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Clinical practice guidelines proposed by the Hellenic Foundation of Osteoporosis for the management of osteoporosis based on DXA results

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On behalf of the Hellenic guidelines on bone densitometry working group*

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Abstract

In recent years guidelines for the testing and treatment of osteoporotic patients have been published by recognised organisations, including the World Health Organisation (WHO), the National Osteoporosis Foundation (NOF) and the International Osteoporosis Foundation (IOF). Dual Energy X-ray Absorptiometry (DXA) has been considered the technique of choice because of its excellent precision and ability to predict osteoporotic fractures. Last December, based on the Appraisal of the Guidelines for Research and Evaluation (AGREE), the Hellenic Foundation of Osteoporosis, in collaboration with other scientific societies, provided guidelines for the use of DXA for the diagnosis, monitoring and treatment of osteoporosis and Quality Assurance (QA) of these systems. According to these guidelines, the adequacy of the present number of DXA units in Greece was assessed. There are 367 DXA units in Greece, and almost 50% are located in the capital city, Athens, where 34.1% of the population lives. The distribution of DXA devices per resident in the Greek provinces (except Attica) is between 4.2 units/100,000 heads (Ionian Islands) and 1.6 units/100,000 heads (Sterea Hellas). These guidelines have resulted in a suggestive yearly repeat of the measurements, to ensure the precision of the method, but mainly for reasons of compliance. Finally, these guidelines are viewed as a work in progress and will be updated periodically in response to advances in this field.

Keywords: Osteoporosis, Clinical Practice Guidelines, Dual Energy X-ray Absorptiometry, Quality Assurance

Introduction

Clinical practice guidelines are systematically developed statements that assist practitioners and patients in their decisions about appropriate health care. Their purpose is to make explicit recommendations with a definite intent to guide and influence clinician practice.

Dual Energy X-ray Absorptiometry (DXA) is the most commonly used technique to measure bone mineral density (BMD). It is easy to use, carries a low radiation exposure, and has the ability to measure BMD in the spine, the hip, the forearm, other peripheral sites and throughout the entire skeleton. It uses two X-ray beams of different energy levels to scan the region of interest and measure the attenuation as the beam passes through the bone.

In Greece the imaging techniques used in the diagnosis of osteoporosis display a certain particularity. DXA is the most widely used method for measuring bone density and is the

Figure 1. DXA unit distribution in Greece.

Provinces	DXA units	Population (2001)	Unit/100,000heads
1. Attica	172	3,761,810	4.5/100,000
2. Salonica	27	1,057,825	2.5/100,000
3. Sterea Hellas	10	605,329	1.6/100,000
4. Western Hellas	18	740,506	2.4/100,000
5. Peloponnesus	18	638,942	2.8/100,000
6. Hepirus	9	353,820	2.5/100,000
7.Thessaly	24	753,888	3.1/100,000
8. Macedonia	36	1,366,940	2.6/100,000
9. Thrace	8	362,038	2.2/100,000
10.Aegean Islands	19	508,807	3.7/100,000
11.Ionian Islands	9	212,984	4.2/100,000
12.Crete	17	601,131	2.8/100,000
Total number	**367**	**10,964,020**	

Table 1. The distribution of DXA units per resident in Greek provinces.

only one that has been valued by the health insurance agencies. Other methods such as vQCT, QUS and pQCT can not be prescribed and are rarely applied in Greece.

The whole country of Greece, which is divided into 49 counties, has 367 DXA units in all, of which 172 units (46.86%) are located in the capital city, Athens, and a mere 27 units (7.35%) are found in the country's second largest city, Salonica[1] (Figure 1).

Taking into account that 34.1% of the Greek population resides in the capital and the surrounding suburban area it can easily be understood why this method is widely accessible in Athens. On the contrary, the dozens of Greek islands have only 45 units (12.26%) at their disposal. This results in the need for a large number of the population to travel to the larger suburban cities to undergo examination by highly trained personnel[1]. Due to the particular geological topography of Greece, DXA units are also unfairly distributed. Many Greek islands are quite isolated and difficult to approach especially during the winter months and therefore more units are required to serve fewer patients. On the other hand, mainland Greece, for example Sterea Hellas, which is near the capital, possess a lower number of DXA units for a larger population[1,2] (Table 1).

