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2011 Guidelines for the Diagnosis and Treatment of Osteoporosis in Greece

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The development of these guidelines followed the decision of the Greek National Medicine Agency for the construction of guidelines that will apply to all diagnostic and therapeutic medical procedures in Greece. An expert panel consisting of physicians from the three major medical specialties (Endocrinology, Orthopedic Surgery, Rheumatology) dealing with osteoporosis in Greece, met to discuss the initial guidelines. Following an extensive literature review as well as a review of the worldwide existed guidelines for the management and treatment of osteoporosis, an initial draft was constructed. The Central Health Council of Greece then reviewed the guidelines. The expert panel endorsed the revised guidelines and the English version of the final manuscript is herein presented.

Evaluation

The diagnosis of Osteoporosis should be established following bone mineral density (BMD) evaluation with Dual energy X-Ray absorptiometry (DXA). Skeletal sites to measure include lumbar spine (L1-L4) and hip; simultaneous measurement at both sites (lumbar spine and hip) is strongly recommended; forearm BMD should be measured in cases of: hyperparathyroidism, obese patients exceeding the weight limit of DXA table, difficulties in measurement and/or interpretation of hip and/or lumbar spine measurements.

Indications for BMD testing (men and women):

Age <50 yrs:
- Fragility fractures,
- Hypogonadism,
- Premature menopause (<45-yr),
- Malabsorption syndromes,
- Primary hyperparathyroidism,
- Medication related with bone loss and/or fractures (e.g. steroids, aromatase inhibitors, etc),
- Other pathologic conditions/diseases related with bone loss and/or fractures (e.g. Rheumatoid Arthrits, Type 1 Diabetes, Cushing syndrome, etc).

Age 50-64 yrs:
- Fragility fracture after the age of 40 yrs,
- Parent hip fracture,
- Vertebral fracture and/or "osteopenic" imaging of skeleton,
- Low weight (<60 kgr) and/or weight loss >10% of weight at the age of 20 yrs,
- Alcohol consumption (≥25-30 gr daily) and/or smoking,
- Other pathologic conditions/diseases related with bone loss and/or fractures (e.g. Rheumatoid Arthrits, Type 1 Diabetes, Cushing syndrome, etc).

Age ≥65 yrs:
- All men and women.

BMD Interpretation – Terms

Postmenopausal women, women in menopausal transition, men ≥50 yrs:
- Normal BMD: T-score ± 1.0,
- Osteopenia: -2.5 <T-score <-1.0,
- Osteoporosis: T-score ≤-2.5,
- Established Osteoporosis: T-score ≤-2.5 and one or more fragility fractures.

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MEDICATION	ANTI-FRACTURE EFFICACY		
	VERTEBRAL	NON – VERTEBRAL	HIP
Alendronate	+	+	+
Risedronate	+	+	+
Ibandronate	+	+	
Zolendronic acid	+	+	+
Denosumab	+	+	+
Raloxifene	+		
Strontium ranelate	+	+	(1)
Calcitonin	+		
Teriparatide	+	+	
PTH 1-84	+		

Footnotes – Comments:
(1) Post hoc analysis: reduction of hip fractures in female patients ≥74 yrs with a a femoral neck BMD T-score <-3.0.

Among women ≤55 yrs lacking risk factors (history of venous thromboembolism, breast cancer, etc) and experiencing menopausal symptoms, ***estrogens (HRT)*** *could be the treatment of choice while reducing all osteoporotic fractures (vertebral, non-vertebral, hip).*

Table 1. Anti-fracture efficacy of anti-osteoporotic treatment in postmenopausal women.

Premenopausal women and men <50 yrs:

The diagnosis of osteoporosis cannot be solely based on BMD measurements and additional indications of decreased bone strength are needed (e.g. prior fragility fracture, disease related with increased fracture risk). Z-scores are preferred over T-scores while the terminology in these ages should be:
• BMD below the expected range for age: Z-score ≤-2.0,
• BMD within the expected range for age: Z-score >-2.0.

