Review Article

Osteoporosis: what the clinician needs to know?

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Abstract: Osteoporosis is a common condition and an important cause of disability. For this reason, early detection of the disease and patients at higher risk of bone fractures is compulsory. In the recent years, conventional quantitative methods have been spreading for the diagnosis of osteoporosis; moreover, new improvements in computed tomography (CT) and magnetic resonance imaging (MRI) have been made in this field and imaging findings may correlate to the morphological and structural changes within the bone.

Keywords: Osteoporosis; quantitative methods; vertebral morphometry; computed tomography (CT); magnetic resonance imaging (MRI)

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Introduction

Osteoporosis is a common bone metabolic disease characterized by loss of bone strength, due to modifications in bone turnover, with the subsequent increased risk of fracture (1). It is a very common condition which mostly affects post-menopausal women and men aged over 50 years (2), rare (but still important) its occurrence in pediatric population (3). Osteoporosis can be distinguished as primary or secondary (4). Primary osteoporosis is caused by changes in normal bone turnover; these can be secondary to reduction of bone matrix production due to low osteoblastic activity, as it happens in postmenopausal women (following the loss of estrogen protection on bone matrix) (4), or in adult population for the aging of cortical and cancellous bone (5); otherwise, primary osteoporosis can be secondary to increased osteoblastic activity, as may result during corticosteroid treatments (2,6)

Secondary osteoporosis can be associated to several conditions, such as congenital (i.e., osteogenesis imperfecta, Ehlers-Danlos syndrome, Marfan syndrome), malnutrition (i.e., vitamin D deficiency, low calcium intake), metabolic, endocrine or iatrogenic diseases (3,5).

Bone strength depends on both bone quantity, which can be expressed in terms of bone mineral density (BMD), and bone quality, which reflects bone microarchitecture (2); these components can be well evaluated on different types of imaging methods.

Imaging techniques

Dual-energy X-ray absorptiometry (DXA)

DXA is the referring technique in the evaluation of osteoporosis, and it consists in a radiogenic tube which delivers an X-ray fan beam with two alternative energy levels (7). BMD is expressed in terms of bone mass per cm^2 (g/cm^2) and can be easily assessed using DXA (8). World Health Organization (WHO) proposed to classify osteoporosis according to BMD values and the difference