There have been consensus development conference panels for the diagnosis and management of osteoporosis over the last ten years in Greece, attended by both clinical and laboratory medical scientific societies. These panels have resulted in a suggestive yearly revision of the measurements, to ensure the long-term precision, but mainly for compliance[3-5].

DXA technique:
Clinical utility and diagnostic ability

DXA estimates the average concentration of bone mineral in the area that is being scanned and allows calculation of BMD in g/cm^2 and bone mineral content (BMC) in grams. Because DXA is a projectional technique, the measured bone density does not reflect true volumetric density but rather an area density, calculated as the quotient of the BMC and the area[6].

Early in life, more bone tissue is formed faster than it is resorbed, allowing the skeleton to grow. By about age 30 BMD is at its lifetime best, or "peak bone mass". After this peak, bone remains in equilibrium until about age 50 in women and 60 in men. After that, bone is absorbed faster than it is formed. The resulting bone loss affects both women and men. In women, this decline is accelerated by menopause.

The choice of the appropriate measurement sites may vary depending on the specific circumstances of the patient. DXA scans of the spine can focus in either a posteroanterior projection or a lateral view of the lumbar vertebrae. Depending on the particular equipment, measurements can be obtained either from the L_1 to L_4 region, or from L_2 to L_4. Because of the increased prevalence of degenerative spinal changes and aortic calcification, falsely elevated BMD values can be obtained when posteroanterior spine scans particularly are used in the elderly. In these patients, lateral spine scans or hip scans may be more reliable and sensitive.

Scans of the hip include the femoral neck, the trochanteric and intertrochanteric region, Ward's triangle and/or the entire hip. With the use of a large region of scanning in the total hip, measurement errors may be minimized.

The method emits high and low X-ray energy and measures the difference in tissue attenuation of each, in turn allowing separation of soft tissue density from bone density. This sepa-

ration is particularly important due to the individual variability in the soft tissue content around the hip and spine. The attenuation of X-rays is also distinctly different between normal bone and osteoporotic bone. DXA measurements can neither sufficiently differentiate between cortical and trabecular bone, nor give details with respect to bone architecture[7-9].

Each patient's bone density is plotted against a healthy young adult or against age-matched control data. In 1994, the World Health Organization (WHO) chose the T-score as its standard for defining BMD[10]. The WHO criteria are intended to provide a reasonable standard for evaluation of individual BMD values in comparison to existing databases. Comparisons are stated as standard deviation (SD) from normal BMD values obtained from young, healthy persons of the same sex, race, and age. These young normal scores, or T-scores, can then be used to decide whether a patient has a reduced BMD consistent with osteoporosis or osteopenia. The Z-score compares one patient's BMD, in standard deviations, with the mean BMD for people of similar age and gender.

Most densitometry equipment contains software that calculates T-scores and Z-scores automatically. The T-score may also be demonstrated by the formula: Patient's BMD-Young adult BMD/1SD of Young adult Mean BMD and the Z-score by the formula: Patient's BMD-Age matched Mean BMD/1SD of age-matched Mean BMD.

A normal bone mineral density (BMD) is one that is within 1 SD of the young adult reference range (T-score > –1), osteopenia a BMD more than 1 SD but less than 2.5 SD below the young adult mean (T-score between –1 and –2.5), osteoporosis the BMD value of 2.5 SD or more below the young adult mean (T-score < –2.5) and severe/established osteoporosis the BMD value of 2.5 SD or more below the young adult mean in the presence of one or more fragility fractures[11].

Unfortunately, there is limited published information on normal values of bone mineral density in Greece[12,13].

The limitations of measuring bone density of the vertebra in the posteroanterior projection include patient age above 65 years, the presence of osteophytes, calcification of paraspinal ligaments, vertebral compression fractures, aortic calcification and vertebral scoliosis. Existing vertebral compression fractures may be interpreted as increased bone density. Lateral scans of the vertebra eliminate the potential artefacts of osteophytes or aortic calcifications. The limitations of lateral scans include the increased amount of soft tissue in this projection, and the overlap of the ribs and pelvis which decrease the number of vertebrae that can be analysed, thus affecting the precision of the measurements[14].

The limitation of hip measurements include the variability of different areas of the femur in regard to the percentage of cancellous bone and thus the potential risk of fracture[15], the presence of metal prostheses, osteoarthritis, recent hip fracture and fibrodysplasia ossificans progressiva.

