Early diagnosis of vertebral fractures

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Summary

Vertebral fractures are a common clinical entity, caused by trauma or related to osteoporosis (benign). Their recognition is especially important in the post-menopausal female population but also important is their differentiation from pathological (malignant) fractures (1). A vertebral fracture is evidenced by vertebral body deformity or reduction in vertebral body height beyond a certain threshold value in the absence of bone discontinuity. For prognosis and treatment it is extremely important to recognize the cause of the fracture. In contrast to fractures that occur in other locations, vertebral fractures often go unrecognized in the acute phase as the pain may be transient and radiographic and evaluation of the spine may be difficult (2).
Objective measurement of the vertebral deformity provides invaluable information to the interpreting physician and helps grade fracture severity. The recognition and diagnosis of vertebral fractures can be performed using additional diagnostic tools.

KEY WORDS: vertebral fractures; plain radiographs; vertebral morphometry; bone densitometry.

Role of imaging

The role of imaging is to make the diagnosis as early as possible in order to initiate treatment and prophylactically prevent further fractures and complications. This requires quantitative and qualitative evaluation of bone tissue. From a qualitative point of view it is possible to identify vertebral and appendicular fractures by following their time course and natural history. Quantitatively: those patients who are at increased risk of fracture can be assessed with good accuracy and precision using bone density/DEXA (3).

Conventional radiography

Conventional radiology is the most frequently used modality to assess the bone. However, this method is able to detect demineralization only when there is significant bone loss (approximately 30%) (4).The signs of osteoporosis described on conventional radiology, are the rarefaction of trabecular bone with a consequent increase radiolucency and thinning of cortical bone with a relative increase in the diameter of the medullary space.
The radiographic characteristics are: reduced density in the vertebral body due to a decrease in the horizontal trabecular bone and apparent increased density/sclerosis of the peripheral margins resulting in the appearance of the an "empty box" as well as the presence of one or more vertebral fractures (5).
A vertebral fracture is defined when there is a loss of height greater than 4 mm (6). The vertebral body deformity may include: "wedge fractures" when the anterior height of the vertebral body is less than posterior, "biconcave or lens fractures" when the central height of the vertebral body is lower than the anterior and posterior, "crush fractures" when the entire vertebral body height is reduced compared to the adjacent vertebrae.
To better assess the alterations of the spine detectable on conventional radiology has been proposed the index of Saville (7); however, this index has not been widely accepted because results are highly subjective. The current classification used for vertebral fractures is that described by Genant, where a semiquantitative evaluation of spine radiographs results in four grades. Grade 0: normal vertebra, Grade 1: mild fracture (reduction in height of 20-25% and 10-20% reduction in surface area than the adjacent normal vertebra), Grade 2: moderate fracture (reduction in height of 25-40% and reduction of 20-40% of the surface area), Grade 3: severe fracture (reduction in height and surface area greater than 40%) (8).
When it is used by trained and experienced observers, this semiquantitative method is considered the gold standard for the assessment of vertebral fractures and is currently the most common method used in multicenter clinical trials.

Techniques of bone densitometry

The diagnosis of osteoporotic fractures has been revolutionized by the introduction of bone densitometry into clinical practice. These techniques allow accurate and precise measurement of bone mineral density at various skeletal sites and have also allowed, in recent years, the assessment of bone mass at various ages, enabling the understanding of the relationship between bone density and fracture risk.
The techniques include: DXA bone densitometry (dual X-ray densitometry energy), QCT (Quantitative Computed Tomography) for

the axial and appendicular skeleton and QUS (Quantitative Ultrasound Bone) for the appendicular skeleton. All densitometric techniques have their advantages and limitations.

The densitometric technique we are most familiar with and most widely used in clinical practice is the DXA at the lumbar spine (L1-L4) and femoral neck.

DXA has the advantage of providing a low radiation dose to the patient and allows a rapid examination at low costs, but it is not able to discriminate cortical from trabecular bone. In addition, DXA is the only modality that can be used for the Assessment of Fracture Risk or FRAX (Fracture Risk Assessment Tool). FRAX allows an assessment of absolute fracture risk in 10 years and is now considered the screening tool of choice in order to initiate pharmacological therapy and allow prevention of initial or first fracture from osteoporosis.

The FRAX tool provides an estimate of fracture risk on the basis of: BMD at the femoral neck, the patient's age, sex, height, weight, presence of previous fractures, parents with hip fractures, smoking habit, use of glucocorticoids, rheumatoid arthritis, secondary osteoporosis and daily ingestion of large quantities of alcohol.

DXA provides a density in g/cm^2 "aerial" and is therefore dependent on the size of region analyzed and this creates problems for the pediatric population and in patients with short stature (9). QCT overcomes these problems by providing a volumetric measurement of the mineral density in mg/cm^3 and allows us to separately measure trabecular and cortical bone (10). Since trabecular bone is approximately 8 times more sensitive to metabolic stimulation compared to the cortical bone, QCT is more sensitive in detecting minimal changes of bone density.