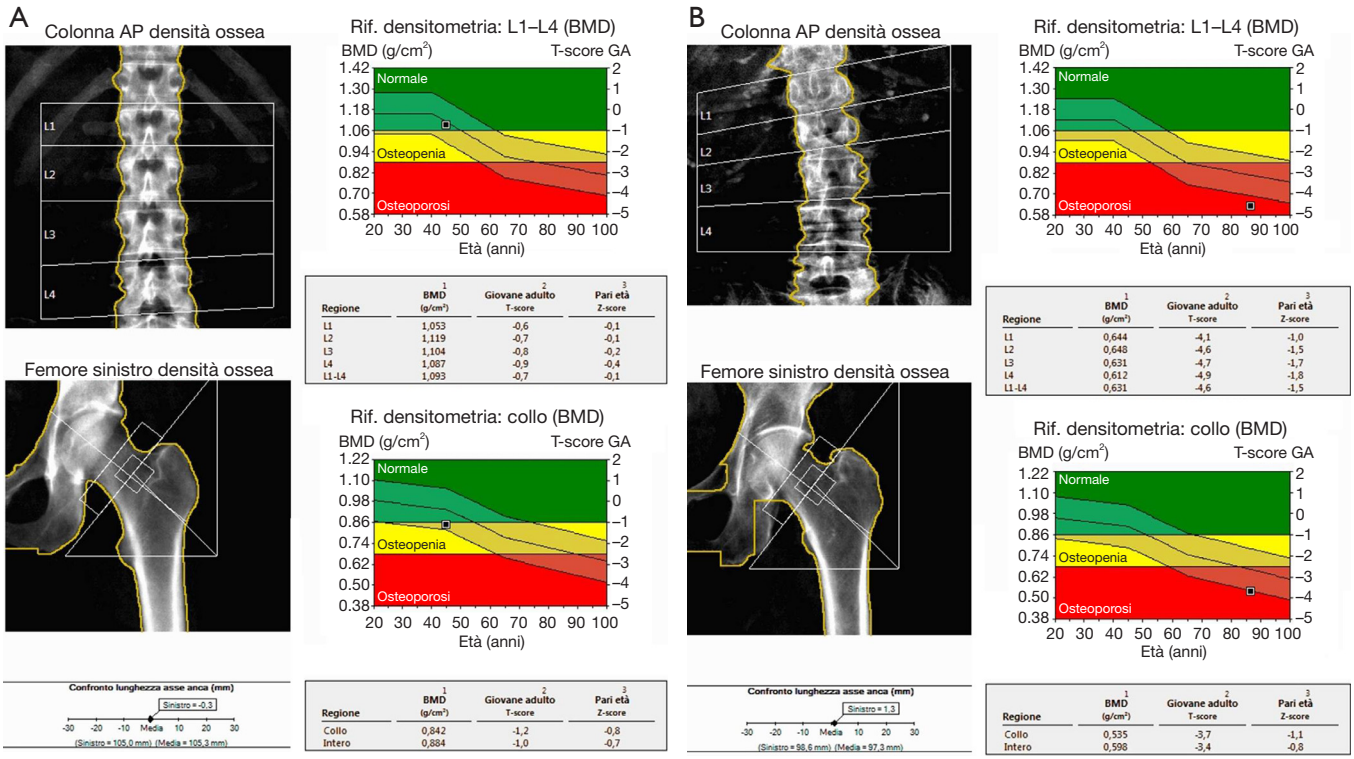


Figure 1 DXA examination. (A) Normal lumbar and femoral DXA; (B) pathological lumbar and femoral DXA. DXA, dual-energy X-ray absorptiometry; BMD, bone mineral density.

[expressed as standard deviation (SD)] from those of a referred population, in terms of T-score or Z-score. T-score is referred to the mean density value measured in 30 years young adults (peak mineral density), while Z-score to the mean density measured in a sample of same age, sex and shape people; osteopenia is defined if the measured BMD value are within –1 and –2.5 SD, osteoporosis if BMD are below 2.5 SD (8,9).

Main sites for BMD evaluation are lumbar spine (L1–L4), femur (femoral neck and total hip) and distal third of the radius (which is mostly composed of cortical bone and its evaluation is relevant in primary and secondary hyperparathyroidism) (2,8) (*Figure 1*).

Even if DXA examination has several advantages, such as the low dose of radiation (1–6 μSv) delivered, the evaluation of anatomical regions which are sensible site of fracture and the short time of acquisition (less the 5 minutes for district) (2,4,10), it cannot distinguish between cortical and trabecular bone and between changes secondary to bone structure or bone density (4,10).

Trabecular bone score (TBS)

BMD calculated with DXA examination, even if is one the most important factor in the determination of bone strength, some patients with fragility fractures may have a normal or osteopenic BMD value (11). For this reason, other factors must be implied in bone strength, such as bone microarchitecture.

TBS consists in measuring the difference pixel by pixel of grey-level texture on DXA image of lumbar spine; even if it does not directly represent the bone microstructure, it is dependent from the three dimensional structure of the vertebral body, which include the trabecular number, the separation between one another and the connectivity density (12): high TBS value indicates a dense, and stronger, bone architecture, while a low value means a fragile bone with an increased risk of fracture. TBS values seem to decrease with aging, more in women than in men, similarly to BMD values (11,12). For postmenopausal women, TBS range above 1.350 is considered normal; if values are between 1.350 and 1.200, TBS is considered