Diagnostic work-up of Osteoporosis

Medical history and clinical examination are necessary and irreplaceable parts in the evaluation of each case and in the differential diagnosis of secondary osteoporosis.

Minimum, baseline, laboratory assessment should include:
• Serum Calcium (corrected for albumin),
• Complete Blood Count,
• Erythrocyte Sedimentation Rate (ESR),
• Serum Creatinine,
• Serum total Alkaline Phosphatase (ALP),
• Thyroid Stimulating Hormone (TSH),
• 25 (OH) vitamin D.

Depending on medical history, clinical examination, and results of the initial laboratory assessment, additional laboratory exams might be necessary such as: parathyroid hormone (PTH), serum testosterone (men), serum tryptase, Anti-Tissue Transglutaminase (tTG) antibodies, etc. Bone markers are useful before and during treatment, however, adequate evidence for their use in the choice of the most suitable treatment is lacking.

Assessment for fracture risk

Osteoporosis is a systemic skeletal disease characterized from decreased bone mass and deterioration of bone micro-architecture resulting in reduced bone strength and increased fracture risk. By definition any anti-osteoporotic treatment should either decrease the possibility of the first fragility fracture or reduce the risk of additional fractures in patients with prevalent fractures. Therefore, the recognition of patients with high fracture risk is of paramount importance.

FRAX tool (http://www.shef.ac.uk/FRAX/) can provide the absolute 10-yr fracture risk in patients ≥40 yrs, who have never been exposed to any anti-osteoporotic treatment, depending on their risk factors and BMD measurement. Necessary data for FRAX calculation tool include: age, gender, prevalent osteoporotic fractures, hip BMD, body mass index (BMI), as well as information regarding: exposure to steroids, rheumatoid arthritis, secondary osteoporosis, parental hip fracture, smoking and alcohol consumption.

A Greek database for the calculation of fracture risk is currently lacking. However, it is recommended to use the Italian database until a Greek one would be available, due to the similarity of both populations regarding their diet and way of living as well as due to the similar latitude of both countries. The use of database from Turkey should be avoided due to the obvious difference of fracture rates between populations.

Medical treatment

Among postmenopausal women a lot of randomized control studies and meta-analyses have been conducted concerning the anti-fracture efficacy of several substances. The anti-fracture efficacy of the available medication in Greece is outlined in Table 1. The initial indication for treatment or re-evaluation in the future is depicted in Figure 1. Women requiring treatment, with an osteoporotic fracture at baseline, should be treated according to the algorithm of Figure 2. The panel accepts that a fragility fracture at baseline increases the possibility of a new fracture at a similar site. Therefore, the patient should be treated accordingly with an agent

Figure 1. Defining the need for initiation of treatment (postmenopausal women and men ≥50 yrs).

