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Imaging of vertebral fracture in osteoporosis

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Summary

Vertebral collapses are the most frequent fractures in osteoporosis. They are often overlooked, although their presence is a strong risk factor for development of new fractures. Lateral radiographs of the spine are the accepted standard for assessment of fractures. Qualitative (visual), semiquantitative and quantitative (morphometric) techniques are useful in determining the compressive deformities of vertebral bodies. In the present paper, the advantages and the disadvantages of these methods are discussed. The improvement of scan quality allows to use DXA technique to diagnose the fractures, in both – the visual and the morphometric way. The vertebral morphologic assessment also seems to be an important diagnostic tool in pediatric osteoporosis.

Application of multidetector CT and especially MR in vertebral imaging of osteoporosis, improves the sensitivity of fracture detection and enables the differentiation of benign from malignant vertebral body collapses.

Key words: osteoporosis • fractures • morphometric radiography • morphometric X-ray absorptiometry • MSCT • MRI

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Significance of diagnostics of vertebral fractures

Osteoporosis is characterized by reduced mechanical strength of the bones, which increases the risk of fractures. Mechanical strength of the bone is a function of its two integral features: bone mineral density and quality [1]. Vertebral collapses are the most frequent fractures in osteoporosis. In the US, vertebral fractures account for as many as 47% of all fractures in women over 50 years of age, the overall annual incidence of which reaches ca. 1.5 million [2]. They lead to deterioration of the quality of life [3] and increased mortality [4]. Whereas the diagnostics of peripheral fractures and fractures of the proximal end of the femur is not associated with any significant problems, most vertebral fractures are difficult to diagnose because of their oligosymptomatic course, as well as due to neglecting, both by the patients and by physicians, such symptoms as backache, deformity of the figure (increased kyphosis) and/or decrease of body height [5].

Information about non-traumatic (low-impact) vertebral fracture is very important for the physician taking care of the patient, as it considerably alters the management of the case. It is a well-known fact that such a fracture, irrespectively of bone mineral density (BMD) values, significantly increases the risk of further osteoporotic fractures: almost 5-fold with respect to next vertebral body fractures [6] and over 2-fold for femoral neck fractures [7]. In subjects with multiple (over 2) vertebral fractures, the risk of subsequent fractures is 7-fold higher than in subjects without fractures [8]. All vertebral body fractures, both manifested clinically and detectable only radiologically, lead to decreased activity, prolonging the time spent in horizontal position because of pain. Therefore, from the practical point of view, a patient with positive fracture history requires much more serious treatment than a person with similar densitometry results but without such a history.

Problems in diagnostics of vertebral fractures

Underestimation of the number of vertebral fractures is a complex phenomenon:

1. Even in as many as 50% of cases such fractures are asymptomatic, and thoracic and lumbar spine X-rays are

not included in routine diagnostic algorithm in osteoporosis – because of costs and the patients' exposure to radiation.
2. Radiologists often overlook fractures vertebral bodies, or do not include their observations in descriptions of radiograms; the rates of false negative X-ray results ranges from 29.5% in Europe, the Republic of South Africa and Australia to 45.2% in North America and 46.5% in South America. The frequency of false positive results amounts to 5% [9].
3. The terminology used in interpretations of radiograms is not always unambiguous and comprehensible for clinicians [10].

Gehlbach et al. in a retrospective analysis of chest X-ray results obtained in 934 female patients aged 60 years or more hospitalized for various reasons detected the presence of 130 vertebral fractures; 52% of them were mentioned in the descriptions of radiograms, 23% in conclusions to the descriptions, in 17% of patients with fractures osteoporosis was included in the case history, and the treatment of osteoporosis was instituted only in 7% of cases [10].

Therefore, improvement in identification of past vertebral fractures is a serious challenge both for clinical practice and for research studies.

Methods of assessment of vertebral fractures

The diagnostics of vertebral fractures utilizes qualitative, semiquantitative and quantitative methods.

From the technical point of view, visualization of the fractured vertebral bodies can be accomplished by classic radiography or densitometry (DXA).

The diagnostics of vertebral fractures includes two problems:
1. Identification of past fractures, which influences the character of the instituted treatment.
2. Detection of new fractures, which is important for monitoring the therapy and also affects further management.