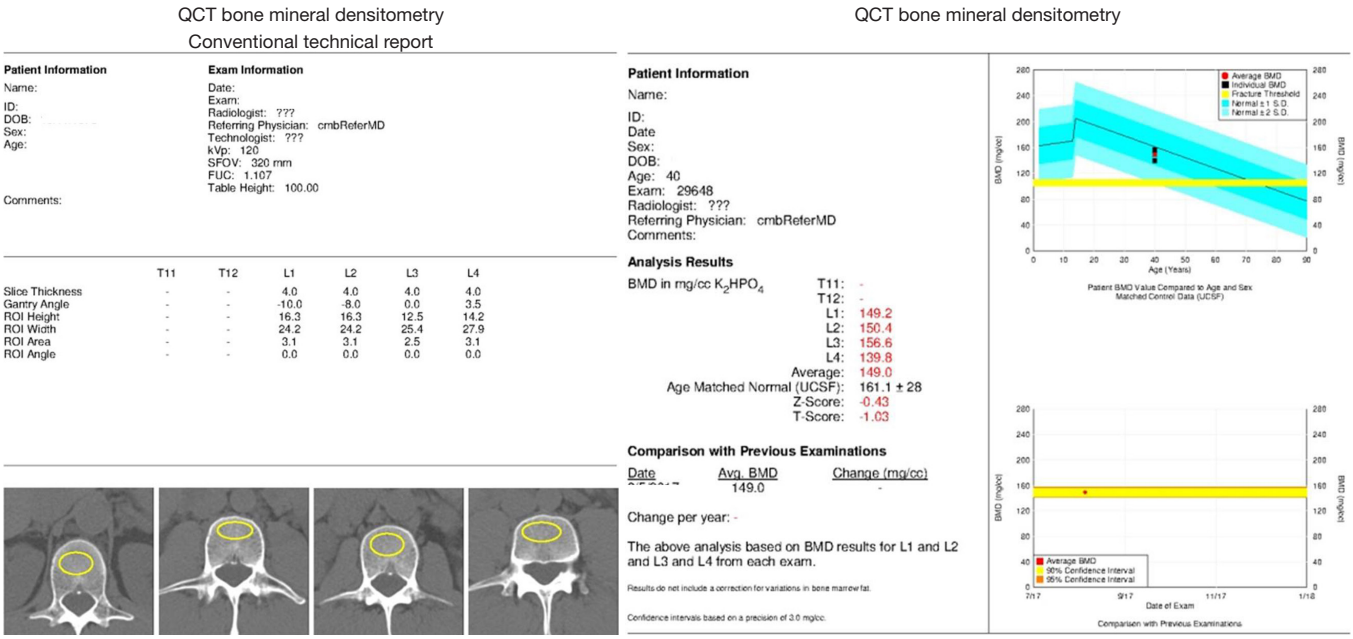


Figure 2 An example of QCT evaluation report. QCT, quantitative computed tomography; BMD, bone mineral density.

compatible with partial microstructural degradation; while a range lower below 1.200 is considered as the degraded microstructure. Considering that TBS has been found a predictor of risk fracture, it may be used with BMD for the selection of patient at high risk of fracture (11).

