.\textsuperscript{[21]} Furthermore, VFA has been shown to be both sensitive and specific in several studies. In 205 women age 65 and older undergoing bone densitometry for BMD measurement, VFA compared to SR was 87%-93% sensitive and 93%-95% specific.\textsuperscript{[18]} In another study including 80 postmenopausal women, clinicians utilizing VFA with a Genant semi-quantitative method identified the vast majority of grade 2 or 3 VFs and normal vertebral bodies (with a false negative rate of 6%) but only identified 50% of grade 1 fractures.\textsuperscript{[22]}

VFA has also a good negative predictive value (NPV) that reaches even 95% in some studies.\textsuperscript{[23]} However, visualization of the upper thoracic spine is of poorer quality for VFA compared to SR, and most of the studies have noted a larger percentage of vertebral bodies that are not visualized clearly with VFA.\textsuperscript{[24]} Non-eligible vertebrae are particularly common superior to the 7th thoracic vertebra (T7) but there are relatively few osteoporotic VFs above T7.

**INDICATIONS FOR VFA**

According to the 2007 Official Positions of the International Society for Clinical Densitometry (ISCD), the candidate indications for VFA were established on the basis that documentation of a prevalent VF may alter treatment of that individual and that there is a reasonable pre-test probability that a prevalent VF is found on VFA.\textsuperscript{[11]} SR following VFA should be performed when grade 2 or milder VFs are present without more severe VFs, VDs are present in patients with a known history of malignancy and when VDs cannot be assigned to benign causes.\textsuperscript{[11]}

The 2013 updated positions of the ISCD simplified the indications, and spine imaging with VFA or SR is recommended when the T-score is less than -1.0 and if one or more of the following factors are present:\textsuperscript{[25]}

(1) Women age > 70 years or men age > 80 years;
(2) Historical height loss > 4 cm (> 1.5 in.);
(3) Self-reported but undocumented prior vertebral fracture;
and (4) Glucocorticoid therapy equivalent to > 5 mg of prednisolone or equivalent per day for > 3 mo.

One of the aims of this study was to develop a regression-based prediction model to be integrated into the densitometric software so that bone technicians can proceed to a VFA in addition to the standard bone density measurement if the likelihood of prevalent VF is > 10%.\textsuperscript{[25]} In fact, Schousboe et al.\textsuperscript{[11]} developed an algorithm to be used by technologists to identify patients for whom VFA should be performed, simplifying the criteria from the ISCD 2007 position statement (T-score < -1.5 or worse and one of the following factors: age 65 years or older, historical height loss > 1.5 in, or systemic glucocorticoid therapy at the time of their DXA test). They concluded that such use can be feasible in clinical practice and that documentation of VFs increased the prescription of fracture prevention medication.\textsuperscript{[26]} However, there are no recommendations about the role of VFA in detecting incident fractures in patients receiving osteoporosis treatment or the interval between consecutive VFAs.

**VFA IN SUBSPECIALTY REFERRAL POPULATIONS**

Models used to form indications for VFA have been developed in general populations and may have little predictive power in special populations such as patients with ankylosing spondylitis (AS), rheumatoid arthritis (RA) or inflammatory bowel disease.

In rheumatology practice VFA has been shown to be useful for revealing VFs.\textsuperscript{[27]} Patients with AS or RA are at increased risk for VFs compared to the general population.\textsuperscript{[28-29]} Known risk factors include age, low BMD, use of glucocorticoids, disease duration and high levels of disease activity.\textsuperscript{[28-33]}
Mohammad et al. performed VFA scans in a cohort of 603 patients with RA of age > 40 years. For the entire cohort, 13% (77/603) of patients had one or more vertebral deformities identified on VFA imaging: 58% of these patients were female with a mean age of 56 years. The prevalence of osteoporosis and osteopenia was 59% and 40%, respectively, with the prevalence and severity of VFs showing significant correlation with spine T-scores and femoral T-scores. In multivariable analyses VFs were significantly and independently associated with a longer duration of RA, markers of disease activity and severity.

In one of the recent studies on the role of VFA in RA, 100 women underwent lateral imaging of the thoracolumbar spine by SR and VFA. All patients with a history of previous VF (n = 13) were visualized with VFA. The sensitivity, positive predictive value, specificity and NPV of VFA compared to SR were 57.3%, 30.9%, 89.1% and 96.1%, respectively, for the total vertebrae.