Qualitative method

Vertebral body fractures are currently assessed most frequently with qualitative method, based on spine radiography performed in lateral projection. Three fracture types are typically distinguished: wedge fractures – with depressed anterior portion of the vertebral body, concave (most often biconcave) – with the height of the central part of the vertebral body decreased and compressive – with the whole vertebral body height decreased in comparison with the adjacent vertebra. However, some authors emphasize that the definition of fracture based only on height reduction criteria can lead to errors and misinterpretations. Certainly, the anatomic variability occurring in normal conditions should be taken into consideration: the wedge-like shape of vertebrae in the mid-thoracic spinal segment and the thoracolumbar junction, and slight biconcavity of the lumbar vertebrae. Extension of the aforementioned method by additional assessment of the lamina limitans, especially in its central part, assessment of parallel position of the superior and inferior laminas and their position in relation to the adjacent vertebral bodies has been proposed [11]. It should be remembered that reduced height of the vertebrae can have other causes than osteoporotic fractures; individual differences in height and shape of the vertebra as well as artifacts due to oblique course of the radiation beam or incorrect positioning of the patient should primarily be ruled out [12]; moreover, other causes of vertebral deformity, listed in table 1 should be taken in to account (Table 1). Comparison of available radiograms obtained at different times of patient monitoring is helpful and indispensable.

Table 1. The causes of fractures and deformities of vertebral bodies which should be differentiated with osteoporosis.

Tumor metastases (breast, prostate, bronchogenic, renal carcinomas)
Primary tumors (multiple myeloma, plasmocytoma, lymphoma)
Langerhans cell histiocytosis (including eosinophilic granuloma)
Inflammatory lesions of the vertebral column (including tuberculotic ones)
Osteomalacia
Developmental deformities of the vertebrae
Genetic bone disorders
Scheuermann disease
Paget disease
Degenerative lesions of the vertebral column

The main advantage, but often also a challenge, associated with visual qualitative method, is an attempt of the radiologist to differentiate between osteoporotic fractures and fractures or deformities caused by other factors. The main disadvantages of the method include limited repeatability, subjective character, possibility of overlooking mild changes and exposure of the patient to relatively high doses of radiation.

Semiquantitative method

Semiquantitative assessment of vertebral fractures according to the algorithm proposed by Genant et al. involves visual evaluation of the degree of deformity of the vertebral bodies [14]. The vertebral body is regarded as fractured if reduction of any height dimension is visible: anterior – ha, middle – hm or posterion – hp (Figure 1). If the height is reduced by 20–25%, it is a mild, grade 1 fracture; over 25% – to 40% the fracture is moderate – grade 2, and above 40% – severe, grade 3 (Figure 2). Genant et al. proposed also summary assessment of fracture severity in a patient by calculation of an appropriate index – SFI (*spinal fracture index*), obtained by adding the grades of severity of the particular vertebral fractures and divided by the number of fractures [14]. In comparison with the qualitative method, the semiquantitative method is characterized by better repeatability (93–99%) and consistency between the observers (90–99%) [15]. It has been applied in epidemiological and clinical studies [16,17].

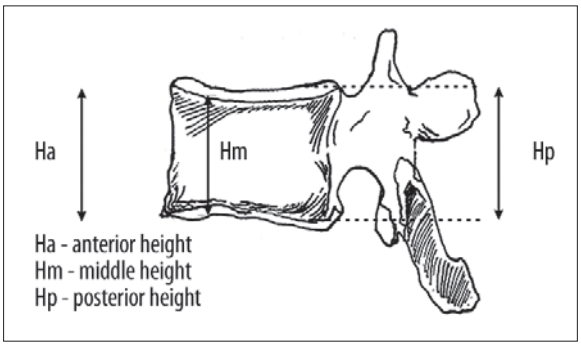


Figure 1. Diagram presenting height measurement of a vertebral body.