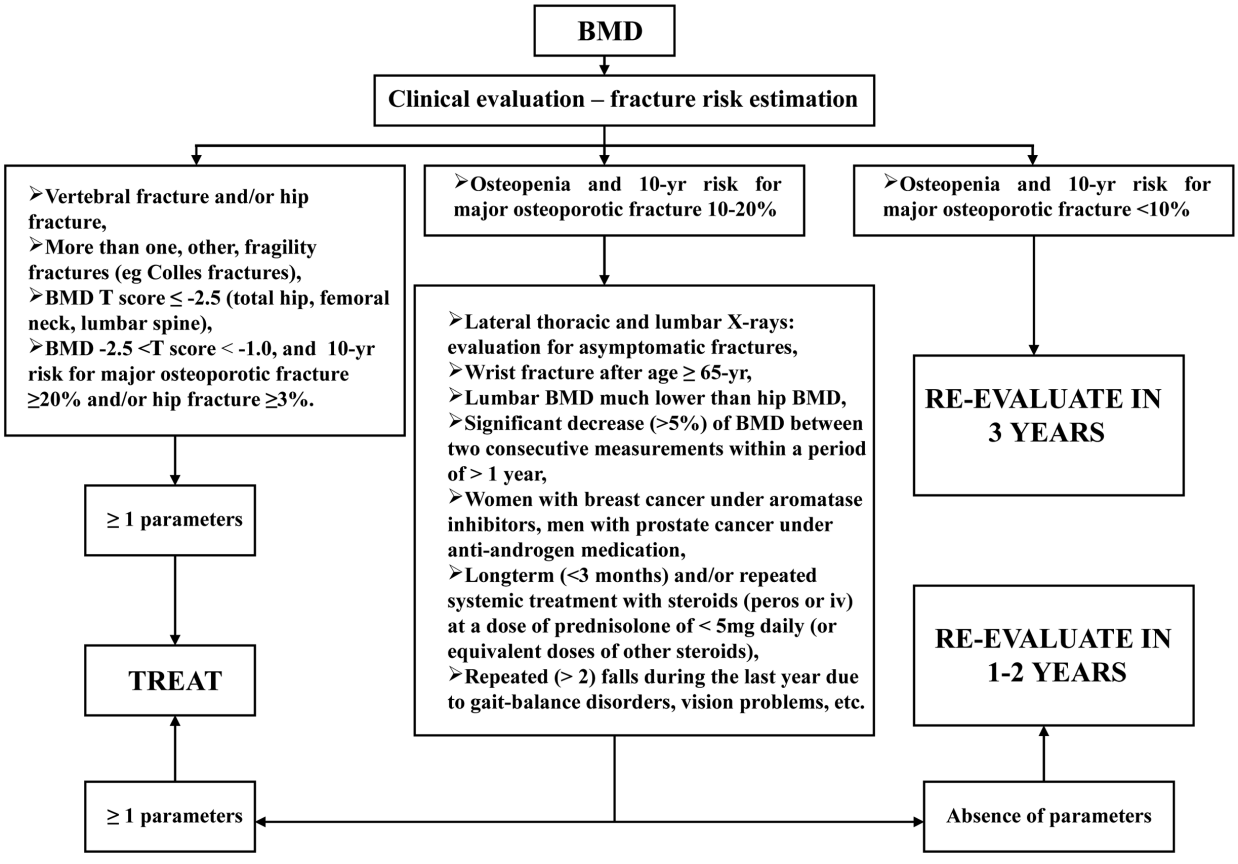
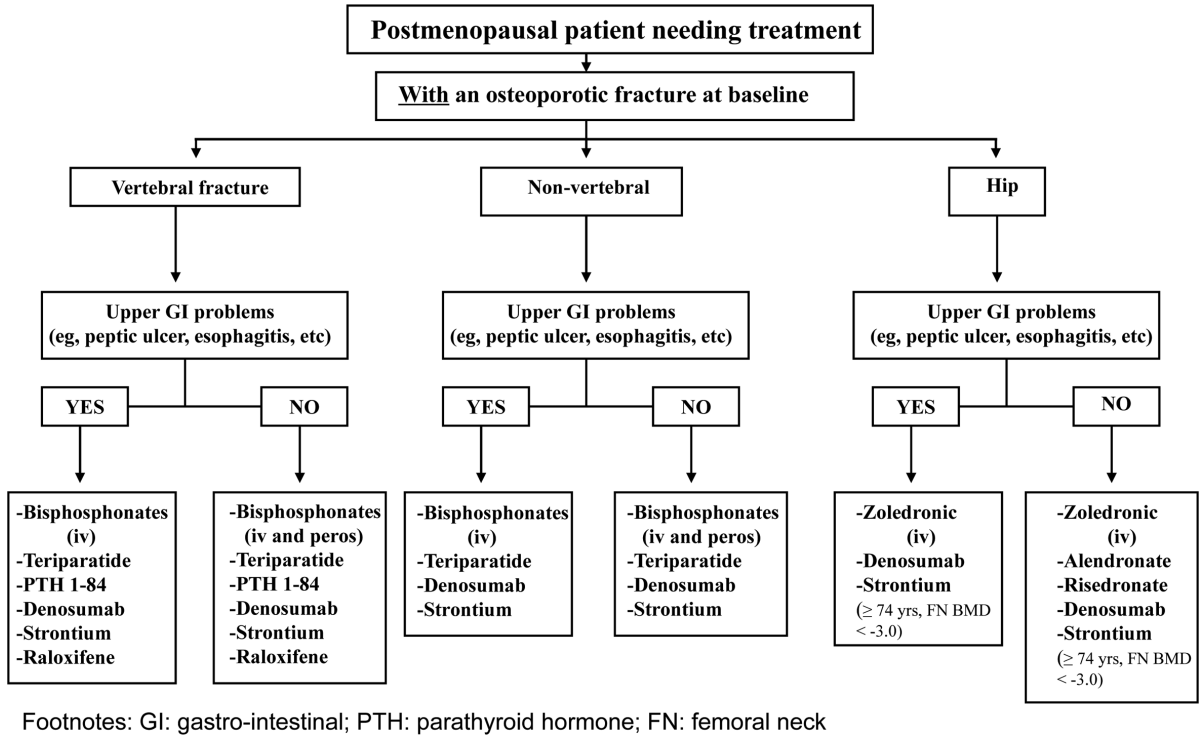