There is less research conducted with regards to VFA in patients with AS. As in rheumatoid arthritis, VFA needs to be validated. Vosse et al. compared VFA with SR in 30 patients with AS. Although the agreement between methods in measuring vertebral wedging [expressed as (mean) A/P ratio] was good, agreement between methods in assessing whether there is a fracture was insufficient. However, as the NPV was high (97%), VFA could be of clinical value to select patients for further evaluation by SR.

According to the 2013 official positions of ISCD, VFA for these subsets populations should be performed on an individual basis taking also in account the guidelines for the general population. On 2012, the French Society for Rheumatology and the Osteoporosis Research and Information Group updated their recommendations for the pharmacological treatment of post-menopausal osteoporosis and suggested the same indications for VFA as recommended by the ISCD.

Finally, the 2010 American College of Rheumatology recommendations for the prevention and treatment of glucocorticoid-induced osteoporosis suggest considering lateral imaging of the spine with SR or VFA for patients starting or currently receiving prednisolone > 5 mg/d.

APPLICATION OF VFA IN PATIENTS TREATED WITH KYPHOPLASTY

Kypohoplasty is new minimal invasive procedure for the treatment of osteoporotic VFs and is being performed with increasing frequency. The technique was developed to provide relief to patients with painful VFs and entails inflation of a percutaneously delivered balloon in the vertebral body, followed by the percutaneous injection of bone cement into the cavity created by the balloon. Chemotoxicity, thermal necrosis during exothermic polymerization, and mechanical stability provided by the cured bone cement are the most likely mechanisms for pain relief in kypohoplasty.

Through the use of a balloon, kypohoplasty is intended to provide restoration of vertebral body height. Based on current evidence, kypohoplasty does not restore substantial vertebral body height in most patients, and the intrinsic value of vertebral body height restoration remains speculative. Patients treated with kypohoplasty are generally quite satisfied with their pain relief and rarely express disappointment in a lack of height restoration.

There may be an additional risk of new VFs developing in adjacent vertebrae subsequent to kypohoplasty. Because new VFs can occur in osteoporotic patients simply due to disease progression rather than as a result of the kypohoplasty, it is difficult to determine the added risk of fracture resulting from this procedure.

The assessment and follow-up of patients who underwent kypohoplasty requires repetitive X-ray imaging with the limitations of radiography in terms of radiation, cost, patient positioning and geometric distortion within vertebrae located above or below the central point of the beam (parallax effect because the endplates are projected obliquely, giving them an elliptical appearance). Thus, VFA is a technique that may facilitate the evaluation of VFs in these patients. In fact, patients treated with kypohoplasty frequently are: (1) Osteopenic or osteoporotic patients with a T-score less than -1.0 and need regular BMD measurements; (2) Women or men age > 70 or even 80; (3) Patients that present with height loss; (4) Patients that have a history of prior VF; or (5) Patients that have an additional risk for new VFs because of the natural course of the osteoporosis or of the kypohoplasty.

Furthermore, chronic rheumatologic patients under treatment with glucocorticoids have an increased risk for VFs and can be treated with kypohoplasty. Considering the above criteria, most of the kypohoplasty patients would fulfill the criteria for VFA according to the 2013 ISCD Official Position.

MATERIALS AND METHODS OF THE STUDY

Before any data collection, local ethics committee approval was obtained for the present cross sectional study.

Twenty-eight patients treated with kypohoplasty for acute symptomatic osteoporotic VFs were included. The patients were evaluated according to a standard protocol, which included measurement of BMD (of both nondominant hip and lumbar spine) and densitometric images of the spine with the patient in the lateral position using a Lunar Prodigy Advance densitometer (GE Healthcare Buckinghamshire, United Kingdom). For the calculation of the mean T-score, the least value between the lumbar spine and hip (femoral neck, or total proximal femur) was included for every patient. At the lumbar spine, at least 3 vertebrae (between L1 and L4) had to be evaluable, that is without kyphoplasty, for the T-score to be taken into consideration. For VFA images, the Lunar software of the densitometer was used to set.
markers on the vertebral margins by two observers (XM and ED), and anterior (A), middle (M) and posterior (P) heights together with their ratios were measured (Figure 2). VFs were assessed by calculating the A/P, M/P ratios.