There are other important limitations to DXA. Because BMD is the average on two-dimensional projection of the bone, while variations in the third dimension are ignored, the estimated BMD can be strongly altered by the size of the bone. This potential source of systematic error may be especially important when patients with different body size are compared. In addition, there is no information about the geometric distribution of trabecular and cortical bone, while the geometric component of bone competence is completely ignored. Finally, these measurements are inherently inaccurate since they are strongly influenced by the composition of the soft tissue surrounding the bone. This is particularly important in frail older women in whom the magnitude of the measurement error can be as high as 20%[16].

According to the International Society of Clinical Densitometry (ISCD) measurement, BMD is recommended for: women 65 years and older; postmenopausal women under 65 years with risk factors; men 70 years and older; adults with a fragility fracture; adults with a disease or condition associated with low bone mass or bone loss; adults taking medications associated with low bone mass or bone loss; anyone being considered for pharmacological therapy; anyone being treated, to monitor treatment effect; and anyone not receiving therapy in whom evidence of bone loss would lead to treatment[17-20].

The first step in the management is a thorough medical history. The National Osteoporosis Foundation (NOF) has identified many risk factors for osteoporosis and related fractures in white postmenopausal women[19,21,22]. Major risk factors include: personal history of fracture as an adult, history of fragility fracture in a first-degree relative, low body weight (<57.5 kg or 127 lbs), current smoking and use of oral glucorticoid therapy for more than 3 months. Additional risk factors include: impaired vision, estrogen deficiency at an early age (<45 years)[23], poor health/frailty, recent falls, lifelong low calcium intake, low physical activity and alcohol in amounts >2 drinks per day. Medical conditions associated with increased risk of osteoporosis are: chronic obstructive pulmonary disease, gastrectomy, hyperparathyroidism, hypogonadism, multiple myeloma, renal failure (patients on dialysis), dementia and celiac disease[19]. Several medications, in addition to oral glucocorticoids, have been implicated with osteoporosis and include: anticonvulsants, GnRH agonists, excessive T4 doses, long-term phenytoin therapy and lithium[19].

Error and artefacts in DXA are correlated to the calibration and the quality assurance of the equipment, patient positioning, image analysis, operator variability, anatomical problems of the patient, misunderstanding of data, as well as the age and ethnicity of the patient.

Bone mineral density measurement with DXA is painless, requires no injections, invasive procedures, sedation, special diet or any other advance preparation. During the examination the patient lies almost fully clothed on a padded table while the system scans one or more areas of bone. The entire exam typically takes just a few minutes to complete (<5 minutes). While DXA uses X-rays, the amount of radiation is very small, less than one-tenth the dose of a standard chest X-ray. DXA is a high precision and accuracy technique, with high resolution and well-documented correlation to fracture risk.

According to Greek guidelines on bone densitometry, all men and women over 65 years of age have a clear indication to undergo a DXA measurement that means, according to recent demographic data, 870,500 men and 1,079,400 women in Greece should have a screening test. Unfortunately, epidemiologic data about the incidence of vertebral osteoporotic frac-

tures in Greece are scarce but according to a large population-based study (1987) about 20% of women above 50 years old presented with significant height reduction which was a sign of multiple spine deformities[24]. If we extrapolate these results to the total number of women of the same age (2,071,203 in year 2001[2]) 415,000 women sustain at least one vertebral fracture in Greece. Furthermore, about 12,000 women and men over 50 years of age sustain a hip fracture every year[25].

These are pools of population consisting of high risk persons that should undergo a DXA measurement at least once to estimate the risk of fracture and diagnose osteoporosis, and subsequently once per year to enhance the compliance to therapy. If we assume that in a 10-years-period about 2,950,000 persons above 65 years old in Greece according to the guidelines have to be measured in DXA units (295,000 persons per year) and taking into account that another 430,000 osteoporotic patients in Greece, as mentioned above, should undergo a DXA measurement once per year, then at least a total number of 725,000 persons should have a DXA measurement every year. If we extrapolate this number to the number of person measurements per working day, then we should measure 3,296 persons per day throughout Greece.

Subsequently, the 367 DXA units throughout Greece should measure at least 9 persons per day. In conclusion, the number of DXA units in Greece almost responds to the needs.