Axial Quantitative Computed Tomography (aQCT) and peripheral Quantitative Computed Tomography (pQCT) are currently the only non-invasive techniques that measures true bone density within a certain volume in mg /cm^3. Unlike other methods, such as DXA, QCT is not affected by the super- imposition of other tissues (not bone) present in a given area of the body. Because QCT is also used to measure trabecular bone density it shows a high sensitivity for the measurement of osteopenia correlated with age after menopause where trabecular vertebral bone turnover is greater than that of the surrounding bone cortical.

Due to its three-dimensional spatial resolution, QCT measures the volumetric density and the micro-architecture of the segment examined, allowing a separate evaluation of bone density and the geometry of the bone. This allows evaluation of the changes associated with progression of osteoporosis and response to drug therapy. This selective evaluation also makes this method sensitive for the assessment of changes during short term follow-up. However QCT also presents a number of disadvantages compared to DXA: high radiation dose delivered to the patient, high cost, is operator dependent and requires considerable space as well as access to the scanner but more importantly is the disadvantage of limited accuracy and lower precision compared to measurements obtained with DXA. This error is related to the presence of adipose tissue in the vertebral body and causes an underestimation of bone mass. This error is not only limited to QCT but also to the use of dual-energy CT, which results in an even greater dose to the patient. Peripheral quantitative CT (pQCT) has been developed to overcome some of the limitations of DXA and aQCT. It allows separate assessments of cortical and trabecular bone and provides direct information on the geometry of the bone in the appendicular skeleton at different locations. QCT is used for the quantitative evaluation of bone structure and bone marrow composition in order to analyze trabecular architecture and its' biomechanical properties in the prediction of the fracture risk's (11).

Magnetic Resonance Imaging (MRI) is the most sensitive and specific technique in the assessment of vertebral fractures. A recent fracture typically shows a band of bone marrow edema adjacent to the end-plate. It is used for the qualitative evaluation of bone structure and provides non invasive evaluation of the entire musculoskeletal system.

Quantitative Bone Ultrasonography (QUS) is a technique where ultrasound pulses are transmitted (transversely or longitudinally) through the bone in question and by measuring the speed of the ultrasound pulse as well as the variations of the ultrasonic wave, it allows evaluation of the mechanical strength of bone. QUS is advantageous for its small size, portability, low cost and absence of ionizing radiation. QUS is performed on the calcaneus and phalanges of the hand. For this reason it is not used for evaluation of early vertebral fractures.

This technique, however, is useful in the diagnosis of osteoporosis and has been extensively studied. Clinical results have proven to be effective in the evaluation of osteoporosis fracture risk. Its' performance has been similar to those obtained with conventional densitometric techniques (DXA, QCT) and it has also been suggested that the combination of results obtained by different methods (QUS, DXA, QCT) would improve fracture risk prediction, though there are discordant results in literature (12). Several studies have also demonstrated the efficacy of QUS as a first level screening tool for identification of postmenopausal women at higher risk of osteoporosis fractures. QUS is a versatile and harmless tool; for this reason it has been introduced in several clinical fields. Evaluation of bone tissue by QUS is often suggested in high risk patients in order to verify a decrease in bone mass and/or architectural deterioration with an increase in fracture risk.

Vertebral morphometry is defined as the technique used to measure anterior, central and posterior vertebral height for the quantitative identification of vertebral fractures. It can be performed on images obtained with conventional X-ray equipment: radiographic morphometry (MRX: morphometric X-ray radiography) or those obtained by DXA: absorbimetric morphometry (MXA: morphometric X-ray absorptiometry). Vertebral morphometry is used in epidemiological studies to identify the prevalence and incidence of vertebral fractures from osteoporosis. These studies have demonstrated the value in having a method to provide quantitative and easily reproducible measurement for each vertebrae, overcoming the subjectivity of the qualitative assessment. The method requires digitization of standardized lateral conventional radiographs of the dorsal and lumbar spine. From standard lateral radiograph two accepted methods for objective measures have been described for the assessment of vertebral fractures. The measurement of vertebral heights can be obtained by measuring the vertebra that appear deformed with the aid of a special ruler and can be measured on high resolution work station from CT scan radiographs of the spine (13). Specific CT software allows first qualitative processing of the images which tends to enhance the visibility of the vertebral cortex thus facilitating subsequent placement with the mouse by the operator of the six landmarks at the 4 corners and midpoints of the upper and lower endplates (14). Manual positioning of the point of reference is the most delicate phase for the accuracy of morphometry and is done according to Hurxthal. This proposed method of measurement excludes the uncinate process along the posterior thoracic vertebra, Schmorl nodes and osteophytes from the overall vertebral height measurement. With careful review and assessment of all these signs, a definitive diagnosis of an osteoporotic fracture can be reached in most cases.