To measure intraobserver reliability for A/P and M/P ratios, each observer read every densitometric image twice in a random order, evaluating vertebrae from T4 to L4. To assess interobserver reliability, VFA images were read independently from the two observers (XM and ED), who were blinded to each other’s assessment.

We estimated the intraobserver and interobserver reliability for A/P and M/P ratios using the intra-class correlation coefficient (ICC) on the “vertebral level” (n = 364), as well as on the “vertebrae with kyphoplasty” level (n = 49) and adjacent to the kyphoplasty vertebrae level (“2 above and 1 below the kyphoplasty vertebrae”, n = 82). Furthermore, following Genant’s method, we used the cut-off ratios of 0.60, 0.75 and 0.80 for the A/P ratio to categorize the vertebrae as grade 0 (non fracture), grade 1 (mild), grade 2 (moderate) and grade 3 (severe) fractures and calculated Cohen’s kappa value (κ) with quadratic weighting. The κ value was determined on a vertebral level with 95% confidence intervals. To interpret the level of agreement based upon Cohen’s κ results the Landis and Koch guidelines were followed.

Thus, a Cohen’s κ value greater than 0.81 was considered almost perfect agreement; between 0.8 and 0.61, substantial agreement; between 0.6 and 0.4, moderate agreement; between 0.4 and 0.2, fair agreement; between 0.2 and 0, slight agreement; and less than zero, poor agreement. All tests were two-sided and statistical significance was set at P < 0.05. All analyses were carried out using the computer software SPSS for Windows (IBM SPSS Statistics 21 NY, United States).

STUDY RESULTS

Ten patients were male, 18 patients were female and the mean age was 72.4 years (range, 54-84). Only 1 patient did not meet the 2013 ISCD criteria for VFA because of a T score > -1. The mean T-score was -2.28 (range, -4.1 to -0.8), and the mean height was 1.52 m (range, 1.38-1.71 m). Furthermore, the mean weight was 70 kg (range, 51-98 kg), the mean body mass index was 30 (range, 22-41) and the mean follow-up from the operation date was 34 mo (range, 14-60 mo).

Of the 364 available vertebrae, 295 could be analyzed. Most instances of missing data (concerning 69 vertebrae) occurred in the thoracic T4-T6 region and were equally distributed across the two readers. Three of the 69 non-eligible vertebrae were vertebrae that had been treated with kyphoplasty. Both of the readers characterized these vertebrae as non-eligible. These vertebrae were three lumbar vertebrae (one L1 and two L2) of three different patients and had the presence of cement leakage from the kyphoplasty in common.

Intraobserver agreement for A/P ratios was very good for both readers (XM and ED), with ICC = 0.98 (95%CI: 0.977-0.988) for XM and ICC = 0.96 (95%CI: 0.957-0.973) for ED. Intraobserver agreement for M/P ratios was also very good for both readers, with ICC = 0.977 (95%CI: 0.971-0.982) for XM and ICC = 0.945 (95%CI: 0.93-0.956) for ED. Interobserver reliability (first assessments of the two readers were compared) for A/P and M/P ratios, the results were again very good, with ICC = 0.951 (95%CI: 0.938-0.961) for A/P and ICC = 0.947 (95%CI: 0.933-0.958) for M/P.
Agreements on the “vertebrae with kyphoplasty” level and on the “2 above and 1 below the kyphoplasty vertebrae”, were also very good. There was very good interobserver reliability for the A/P ratio on the “vertebrae with kyphoplasty” level with ICC = 0.94 (95%CI: 0.894-0.966) and for the A/P ratio on the “2 above and 1 below the kyphoplasty vertebrae” level with ICC = 0.969 (95%CI: 0.951-0.98).

With regards to Genant’s method, after using the cut-off ratios of 0.60, 0.75 and 0.80 for A/P ratio and classifying the vertebrae, interobserver agreement was almost perfect calculating a κ value with Quadratic Weighting = 0.833 (95%CI: 0.82-0.95). Furthermore, using Genant’s method and taking in account the first observer’s measurements (XM), 15 VFs were found on the “2 above and 1 below the kyphoplasty vertebrae” level. More specifically, there were nine VFs on the adjacent-superior to the kyphoplasty vertebrae, one VF on the adjacent-inferior to the kyphoplasty vertebrae and five VFs were identified in two vertebrae above the kyphoplasty. Eleven of these 15 VFs were at the thoracolumbar junction (T12-L1), three were on T11 and one was on T9. Seven more VFs were found on the rest of those not adjacent to the kyphoplasty vertebrae.