Quality Assurance (QA) Guidelines

Any medical device using radiation requires testing after installation in order to ensure that the system is functioning properly and the radiation dose is within the specified limits. This is carried out by a Medical Physicist at the time of installation, who should review these data and compare the results with the specifications of the instrument given by the manufacturer. The essay of QA results concerning the DXA system is sent to the Hellenic Committee of Atomic Energy, Department of License and Quality Control (QC) in order to certificate the declaration of conformity. At times, it may be necessary to repeat some measurements, particularly if a new brand of instrument is installed. It may also be necessary to evaluate the instrument for new applications or to determine measurement errors under certain experimental conditions. Besides these occasional evaluations, there are also daily quality control requirements. Instrument calibration and, if indicated, radiation dose to the patient should be measured after each major maintenance or repair[26]. These different aspects of instrument evaluation and quality control are summarized in Table 2[26].

Conclusion

DXA is a useful technique for the estimation of fracture risk as well as an important aid in the decision process of who qualifies for therapy for osteoporosis (level 1)[5].

DXA aids in the investigation and differential diagnosis of patients with radiographic osteopenia or medical condition compatible with primary osteoporosis[27] (level 1)[5].

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1. At installation of a new instrument:
   - Acceptance testing at time of installation.
   - Performed by a medical physicist.
   - Review by user recommended.
2. Routine quality control procedures:
   - Set up of a routine quality control procedure and a routine recording and review procedure (QC log). Most instruments have software supported QC routines. Additional QC tests may be needed.
   - Start a book to enter any repair or malfunction of the instrument, as well as results of inspections and performance reviews.
3. Evaluation of instrument performance (Accuracy, Reproducibility, Linearity):
   - Special phantoms and, if still needed, patients.
   - Radiation dose measurements.

Table 2. Instrument evaluation and quality control.

Recommendations

Measurement of BMD by central DXA is the best method to estimate the fracture risk in postmenopausal women (grade A)[5].

DXA's T-score as a standard for defining BMD, is a useful diagnostic tool which can aid in the determination of treatment plan, particularly when used in combination with co-existing clinical risk factors (grade B)[5].

In postmenopausal women without indications for the initiation of pharmacologic treatment, DXA should be repeated every two years (grade D)[5].

In postmenopausal women under pharmacologic treatment, for reasons of compliance, DXA should be repeated every year (grade D)[5].

Any patient with very low BMD values should be suspected for secondary osteoporosis (grade D)[5].

Measurement of BMD should be performed on all individuals, independent of age and sex, in whom evidence of bone loss would lead to a treatment plan (grade D)[5].

Appendix
Grades of evidence and recommendations

Levels of evidence are defined as follows:

1+/1++ (high quality designed meta-analysis of randomised controlled trials/RCT or randomized studies with very low risk of directed results)

1- (meta-analysis, randomized controlled trials/RCT or randomized studies with high risk directed results)

2++ (high quality controlled study, case control/cohort studies or case control/cohort studies with very low risk of directed results and high probability of causative cross-correlation)

2+ (case control/cohort studies with low risk of directed results and moderate probability the correlation to be causative)

2- (case control/cohort studies with high risk of directed results and high probability the correlation not to be causative)

3 (non-experimental descriptive studies, e.g., case control studies, case reports)

4 (from expert committee reports or opinions and/or clinical)

Grade A evidence (at least one meta-analysis of randomized controlled trials/RCT, or RCTs level 1++, corresponding at the population that we study or studies level 1+ with condition they agree between them)

Grade B evidence (data studies level 2++ that present unanimity or prospective data of studies level 1+/1++)

Grade C evidence (data studies level 2+ that present unanimity or prospective data of studies level 2++)

Grade D evidence (levels of evidence 3 or 4 and prospective data of studies level 2+)

These guidelines are viewed as a work in progress and will be updated periodically in response to advances in this field.