In Italy, a new software has been recently introduced for vertebral morphometry referred to as the Spine Analyzer (MorphoXpress, Procter & Gamble, Cincinnati, Ohio, USA). This software improves the analysis of radiographs of the lumbar spine. Spine-Analyzer software is an invaluable tool in the recognition of vertebral fractures and is well suited to a modern digital ima-

Figure 1 - Spine Analyzer tool: morphometric points are chosen and automatic assessment of the degree of deformity is performed highlighting deformities that exceed 20% (mild - yellow), 25% (moderate - orange), or 40% (severe - red), consistent with the criteria proposed by Genant.

ging department. The current version of the Spine-Analyzer software allows easy identification of normal vertebrae and those that have a slight deformity. It also highlights those with severe fractures. These features are very important as it is often difficult to recognize a normal vertebra from another, especially when there is only slight deformity (15).

Recognition of vertebral deformities is performed by the calculation of the relationship between the height of the vertebral body:

1. Wedge deformity (reduction of the ratio Ha/Hp);
2. Deformity biconcave lens (decrease in the ratio Hm/Hp);
3. Deformity crush (decrease of the ratio between back height or front, and front or back height of the vertebra over and/or below (Ha/Hp). Ha: is the anterior height, Hm: is the middle or central height and Hp: is the posterior height of the vertebrae from T4 to L4 (16).

The data obtained are compared with the data of a normal reference population included in the program, which thus identifies, based on the threshold of fracture chosen, which vertebrae are fractured (17,18). Then a combination of semi-quantitative view and morphometric quantitative methods may be the best approach for the definition of the fracture, as suggested by the National Osteoporosis Foundation and the International Osteoporosis Foundation (IOS) (Figure 1).

Conclusion

In reviewing the above techniques we recognized that QUS is of limited use for the diagnosis of early vertebral fractures. However the use of the other techniques are often complementary.

Vertebral deformities can be seen related to variable causes i.e.: osteoporosis, trauma, degenerative disease, Scheuermann's disease, congenital anomaly, neoplastic disease, and haematopoietic disorders, infectious disease and Paget's disease could all be a cause for vertebral deformity. The correct diagnosis however is only achievable when radiographs and other imaging modalities performed are carefully evaluated and integrated. Vertebral deformities can careful evaluation of the radiographs and other imaging modalities are integrated (19,20). Quantitative morphometry is unable to distinguish osteoporotic vertebral fractures from vertebral deformities from other causes such as degenerative spine and disc disease.

This limitation is characteristic to any method of quantitative morphometry while the limited spatial resolution of the DXA images in MXA may increase this problem (21). However given the superior image quality of MRX it has the potential for improved qualitative evaluation of the radiographs in order to help differentiate the possibilities or make a confirmed diagnosis. In fact, although it is recognized that visual interpretation of radiographs is subjective, it is also true that an expert eye can better distinguish between true fractures and vertebral anomalies than quantitative morphometry. For example, the distinction between a fractured endplate and the deformity associated with Schmorl's nodes can only be made visually by an experienced observer, as is the case for the diagnosis of the wedge-shaped appearance caused by remodeling of the vertebral bodies in degenerative disc disease (22,23). A combination of semiquantitative, visual and quantitative morphometric methods may be the best approach to fracture definition, as suggested by the National Osteoporosis Foundation (24), by Kanis et al. (25), and by the International Osteoporosis Foundation (IOF) (26). Currently, there is no consensus on which morphometric technique should be used, or how, to evaluate patients at risk of osteoporosis. MRX, based upon assessment of conventional radiographs, has, unlike MXA, the potential for qualitative reading of the radiographs by a trained radiologist or highly experienced clinician who can distinguish between vertebral anomalies and true fractures and detect technical artefacts on the films, which might increase the errors on quantitative morphometry.

However, in view of the relatively low radiation dose to the patient and the excellent agreement with the visual SQ method

for the identification of vertebral deformities, the visual or morphometric assessment of lateral DXA spine images may have the potential for use as a prescreening tool. If all vertebrae are visualized adequately by lateral DXA images and classified as normal by IVA or MXA, the patient could be classified as normal. If all vertebrae are not visualized by DXA and if one or more deformities are detected by IVA or MXA, it will be necessary to acquire conventional radiography to check for further prevalent deformities and to identify the nature of the deformity. The availability of a rapid, low-dose method for assessment of vertebral fractures, using advanced fan-beam DXA devices, provides a practical means for integrated assessment of BMD and vertebral fracture status. This approach allows the identification of most vertebral fractures, even those that are asymptomatic, in patients with low BMD, improving the selection of candidates for therapeutic intervention.

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