Quantitative method – morphometric radiography

On assessment of spine radiograms, also a quantitative method – morphometric radiography (MRX), involving mathematic analysis of conventional X-rays of the spine in lateral projection, can be used. It is a repeatable and objective method, characterized by high sensitivity, but significantly lower specificity than the visual methods. For this reason, morphometric assessment often uses the term „deformity". Deformity is a wider notion, including, besides fractures, also other causes of vertebral anomalies listed in Table 1.

Morphometric analysis involves initial selection of 6 points on the surface of each examined vertebral body, which allows to determine the height of its anterior (ha), middle (hm) and posterior (hp) portion.

There is a number of proposals concerning mathematical definition of vertebral deformity (equivalent to past fracture). Melton proposed the criterion of 15% height reduction. The vertebral body was considered to be deformed if any of the ha/hp, hm/hp quotient values, or hp/hp of the next vertebral body, or hp/hp of the previous vertebral body was lower than 85% [18]. According to Eastell et al, to diagnose deformity of the vertebral body, its height should be at least 3 SD (standard deviations) lower than the mean value (grade 1 fractures) or 4 SD lower than the mean value (grade 2 fractures). This classification takes into account individual variability of vertebral shape and height [19]. McCloskey et al. [20] modified this approach, maintaining the 3 SD criterion as the cut-off point, but took the vertebral height of healthy population as a reference. They also introduced the hpp parameter as predicted posterior height, obtained as a result of analysis of adjacent vertebral heights and population standards. According to this method, the vertebral body was regarded as fractured if it meet any of the following criteria ha/hp and ha/hpp below 3SD or hm/hp and hm/hpp below 3 SD, or hp/hpp and ha/hpp below 3SD.

In turn, Minne et al. [21] related the height of the assessed vertebral bodies (ha, hm, hp) to the appropriate heights of Th 4 and compared such „corrected Th 4 heights" with the mean height obtained from population studies. On that basis, vertebral deformity index (VDI) was calculated for each of the examined vertebra; by adding VDI obtained for the 13 analyzed vertebra (Th 4 – L4), the spinal deformity index (SDI) was obtained.

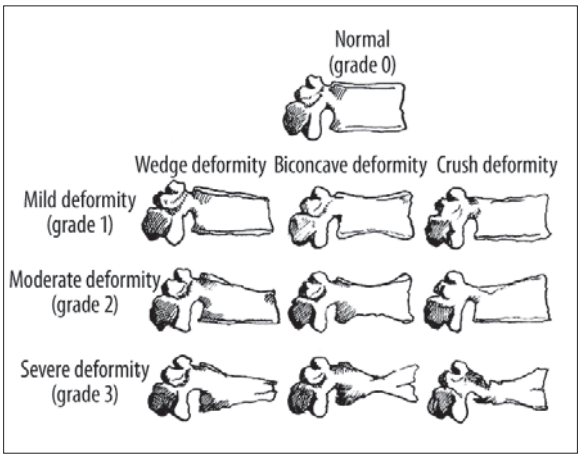


Figure 2. Semiquantitative method of vertebral fracture assessment –classification of the wedge, biconcave and crush deformities according to Genant et al. [14]. Diagram modified from [14].

From the epidemiological point of view, it would seem most appropriate to compare the vertebral heights with those of the reference population of healthy subjects of the same gender. However, it is known that vertebral heights differ, depending on age of the examined subject. Search for so-called normal values in the group where fracture probability is low, e.g. in premenopausal women, may not provide appropriate reference and lead to incorrect selection of the reference group. Therefore, Black et al. [22] proposed a mathematical model allowing to identify normal values in the study group, where both normal and pathologic values can be distinguished.