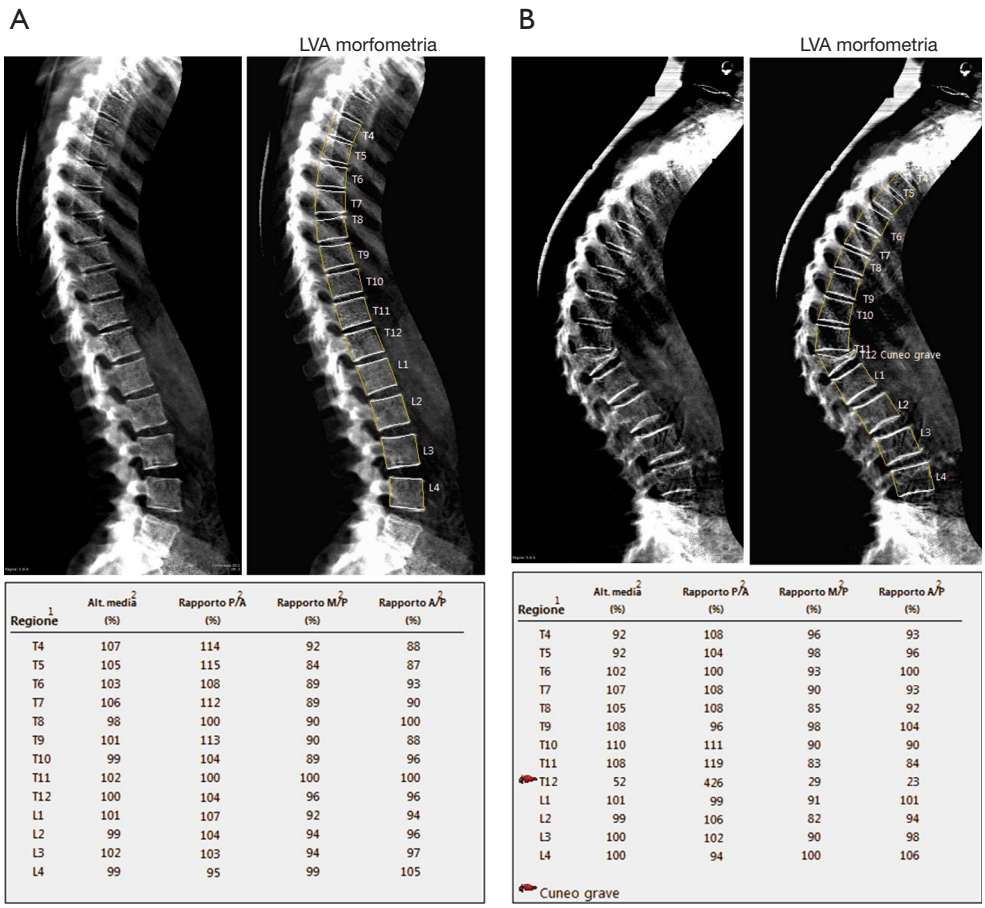
Quantitative computed tomography (QCT)

QCT allows a volumetric estimation of bone density and also permits separate measurement of cortical and trabecular bone (2). QCT is generally performed at the lumbar spine (so called axial QCT) and it well correlates with the bone volume fraction, over the total volume, and the trabecular spacing, while it is poorly correlated with trabecular number and thickness; the result can be represented in terms of absolute T-score and Z-score values or expressed as g/cm^3 (13) (*Figure 2*): a BMD ranging from 80 to 110 mg/cm^3 is associated to mild risk of fracture, a BMD value between 80 and 50 mg/cm^3 is associated with a moderate risk of fracture, while a BMD value lower than 50 mg/cm^3 is associated to severe risk of fracture (14). QCT has shown a great ability in the prediction of fracture risk and importance in the treatment follow-up, but as it delivers a high dose of radiation and also several other bone marrow changes may affect the measurements, its application in clinical use has been narrowed (2,14).

Vertebral morphometry

As previously stated, osteoporosis is a condition on which lays an increased risk of fracture. Theoretically, every bone site is at risk, but fractures generally occur at the level of spine, hip or distal radius. In particular, vertebral fractures are the most common type of fractures, for which a semi-quantitative grading system have been developed by Genant *et al.* (15): according to the reduction in the vertebral anterior, middle or posterior height with respect to the normal adjacent vertebra, fractures can be defined as grade 1 (mild) if the reduction is 20–25%, grade 2 (moderate) if reduction ranges between 25–40% or grade 3 (severe) if it is higher than 40% (*Figure 3*).

Evaluation of vertebral fractures can be performed on both lateral standard radiograms or lateral DXA images of the thoracolumbar spine (from T4 to L4) and the evaluation of vertebral fractures is made accordingly to Genant's criteria (16). In addition, a semi-quantitative method may be used in order to make the evaluation of vertebral fractures clearer and more reproducible among observers: in this view, six points are placed within the vertebral body, four at the margins and two at the middle of vertebral endplates, for the measurement of the anterior, middle and posterior height (16,17). Even if both kinds of imaging evaluation reported a similar detection of vertebral fractures, the assessment on DXA might be preferred for at least two reasons: it delivers a