**DISCUSSION**

In our hands, VFA was highly reproducible when applied to patients treated with kyphoplasty, demonstrating very good agreement in terms of intraobserver and interobserver reliability. Agreement was very good on the vertebral level, “vertebrae with kyphoplasty” level and “2 above and 1 below the kyphoplasty vertebrae” level. Application of Genant’s method on these patients also resulted in perfect agreement.

With regards to the patient who did not meet the criteria for VFA, the lowest T-score = -0.9 of the hip was considered. She was a woman aged 68 years with two kyphoplasty vertebrae (T11 and T12). Being under treatment with intravenous zoledronic acid for the last two years, post-kyphoplasty may have improved her BMD. The 69 individual non-eligible vertebra (most of them in the thoracic T4-T6 region) were in concordance also with studies where VFA was applied in general population groups or in subgroups such as patients with ankylosing spondylitis. Three of the 69 non-eligible vertebrae were kyphoplasty vertebrae in 3 patients presenting cement leakage (Figure 3). In fact, cement extravasation alters vertebral shape, and as a result, it is extremely difficult for the reader to assess the vertebra.

It is still a matter of debate as to whether vertebrae neighboring the kyphoplasty are more likely to fracture. According to our database, most of the fractures on the vertebra without kyphoplasty were on the “2 above and 1 below the kyphoplasty vertebrae” level (15 VFs), but we have no data on whether these were new fractures or present before the kyphoplasty.

We believe that the potential value of VFA in patients treated with kyphoplasty needs further evaluation, in particular, evaluations comparing VFA with SR and including longitudinal follow-up. Although we did not perform longitudinal VFA assessments, VFA has the potential to be a very useful test for longitudinal follow-up. Our pilot study demonstrated that VFA could be a valuable technique in terms of intraobserver and interobserver reliability for the determination of the height ratios of the vertebrae or using Genant’s method. A larger study, comparing the agreement between VFA and SR in patients who underwent kyphoplasty is currently underway. Moreover, considering the guidelines for monitoring BMD in populations at high risk for VFs, patients who underwent kyphoplasty should have their DXA measurement regularly at least every 1 or 2 years. In an era in which all dimensions of pathology should be accounted for, serial BMD testing and VFA should probably be part of routine practice in this at-risk population, and having a single exam that entails minimal irradiation and allows for the assessment of major structural changes certainly warrants further systematic evaluation.

Overall, assessing structural damage is essential in patients treated with kyphoplasty and has key implications for treatment outcomes. SR remains the gold standard to evaluate the spines of these patients, despite all its disadvantages and limitations. Our study demonstrates a potential for VFA in these patients. The technique of VFA is much less irradiating than standard radiographs, easily available during the BMD determination and inexpensive in the modern era of economic crisis.

**CONCLUSION**

Future research is needed to determine if other predictors can be established that may improve the efficiency of lateral spine imaging to identify those with
clinically unrecognized VFs. Because models used to form general indications for VFA may have little predictive power in subsets of populations, such as patients with RA or kyphoplasty power, further studies are needed on new care processes within healthcare systems to identify those who should have VFA. Furthermore, although VFA has the potential to be a very useful test for longitudinal follow-up; there are currently no recommendations on how often the assessment should be repeated. It is important to also mention that, according to evidence, VFA studies revealing a VF do affect patient’s and physician’s fracture prevention behavior. In conclusion, more research will help the adoption of care processes to determine which patients require VFA and how often VFA should be performed, while also considering the impact of such cost on healthcare organizations.