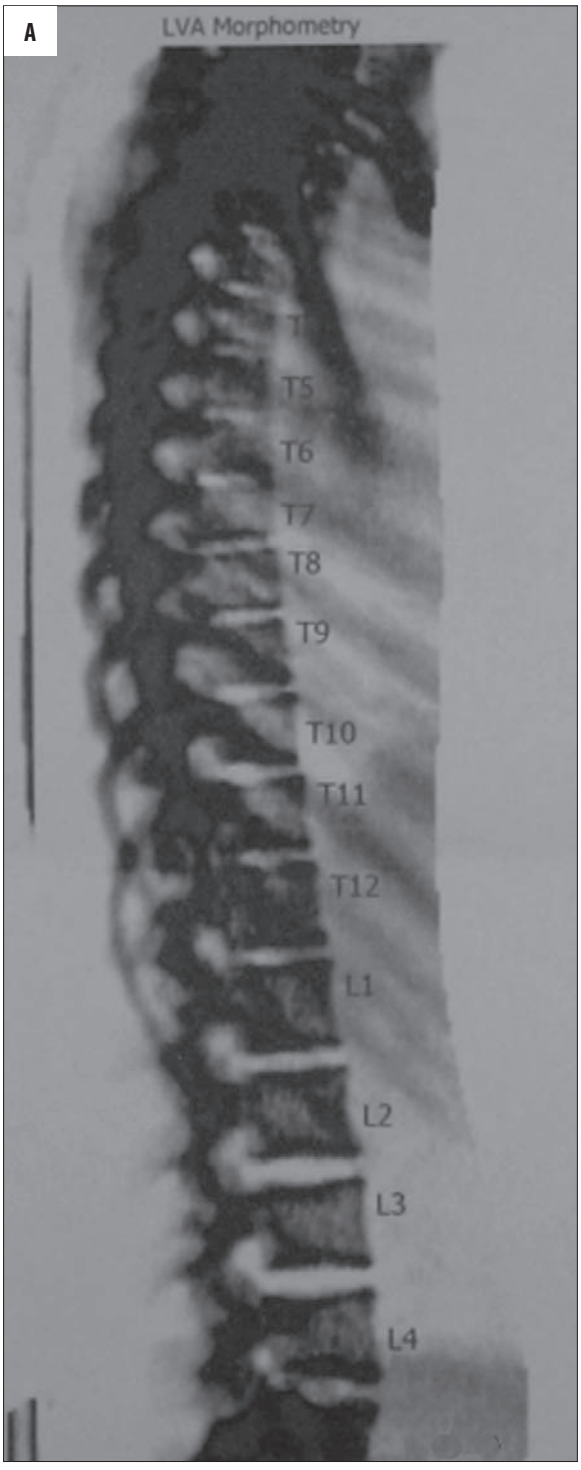
Morphometry makes it possible to monitor the treatment and to analyze potential new fractures. To diagnose a new fracture, any of the three determined heights of the vertebral body should be reduced by at least 20%, and by more than 4 mm.

Morphometry of the vertebral bodies also seems to be an important tool in the diagnostics and monitoring of pediatric osteoporosis.

In the analyzed group of 32 with suspected secondary osteoporosis (low BMD, long-term use of glucocorticoids, pains in the bones and/or past fractures), compressive vertebral fractures were diagnosed in 11 (34%); in most cases (82%), they were asymptomatic; no other, extraspinal, fractures were diagnosed in any of these patients. Additionally, in 8 (73%) of the patients in that group, normal BMD values were observed [23]. Thus, morphometric assessment of the spine should be included in the diagnostic criteria of pediatric osteoporosis, supplementary to clinical data, BMD measurements and history of peripheral fractures.

Application of DXA technique in fracture diagnostics

Improvement of the quality of scans obtained with DXA technique enables both qualitative (visual identification of fractures) [24], and quantitative analysis – morphometric X-ray absorptiometry, (MXA) [25] (Figure 3).