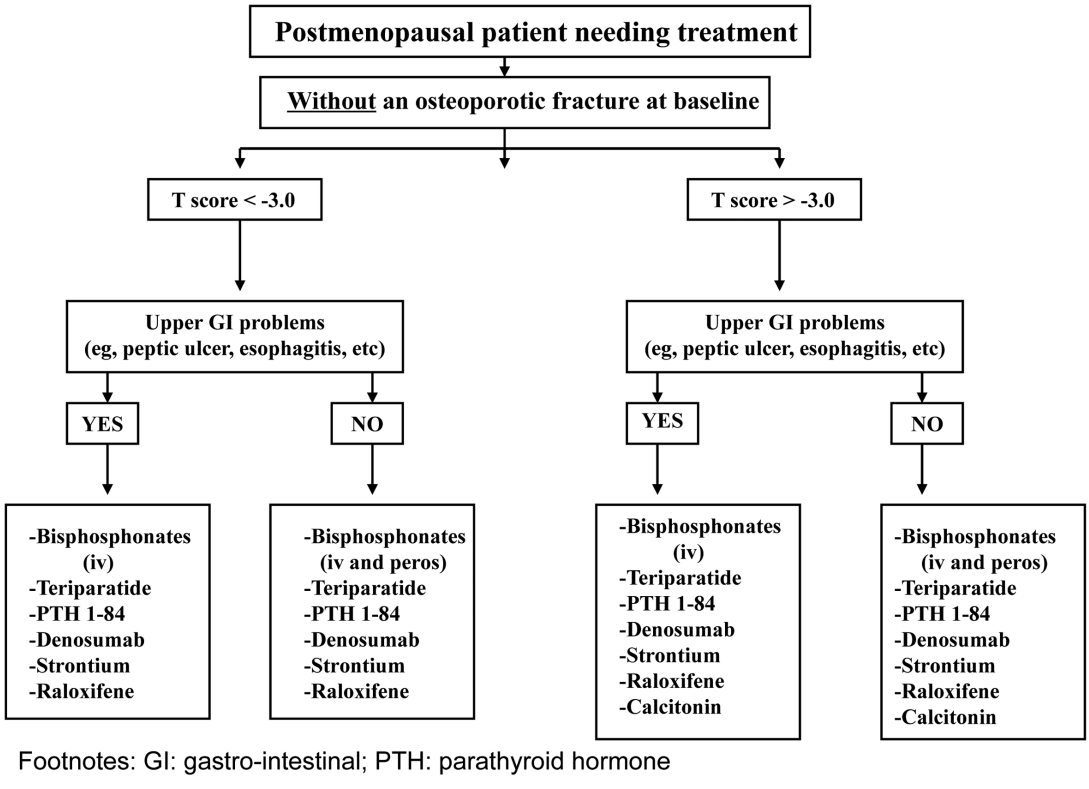