Regione [1]	Alt. media [2] (%)	Rapporto P/A [2] (%)	Rapporto M/P [2] (%)	Rapporto A/P [2] (%)
T4	107	114	92	88
T5	105	115	84	87
T6	103	108	89	93
T7	106	112	89	90
T8	98	100	90	100
T9	101	113	90	88
T10	99	104	89	96
T11	102	100	100	100
T12	100	104	96	96
L1	101	107	92	94
L2	99	104	94	96
L3	102	103	94	97
L4	99	95	99	105

Regione [1]	Alt. media [2] (%)	Rapporto P/A [2] (%)	Rapporto M/P [2] (%)	Rapporto A/P [2] (%)
T4	92	108	96	93
T5	92	104	98	96
T6	102	100	93	100
T7	107	108	90	93
T8	105	108	85	92
T9	108	96	98	104
T10	110	111	90	90
T11	108	119	83	84
T12	52	426	29	23
L1	101	99	91	101
L2	99	106	82	94
L3	100	102	90	98
L4	100	94	100	106

Cuneo grave

Figure 3 Example of vertebral morphometry evaluated on lateral thoracolumbar DXA. (A) Normal vertebral morphometry (left) and semiautomatic drowning algorithm of vertebral body (right); (B) vertebral morphometry (left) documents severe collapse of T12, which is also detected with the semiautomatic algorithm. LVA, lateral vertebral assessment.

low radiogenic dose than lateral conventional radiogram and also vertebral deformations, due to other spine deformations not related to vertebral fractures, are less common than in standard lateral radiograms, for the image acquisition is performed with a parallel photon beam (16,18).

Quantitative ultrasound (QUS)

QUS is a novel technique which provides information not only on bone mass but also mechanical and microstructural properties; it uses sound waves with a length ranging from 0.5 and 1.25 kHz (2,19). The rationale of this methodic is based on the modification in shape, intensity and speed of the wave while passing through the bone and soft tissues. In particular, the two main parameters evaluated are the speed of sound (SOS) and the broadband ultrasound (intensity) attenuation which have been shown to be related to bone microstructure and density, but other more complex ones [such as stiffness index (SI), QUS index (QUI) and amplitude dependent speed of sound (AD-SoS)], derived from their combination, may help to distinguish patients at increased risk of fracture (2,19-21).

QUS is performed on peripheral sites, such as phalanges, radius, tibia and calcaneus. In particular, this latter well lends itself to the evaluation because it is easily accessible, is predominantly composed of trabecular bone and delimited by the medial and lateral aspects which are flat and run almost parallel one to another, characteristics that make this site very suitable for the evaluation (19,20,22-24).

Other techniques

Recent studies have reported that some other imaging

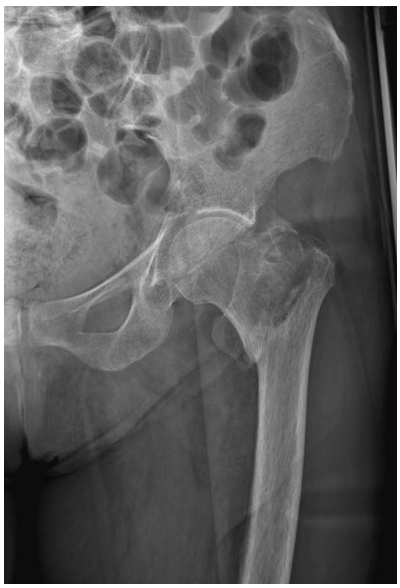


Figure 4 A 75-year-old patient with osteoporosis. Post fallen radiography shows femoral neck fracture.

modalities may play in the quantification of bone mass and its quality (14).

Multidetector CT (MDCT)

In the recent literature, some studies have proposed that early detection of osteoporosis, the patients who underwent MDCT for other reasons, may be achieved calculating the BMD from the same scan (25-27). In fact, CT findings were found in correlation to bone microstructure changes in some diseases and during some therapy regimens (28-31).