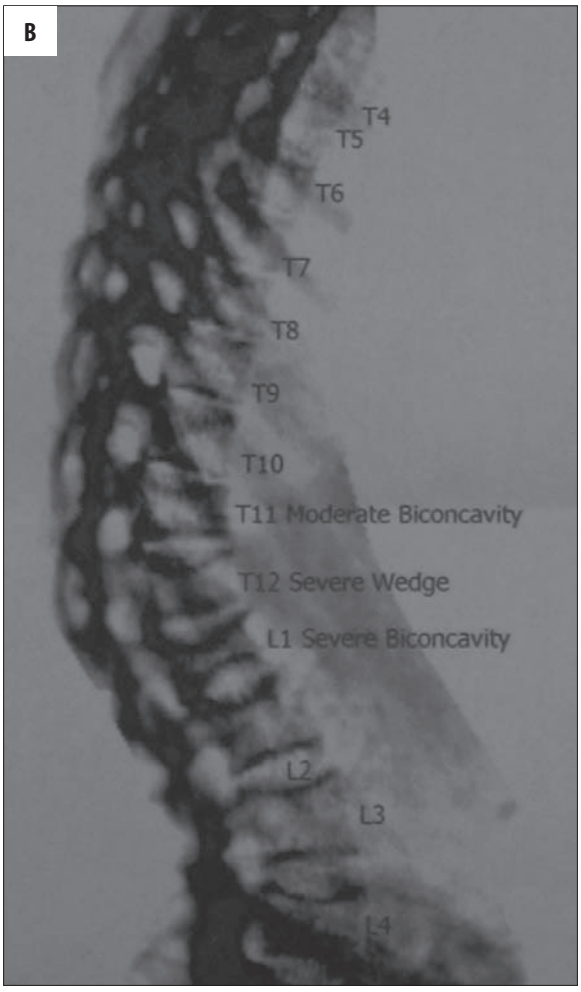


Figure 3. Visualization of thoracic and lumbar spine (Th 4 – L4) from DXA study for vertebral deformity (fracture) assessment – termed MXA (morphometry of X-ray absorptiometry). (A) Normal vertebral morphology of a woman at the age of 21 years old. (B) Spine of a woman aged of 32.5 years old with severe osteoporosis, biconcave fractures of Th11 and L1 and a wedge fracture of Th12.

In comparison with classic radiography, MXA has several advantages:

1. MXA uses a fan-like radiation beam, which eliminates artifacts associated with the use of conical beam used in classic X-ray studies [26]. This allows to assess the thoracolumbar spine in lateral projection during one exposure, whereas classic radiography of the Th4 – L4 segment requires two exposures.
2. 80-fold lower dose of ionizing radiation: 800 μSv in classic X-ray versus10 μSv in MXA [27].
3. Possibility of storage, comparison and processing of data in electronic form, always available for MXA, and for X-ray only in case of digital systems.
4. Organizational and technical reasons: the examination can be performed on the same equipment and at the same time with absorptiometry and is short – only over ten seconds. It is important in case of elderly patients with impaired locomotor functions. On the other hand, the advantage of classic X-ray is better,10-fold higher resolution in comparison with MXA. The number of reports concerning the applicability of MXA in both diagnostics of past vertebral fractures and their monitoring is increasing, because MXA is characterized with high consistency both with qualitative assessment and with MRX results [26,28].

Roles of multidetector CT and MR in assessment and differentiation of pathologic vertebral body fractures

Multidetector CT has been demonstrated to allow much better assessment of vertebral column fractures in com-

Table 2. Characteristic imaging signs of osteoporotic and malignant vertebral collapse (based on 36).

Osteoporotic fractures	Malignant fractures
Presence (at least partial) of normal fatty bone marrow signal	Absence of normal fatty bone marrow signal
No multifocal lesions	Multifocal lesions
No vertebral arch base involvement	Vertebral arch base involvement
Presence of collapse line	No collapse line
No convex cortical outline	Convex cortical outline
No epidural and extraosseous soft tissue lesions	Epidural and extraosseous soft tissue lesions
Intravertebral fluid (T2-weighted images)	Intravertebral fluid absent
Vertebral body fragments directed backwards	No vertebral body fragments directed backwards
Fragmentation of the vertebral body	No fragmentation
Hypointense signal in DWI	Hyperintense signal in DWI
High ADC	Low ADC