REFERENCES

1. Cummings SR, Melton LJ. Epidemiology and outcomes of osteoporotic fractures. *Lancet* 2002; 359: 1761-1767 [PMID: 12049882 DOI: 10.1016/S0140-6736(02)08657-9]

2. Fiak HA, Milavetz DL, Palermo L, Nevitt MC, Cauley JA, Genant HK, Black DM, Ensrud KE. What proportion of incident radiographic vertebral deformities is clinically diagnosed and vice versa? *J Bone Miner Res* 2005; 20: 1216-1222 [PMID: 15940375 DOI: 10.1359/JBMR.050314]

3. Melton LJ, Lane AW, Cooper C, Eastell R, O’Fallon WM, Riggs BL. Prevalence and incidence of vertebral deformities. *Osteoporosis Int* 1993; 3: 113-119 [PMID: 8481586 DOI: 10.1007/BF01623271]

4. Bouxsein ML, Melton LJ, Riggs BL, Muller J, Atkinson EJ, Oberg AL, Robb RA, Camp JJ, Rouleau PA, McCollough CH, Khosla S. Age-specific differences in the factor of risk for vertebral fracture: a population-based study using QCT. *J Bone Miner Res* 2006; 21: 1475-1482 [PMID: 16939406 DOI: 10.1359/jbmr.060606]

5. Jinbayashi H, Aoyagi K, Ross PD, Ito M, Shindo H, Takemoto N, Drampalos E, Genant HK, Wu CY, van Kuijk C, Nevitt MC. Vertebral fracture assessment: the 2007 ISCD Official Positions.

6. Aoyagi K, Ross PD, Ito M, Shindo H, Takemoto N, Drampalos E, Genant HK, Wu CY, van Kuijk C, Nevitt MC. Vertebral fracture assessment using a semiquantitative technique. *J Bone Miner Res* 2008; 13: 1137-1148 [PMID: 18237484]

7. McCloskey EV, Spector TD, Eyres KS, Fern ED, O’Rourke N, Vaskaran S, Canis JA. The assessment of vertebral deformity: a method for use in population studies and clinical trials. *Osteoporos Int* 1993; 3: 138-147 [PMID: 8481590 DOI: 10.1007/BF01623275]

8. Eastell R, Cedel SL, Wahner HW, Riggs BL, Melton LJ. Classification of vertebral fractures. *J Bone Miner Res* 1991; 6: 207-215 [PMID: 2035348 DOI: 10.1002/jbmr.560090207]

9. Melton LJ, Kan SH, Frye MA, Wahner HW, O’Fallon WM, Riggs BL. Epidemiology of vertebral fractures in women. *Am J Epidemiol* 1989; 129: 1009-1011 [PMID: 2784934]

10. Ross PD, Yhee VK, He YF, Davis JW, Kamimoto C, Epstein RS, Wasnich RD. A new method for vertebral fracture diagnosis. *J Bone Miner Res* 1993; 8: 167-174 [PMID: 8442434 DOI: 10.1002/jbmr.5605080207]

11. Jiang G, Eastell R, Barrington NA, Ferrar L. Comparison of methods for the visual identification of prevalent vertebral fracture in osteoporosis. *Osteoporos Int* 2004; 15: 887-896 [PMID: 15071725 DOI: 10.1007/5400198-004-1626-1]

12. Schousboe JT, Debold CR. Reliability and accuracy of vertebral fracture assessment with densitometry compared to radiography in clinical practice. *Osteoporos Int* 2006; 17: 281-289 [PMID: 16172798]

13. Rea JA, Chen MB, Li J, Marsh E, Fan B, Blake GM, Steiger P, Smith IG, Genant HK, Fogelman I. Vertebral morphometry: a comparison of long-term precision of morphometric X-ray absorptiometry and morphometric radiography in normal and osteoporotic subjects. *Osteoporos Int* 2001; 12: 158-166 [PMID: 11303717 DOI: 10.1007/s001980170149]

14. Pavlov I, Gamble GD, Reid IR. Comparison of dual-energy X-ray absorptiometry and conventional radiography for the detection of vertebral fractures. *J Clin Densitom* 2005; 8: 379-385 [PMID: 16311421]

15. Fuerst T, Wu C, Genant HK, von Ingersleben G, Chen Y, Johnston C, Econs MJ, Binkley N, Vokes TJ, Crans G, Mitlak BH. Evaluation of vertebral fracture assessment by dual X-ray absorptiometry in a multicenter setting. *Osteoporos Int* 2009; 20: 1199-1205 [PMID: 19038074 DOI: 10.1007/s00198-008-0806-9]

16. Binkley N, Krueger D, Gangnon R, Genant HK, Dreznner MK. Lateral vertebral assessment: a valuable technique to detect clinically significant vertebral fractures. *Osteoporosis Int* 2005; 16: 1513-1518 [PMID: 15834512 DOI: 10.1007/s00198-005-1891-7]