References

1. Hellenic Committee of Atomic Energy (www.eeae.gr).
2. The 2001 demographic data of Greek National Statistics Organization (www.statistics.gr).
3. Dimitriou P, Kalef-Ezra J, Raptou P. Quality assurance and quality control of DPA units. Consensus Conference Panels. 3rd Hellenic Congress of Hellenic Society for the Study of Bone Metabolism, Ostoun; 1995.
4. Guidelines for the diagnosis and management of osteoporosis in Greece. Hellenic Foundation of Osteoporosis. Athens; 2004.
5. Laboratory assessment of osteoporosis and quality assurance guidelines. Hellenic Foundation of Osteoporosis. Athens; 2005.
6. Genant HK. Measurement of axial and bone mass by DXA. Bone mass measurement in osteoporosis and other bone diseases. National Osteoporosis Foundation; November 1995.
7. Milos G, Spindler A, Ruegsegger P, Seifert B, Muhlebach S, Uebelhart D, Hauselmann HJ. Cortical and trabecular bone density and structure in anorexia nervosa. Osteoporos Int 2004; Sep 28.
8. Boyanov MA, Popovanov PR, Roux C. Separate assessment of forearm cortical and trabecular bone density from standard densitometry data. Ann Med 2001; 33:497-506.
9. Hergenroeder AC. Bone mineralization, hypothalamic amenorrhea, and sex steroid therapy in female adolescents and young adults. J Pediatr 1995; 126:683-689.
10. Assessment of fracture risk and its application to screening for postmenopausal osteoporosis. Report of a WHO Study Group. World Health Organ Tech Rep Ser 1994; 843:1-129.
11. Kanis JA. Assessment of fracture risk and its application to screening for postmenopausal osteoporosis: Synopsis of a WHO report. Osteoporos Int 1994; 4:368-381.
12. Giatzidis A, Tsekoura M, Lyritis G. Bone mineral density estimation of the lumbar spine, the femur and the forearm in Greek women, with single and dual photon absorptiometry. Ostoun 1990; 1:34-42.
13. Hadjidakis D, Kokkinakis E, Giannopoulos G, Merakos G, Raptis SA. Bone mineral density of vertebrae, proximal femur and os calcis in normal Greek subjects as assessed by dual energy X-ray absorptiometry: comparison with other populations. Eur J Clin Invest 1997 Mar; 27:219-227.
14. Rizzoli R, Slosman D, Bonjour J. The role of dual energy X-ray absorptiometry of lumbar spine and proximal femur in the diagnosis and follow-up of osteoporosis. Am J Med 1995;98:33S-36S.
15. Wahner HW. Use of densitometry in the management of osteoporosis. In: Meunier PJ (ed) Osteoporosis: Diagnosis and Management. 1st ed. Martin Duntz, London; 1998.
16. Russo CR, Lauretani F, Bandinelli S, Bartali B, Di Iorio A, Volpato S, Guralnik JM, Harris T, Ferrucci L. Aging bone in men and women: beyond changes in bone mineral density. Osteoporos Int 2003; 14:531-538.
17. Brown JP, Josse RG for the Scientific Advisory Council of the Osteoporosis Society of Canada. Clinical practice guidelines for the diagnosis and management of osteoporosis in Canada. CMAJ 2002; 167(Suppl.10):S1-S31.
18. National Osteoporosis Foundation. Osteoporosis. Review of the evidence for prevention, diagnosis, treatment and cost-effectiveness analysis. Osteoporos Int 1998; 8(Suppl 4):S7-S80.
19. Lewiecki EM, Watts NB, McClung MR, Petak SM, Bachrach LK, Shepherd JA, Downs RW. International Society for Clinical Densitometry: Official positions of the International Society for Clinical Densitometry. J Clin Endocrinol Metab 2004; 89:3651-3655.
20. Lawrence GR. Screening for Osteoporosis. N Engl J Med 2005; 353:164-171.
21. National Osteoporosis Foundation 2003 Physician's guide to prevention and treatment of osteoporosis. National Osteoporosis Foundation,Washington DC.
22. National Osteoporosis Foundation. Physician's Guide to prevention and treatment of osteoporosis. Excerpta Medica, Belle Meade, NJ; 1998.
23. Notelovitz M. Adjustive estrogen therapy: a rational approach to HRT. Contemporary Obstetrics/Gynecology 1999; 44:54-64.
24. Lyritis GP. Epidemiology and socioeconomic cost of osteoporotic fractures in Greece, Editorial in Calcif Tissue Int 1992; 51:93-94.
25. Paspati I, Galanos A, Lyritis GP. Hip fracture epidemiology in Greece during 1977-1992. Calcif Tissue Int 1998; 62:542-547.
26. Wahner HW, Fogelman I. The evaluation of osteoporosis: DEXA in clinical practice, Chapter 5, Mayo Foundation and Ignac Fogelman; 1994.
27. Compston JE, Cooper C, Kanis JA. Bone densitometry in clinical practice. BMJ 1995; 310:1507-1510.