parison with conventional radiography, with the respective sensitivity of fracture detection and inter-observer consistency for CT – 97.2% and 0.95 and for radiography 33.3% and 0.37 [29]. CT image reconstructions in sagittal and coronal planes, visualizing vacuum sign in the fractured vertebral bodies (intravertebral gas-filled spaces, usually parallel to the vertebral end plates), indicate compressive fractures due to necrosis of bone trabeculae [30–32]. The histological picture of osteonecrosis is usually preceded by osteoporosis and is its consequence [32]. Osteoporosis is associated with markedly reduced perfusion indexes within the vertebral bone marrow in comparison with healthy subjects, and even subjects with osteopenia [33]. The presence of gas within the vertebral bodies was associated, until recent times, with Kuemmell disease, involving delayed occurrence of fractures after usually slight traumas [34,35]. As demonstrated by MR, the so-called "occult" fractures observed in osteoporosis are probably due to Kuemmell disease. In T1- and T2-weighted images obtained from patients with spinal pain and normally shaped vertebral bodies, signs of recent vertebral fractures were detected, which included: bone marrow edema – in the form of a horizontal layer of signal alteration, or altered signal of the whole vertebral body, as well as a horizontal or oblique fissure at the fracture site. Classic X-ray images of vertebral deformity were observed in those patients after 4–24 weeks [36].

Veratebral deformity symptomatology in acute phase of the fracture in MR includes bone marrow edema, involving the whole vertebral body or, more frequently, its fragment – in the form of a transverse band, as well as the fluid sign – a hyperintense (in T2-weighted images) space, most often transverse, parallel to the vertebral end plate; This sign is more characteristic of severe fractures [37–40].

Long-lasting, chronic vertebral fractures demonstrate during ca. 3 months a conversion from abnormal bone marrow signal, associated with edema, to intensity corresponding with that of normal bone marrow [41]. Such conversion, from hyperintense to isointense (in T2-weighted images) indicates fractures not connected with a malignant process.

In case of osteoporotic, benign, fractures, the posterior outline of the vertebral body is usually normal, sometimes slightly concave; the fragments of superior posterior and inferior posterior margins of the fractured vertebral body are oriented posteriorly towards the spinal canal. The arch bases are usually normal, with respect both to their shape and to signal intensity [38,40]. MR images allow to differentiate osteoporotic and tumor-related fractures, although some problems may appear, especially in case of acute fractures and changes of signal intensity involving the whole vertebral body. Both fracture types show contrast enhancement. Morover, ca. 1/3 of patients diagnosed with tumors has fractures benign in character; therefore diagnosis of the character of fractures is of utmost importance when there is a history of a malignant process [41]. The possibility of differentiation between both fracture types has been considerably improved owing to diffusion imaging technique – DWI. Baur et al, as the pioneers in diffusion studies, found that benign fractures are iso- or hypointense, and those secondary to neoplastic infiltration – hyperintense [38,42]. Also the mean values of diffusion coefficients (measured in 3 directions – x,y,z) demonstrate significant differences: the lowest values of ADC_{cmb} (combined apparent diffusion coefficient) i.e. minimal diffusion of free water molecules, were detected in normal vertebra ($0.23\times10^{-3}mm^2s^{-1}$), almost 3-fold higher values – in fractures due to malignant lesions, whereas the highest diffusion values were found in the vertebra with acute osteoporotic fractures – ADC was over 2-fold higher than in tumor patients [38,43]. It should be emphasized that the diffusion coefficient for the vertebral bodies with osteosclerotic metastases of prostate cancer was similar to the values obtained for normal vertebra, whereas in fractures due to tuberculotic inflammatory lesions the diffusion coefficient approximated the values observed in case of neoplastic changes [43] .Table 2 presents the most important imaging differentiation criteria in osteoporotic fractures and those due to neoplasia. The signs highly suggestive of infection as the cause of fracture (most frequently *Staphylococcus aureus, Streptococcus epidermidis* and *Mycobacterium tuberculosis*) include: intensive disc enhancement, enhancement of perivertebral soft tissue

and/or the epidural space, as well as intensive enhancement of the lamina limitans and adjacent bone marrow [38,44].

The development of new techniques, densitometric imaging in particular, as well as the use of MR in differentiation of compressive vertebral fractures gives hope for improvement in the diagnostics of osteoporotic fractures of the vertebral bodies and identification of the patients for whom the treatment will be most beneficial.

Effective treatment of osteoporosis is commonly available and can reduce the number of fractures by 30–65% [45].

Percutaneous vertebroplasty is gaining increasing popularity. This technique, first used twenty years ago for treatment of vertebral angiomas and osteolytic tumors, in fractures due to osteoporosis considerably alleviates or eliminates pain, ensures mechanical stability and can be an effective element of fracture therapy [46–48].

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