17. Damiano J, Kolta S, Porcher R, Tournoux C, Dougdos M, Roux C. Diagnosis of vertebral fractures by vertebral fracture assessment. *J Clin Densitom* 2006; 9: 66-71 [PMID: 16731433 DOI: 10.1016/j.jcdr.2005.11.002]

18. Rea JA, Steiger P, Blake GM, Fogelman I. Optimizing data analysis and acquisition of morphometric X-ray absorptiometry. *Osteoporos Int* 1998; 8: 177-183 [PMID: 9666943 DOI: 10.1007/BF02872516]

19. Rosen HN, Vokes TJ, Malahanan AO, Deal CL, Aleje JD, Olenfgangski TP, Schousboe JT. The Official Positions of the International Society for Clinical Densitometry: vertebral fracture assessment study. *J Clin Densitom* 2013; 16: 482-488 [PMID: 24063846 DOI: 10.1016/j.jcdr.2013.08.003]

20. 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: 965-972 [PMID: 24121999 DOI: 10.1007/s00198-013-2519-9]

21. Ghazi M, Kolta S, Briot K, Fichtenbaum J, Paternotte S, Roux C. Prevalence of vertebral fractures in patients with rheumatoid arthritis: revisiting the role of glucocorticoids. *Osteoporos Int* 2012; 23: 581-587 [PMID: 21350894 DOI: 10.1007/s00198-011-1584-3]

22. van Staa TP, Geusens P, Bijlsma JW, Leufkens HG, Cooper C. Clinical assessment of the long-term risk of fracture in patients with rheumatoid arthritis. *Arthritis Rheum* 2006; 54: 3104-3112 [PMID: 17009229]

23. Prieto-Alhambra D, Muñoz-Ortega J, De Vries F, Visse D, Arden NK, Bouxess P, Cooper C, Diaz-Perez A, Vostergaard P. Anklyosing spondylitis confers substantially increased risk of clinical spine
fractures: a nationwide case-control study. Osteoporos Int 2015; 26: 85-91 [PMID: 25341971 DOI: 10.1007/s00198-014-2939-3]

30 Ghoozani I, Ghazi M, Nouajai A, Mounach A, Rezaei A, Achemlal L, Bezza A, El Maghraoui A. Prevalence and risk factors of osteoporosis and vertebral fractures in patients with ankylosing spondylitis. Bone 2009; 44: 772-776 [PMID: 19442629 DOI: 10.1016/j.bone.2008.12.028]

31 Mohammad A, Lohan D, Bergin D, Mooney S, Newell J, O’Donnell M, Coughlan RJ, Carey JJ. The prevalence of vertebral fracture on vertebral fracture assessment imaging in a large cohort of patients with rheumatoid arthritis. Rheumatology (Oxford) 2014; 53: 821-827 [PMID: 24249032 DOI: 10.1093-rheumatology/kct553]

32 Orstavik RE, Haugeberg G, Uhlig T, Mowinckel P, Falch JA, Halse JI, Kvien TK. Incidence of vertebral deformities in 255 female rheumatoid arthritis patients measured by morphometric X-ray absorptiometry. Osteoporos Int 2005; 16: 35-42 [PMID: 15197538]

33 Lodder MC, Haugeberg G, Lems WF, Uhlig T, Orstavik RE, Kostense PJ, Dijkmans BA, Kvien TK, Woolf AD. Radiographic damage associated with low bone mineral density and vertebral deformities in rheumatoid arthritis: the Oslo–Truro–Amsterdam (OSTRA) collaborative study. Arthritis Rheum 2003; 49: 209-215 [PMID: 12687512 DOI: 10.1002/art.10996]

34 Lee JH, Cho SK, Han M, Lee S, Kim JY, Ryu JA, Choi YY, Bae SC, Sung YK. Validity and role of vertebral fracture assessment in detecting vertebral fracture in patients with rheumatoid arthritis. Joint Bone Spine 2014; 81: 149-153 [PMID: 23932727 DOI: 10.1016/j.jbspin.2013.07.003]