High-resolution (HR) peripheral QCT

HR-peripheral QCT is a novel imaging modality that has been implemented for the evaluation of bone structure (32); it also may play a role in monitoring therapies (33). The examination is performed at the level of radius, tibia and metacarpal bones and permits the quantification of BMD in both cortical and trabecular bone, together or separately (10,20,34,35). Even if it delivers a low radiation dose in comparison to QCT, it does not evaluate the lumbar spine or the hip, which are sensible sites at risk of fracture (14).

Magnetic resonance imaging (MRI)

In the recent years, the role of MRI in the evaluation of osteoporosis has been spreading. Basing on the assumption that during osteoporosis there is an adipose involution of bone marrow, different methods have been proposed to quantify the amount of fat fraction, such as T1-weighted images, the Dixon method (which provide fat and water images), diffusion weighted imaging (DWI) or metabolic evaluation using proton magnetic resonance spectroscopy (^{1}H-MRS) (36-40); perfusion studies have also demonstrated a reduced blood supply to the bone marrow, in course of osteoporosis (39,41). Moreover, some research studies have shown that HR imaging sequences, scanning peripheral sites such as tibia or calcaneus, may be helpful in the evaluation of bone microstructure and correlate with spinal BMD (42,43). Functional imaging, such as diffusion tensor imaging (DTI), may also provide further information on bone density and structure (44).

Qualitative evaluation

Radiological evaluation of osteoporosis, with conventional methods, it's often the first step in the radiological work-up of the disease and still has its validity.

Changes in bone density do not become evident on standard radiograms until a certain amount of bone mass is loss (estimated around 30%). Findings can be better appreciated in the axial skeleton and at the proximal portion of long bones and consist in increased bone radiolucency, changes of trabecular pattern network (at the beginning resorption involves mainly the horizontal trabeculae with relative accentuation of vertical ones, in later stages resorption extends also to the vertical trabeculae) and cortical thinning (4,45). These features may be better evaluated with CT scan.

Complications of osteoporosis comprehend bone fractures (compression fractures), which may be even secondary to minor traumas and often involves the spine; other sites are hip (*Figure 4*), sacrum and distal radius (*Figure 5*) (4,45). As previous stated, vertebral fractures may at first be assessed with lateral conventional radiology and be described according to Genant's. On anteroposterior projection, the fracture is usually symmetrical on both sides; the integrity of the posterior must be also checked, for it is lost it may be a sign of malignancy (4,45) and need further investigations. A characteristic vertebral fracture sign, which is strongly indicative of compression fractures, is the Kümmel phenomenon, that represents the avascular necrosis of the collapsed vertebral body and appears as intravertebral vacuum on X-ray images (46), while on MRI has a fluid signal (47).

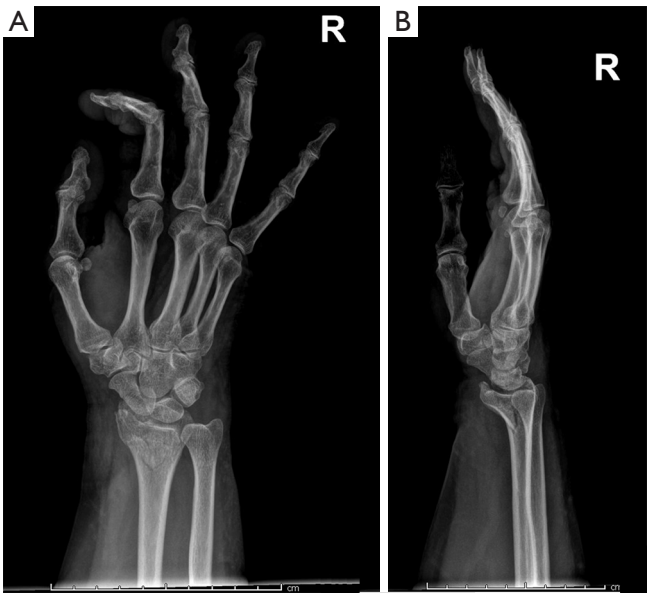


Figure 5 A 71-year-old patient with osteoporosis. Anteroposterior (A) and lateral (B) radiograms show radial fracture after fallen.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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