Figure 2. Algorithm for osteoporosis treatment: postmenopausal patients with a fracture at baseline.



Footnotes: GI: gastro-intestinal; PTH: parathyroid hormone; FN: femoral neck

Figure 3. Algorithm for osteoporosis treatment: postmenopausal patients without a fracture at baseline.



Footnotes: GI: gastro-intestinal; PTH: parathyroid hormone

exhibiting a corresponding efficacy of preventing fractures. In women requiring treatment but lacking an osteoporotic fracture at baseline the algorithm in Figure 3 should be followed. The panel also accepts that the most common cause of defective compliance to anti-osteoporotic treatment in Greece is either the treatment-induced problems of the upper gastrointestinal tract or the aggravation of the already existed gastrointestinal symptoms and signs. Thus, the treatment algorithms in Figures 2 and 3 are taking into consideration the presence of these problems and/or conditions.

In men requiring treatment alendronate, risedronate, zolendronic acid and teriparatide can be used. Denosumab should be administered only in patients with prostate cancer under anti-androgen therapy with an increased risk of vertebral fractures.

In all occasions (men and women), daily co-administration of 400-800 I.U. of vitamin D3 or an equivalent vitamin D analogue is strongly recommended. In addition, a total calcium consumption (dietary and/or through supplements) of 1200 mg per day must be ensured. Physicians should continuously encourage physical exercise, smoking cessation and avoidance of alcohol consumption. Consultation regarding protection from falls is recommended, too.

Other recommendations - comments

- In patients with recent vertebral fractures co-administration of calcitonin can be considered for analgesia. Teriparatide has also analgesic effect in back pain.
- Consider denosumab in renal insufficiency.
- Among women with an increased risk of breast cancer raloxifene might be considered as the initial treatment approach.
- Anabolic treatment with teriparatide or PTH 1-84 should be immediately followed by bisphosphonates.
- Patients with a poor response to treatment should be re-evaluated for secondary causes of osteoporosis.
- Patients with a poor compliance to treatment should be treated with medications requiring longer between-treatments intervals.

In conclusion, the treating physician should choose the most suitable treatment for the patient based on medical history, fracture risk, previous treatment for osteoporosis and concomitant treatment for other diseases, treatment-induced risks and benefits, as well as future follow-up. Finally, the relation of financial cost and potential benefit is an issue that should be always considered in all diagnostic procedures and therapeutic decisions.

References

1. Papaioannou A, Morin S, Cheung AM, Atkinson S, Brown JP, Feldman S, Hanley DA, Hodsman A, Jamal SA, Kaiser SM, Kvern B, Siminoski K, Leslie WD; Scientific Advisory Council of Osteoporosis Canada. 2010 clinical practice guidelines for the diagnosis and

management ofosteoporosis in Canada: summary. CMAJ 2010;182(17):1864-73.
2. National Osteoporosis Foundation. The Clinician's Guide to Prevention and Treatment of Osteoporosis. 2010. www.nof.org
3. 2010 Official Positions of the ISCD/IOF on the Interpretation and Use of FRAX in Clinical Practice. www.iscd.org
4. International Society for Clinical Densitometry Official Positions. 2007. www.iscd.org
5. Hellenic Osteoporosis Foundation (HELIOS). Guidelines for the Diagnosis and Treatment of Osteoporosis in Greece. 2009. www.heliost.gr
6. Baltas CS, Balanika AP, Raptou PD, Tournis S, Lyritis GP; Hellenic guidelines on bone densitometry working group. Clinical practice guidelines proposed by the Hellenic Foundation of Osteoporosis for the management of osteoporosis based on DXA results. J Musculoskelet Neuronal Interact 2005;5(4):388-92.
7. Hellenic Endocrine Society (Bone Section). Brief Guide for the Diagnosis, follow-up and treatment of Osteoporosis. 2011. www.endo.gr