35 Vosse D, Heijckmann C, Landewé R, van der Heijde D, van der Linden S, Geusens P. Comparing morphometric X-ray absorptionmetry and radiography in defining vertebral wedge fractures in patients with ankylosing spondylitis. Rheumatology (Oxford) 2007; 46: 1667-1671 [PMID: 17804453 DOI: 10.1093/rheumatology/kem113]

36 Briot K, Cortet B, Thomas T, Audran M, Blain H, Breuil V, Chapuis L, Chapurlat R, Fardellone P, Feron JM, Gauvain JB, Guggenbuhl P, Trémiot A, Ruel C. 2012 update of French guidelines for the pharmaceutical treatment of postmenopausal osteoporosis. Joint Bone Spine 2012; 79: 304-313 [PMID: 22521109 DOI: 10.1016/j.jbspin.2012.02.014]

37 Grossman JM, Gordon R, Ranganath VK, Deal C, Caplan L, Chen W, Curtis JR, Furst DE, McMahon M, Patkar NM, Volkman E, Saag KG. American College of Rheumatology 2010 recommendations for the prevention and treatment of glucocorticoid-induced osteoporosis. Arthritis Care Res (Hoboken) 2010; 62: 1515-1526 [PMID: 20662044 DOI: 10.1002/acr.20295]

38 Lieberman IH, Dudénys S, Reinhardt MK, Bell G. Initial outcome and efficacy of “kyphoplasty” in the treatment of painful osteoporotic vertebral compression fractures. Spine (Phila Pa 1976) 2001; 26: 1631-1638 [PMID: 11464159]

39 McGraw JK, Lippert JA, Minkus KD, Rami PM, Davis TM, Budzik RF. Prospective evaluation of pain relief in 100 patients undergoing percutaneous vertebroplasty: results and follow-up. J Vasc Interv Radiol 2002; 13: 883-886 [PMID: 12354821 DOI: 10.1016/S1051-0443(07)61770-9]

40 McKiernan F, Faciszewski T, Jensen R. Reporting height restoration in vertebral compression fractures. Spine (Phila Pa 1976) 2003; 28: 2517-2521; discussion 3 [PMID: 14624087 DOI: 10.1097/01.BRS.0000092424.29886.C9]

41 Cloft HJ, Jensen ME. Kyphoplasty: an assessment of a new technology. AJNR Am J Neuroradiol 2007; 28: 200-203 [PMID: 17296979]

42 Berlemann U, Ferguson SJ, Nolte LP, Hein P. Adjacent vertebral failure after vertebroplasty. A biomechanical investigation. J Bone Joint Surg Br 2002; 84: 748-752 [PMID: 12188498 DOI: 10.1302/0301-620X.84B5.11841]

43 Banks L, van Kuijk C, Genant H. Radiographic technique for assessing osteoporotic vertebral deformity. In: Genant H, Jergas M, van Kuijk C (eds.) Vertebral fracture in osteoporosis. USA: Radiology Research and Education Foundation, San Francisco, CA, 1995: 131-147

44 van Bodegom JW, Kuiper JW, van Rijn RR, van Kuijk C, Zwamborn AW, Grashuis JL. Vertebral dimensions: influence of X-ray technique and patient size on measurements. Calcif Tissue Int 1998; 62: 214-218 [PMID: 9501954 DOI: 10.1007/s002239900420]

45 Landis JR, Koch GG. The measurement of observer agreement for categorical data. Biometrics 1977; 33: 159-174

46 Schouboe JT, Shepherd JA, Bilezikian JP, Bain S. Executive summary of the 2013 International Society for Clinical Densitometry Position Development Conference on bone densitometry. J Clin Densitom 2013; 16: 455-466 [PMID: 24183638 DOI: 10.1016/j.jocd.2013.08.004]

47 Schouboe JT, Davison ML, Dowd B, Thiede Call K, Johnson P, Kane RL. Predictors of patients’ perceived need for medication to prevent fracture. Med Care 2011; 49: 273-280 [PMID: 21224740 DOI: 10.1097/MLR.0b013e318202915c]

48 Schouboe JT, McKiernan FE, Binkley N. A performance algorithm improves appropriate vertebral fracture assessment use among those referred for DXA and improves utilization of fracture prevention medication for those with prevalent vertebral fracture. J Bone Miner Res 2011; 27 (1Suppl)

P- Reviewer: Rodlinghoff M, Vokes T  S- Editor: Ji FF  L- Editor: A  E- Editor: Liu SQ
