How should a DEXA scan be used to evaluate bisphosphonate therapy for osteoporosis?

EVIDENCE-BASED ANSWER

If bone density is evaluated after initiating bisphosphonate drug therapy, it should be tested no earlier than 2 years (strength of recommendation [SOR]: **B,** based on case series of dual energy x-ray absorptiometry [DEXA] scanning precision and bisphosphonate efficacy). Currently no prospective, randomized trials investigate the impact of bone density follow-up testing on osteoporotic patients receiving bisphosphonate therapy.

EVIDENCE SUMMARY

Testing the effectiveness of therapy for osteoporosis by measuring changes in bone mineral density (BMD) is difficult because changes are often small and occur slowly, and a decrease in BMD does not necessarily mean treatment failure. Testing patients after starting bisphosphonate therapy has been part of many drug trials to assess the effectiveness of therapy. Follow-up testing in clinical practice has not been the focus of a prospective trial and therefore remains controversial.[1]

DEXA is considered the gold standard because it is the most extensively validated test for predicting fracture outcomes.[2] Understanding the rate of bone density response to therapy, and the precision error of DEXA, helps to determine monitoring intervals. The larger the responses in BMD to therapy and the more precise the DEXA scan result, the shorter the period between testing in which clinically relevant differences can be found. Precision error rates are estimated at <1% for the anterior-posterior spine and 1% to 2% for the hip.[3] The BMD change after the initiation of treatment must escape the precision error of the testing device or exceed the least significant change (LSC) value.[4] The LSC—roughly analogous to a 95% confidence interval—is 2.8 times the precision error of the test on a specific machine and site of measurement. If the precision error for DEXA of the femoral neck BMD is 2%, then the LSC is 5.6%.[5] Changes in BMD of <2%–4% in the vertebrae and 3% to 6% at the hip could be due to inherent measurement error.[6]

A clinician must also understand the anticipated response to the prescribed therapy. It is not

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FIGURE

Bone mineral density in osteoporosis

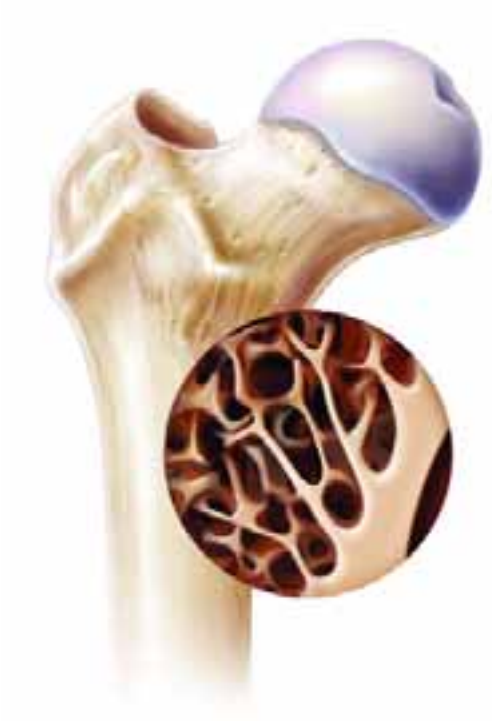

ILLUSTRATION BY JENNIFER FAIRMAN

DEXA scanning is useful if its limitations are understood

Imprecision is a reality with the DEXA scan. Clinical experience has shown that, for patients receiving biphosphonate therapy to increase bone mineral density (BMD) in the femoral neck, any change in BMD of less than 5.6% may be due to measurement error and should not necessarily prompt a change in treatment. BMD response to bisphosphonates vacillates in the first few years of use but can be expected to increase femoral neck BMD by 3% to 6% over 3 years. If serial DEXA scanning is made part of the management plan, it should be considered no sooner than 2 to 3 years following the start of therapy.

clinically useful to retest BMD before a therapy would have time to affect bone turnover. Alendronate and risedronate increase lumbar spine BMD by 5% to 7% and hip BMD by 3% to 6% when used for approximately 3 years.[7,8] These increases in BMD are associated with 30% to 50% reductions in vertebral and hip fractures.[6] Alendronate continues to increase BMD: following 10 years of treatment, it increased BMD by 13.7% in the lumbar spine, 6.7% in the total hip, and 5.4 % in the femoral neck.[9]

Frequent testing, as seen in bisphosphonate clinical trials, demonstrates the phenomenon of regression to the mean. One analysis of the FIT trial, which compared alendronate with placebo in postmenopausal women with low BMD and at least 1 vertebral fracture, focused on the early evaluation of BMD. The study found a high degree of variability in BMD when tested after 1 year of treatment. This wide variety of response in the first year normalized in the second year.[10] A second analysis showed that when women were divided into 8 groups, the group with the greatest increase in BMD in the first year (10.4%) also had the greatest decrease (1.0%) in year 2. In addition, the group with the greatest decrease in year 1 (6.6%) had the greatest increase in year 2 (4.8%). The variability in response among the 8 groups was approximately 17% (+10.4% and –6.6%) in year 1 and narrowed to a 6% difference in year 2 This regression to the mean leads to a normalization of bone density results.[11,12] This patient variability in BMD response to the prescribed therapy should be considered when deciding to retest.

In summary, limitations in DEXA precision mean any changes in BMD of less than 5.6% at the femoral neck may be due to measurement error, and BMD response to bisphosphonates vacillates in the first few years of use but can be

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TABLE

Recommendations on monitoring the clinical response to DEXA in osteoporosis therapy

Organization	Method used to formulate responses recommendation	Recommendations for monitoring treatment to anti-resorptive therapy
AHRQ Evidence Report (*Osteoporosis in Postmenopausal Women*)[14]	Systematic review	Advises against repeating bone density tests within the first year of treatment. Insufficient evidence to determine whether repeating tests 2 years after starting therapy is useful
American Association of Clinical Endocrinologists[13]	Rating scheme (Statement not rated)	Yearly for 2 years and if bone mass has stabilized, follow-up measurements are recommended every 2 years
Canadian Panel of Int'l Society for Clinical Densitometry[15]	Not stated	Repeat scan should be considered after 1 to 3 years if concerned about progressive bone loss or with new intervention
Institute for Clinical Systems Improvement[1]	Not stated	Controversy exists as to whether follow-up testing is necessary in all patients, but if performed, it should be done after 1 to 2 years of therapy
National Institute of Health[16] change	Expert consensus	Monitoring has not been shown to improve compliance. Physicians should not stop or therapies because of modest bone density loss
National Osteoporosis Foundation[6]	Expert consensus	Recommended 1 to 2 years following initiation of therapy
North American Menopause Society[17]	Expert consensus	Monitoring before 2 years of treatment would not be useful
Osteoporosis Society of Canada[18]	Not stated	Suggests at least 1 follow-up measurement is necessary. Central bone densitometry 1 to 2 years following initiation of bisphosphonate therapy. For patients receiving hormone therapy, repeat BMD is recommended at 2 to 4 years
University of Michigan[19]	Evidence rating scheme	For most persons an interval of >2 years between DEXAs provides the most meaningful information

expected to increase femoral neck BMD 3% to 6% over 3 years. Therefore, if serial DEXA scanning is preformed on patients prescribed bisphosphonate therapy, it should be considered no earlier than 2 to 3 years after therapy begins. When monitoring osteoporosis therapy, a BMD change within the LSC should be interpreted as "no change" and should not lead to changes in patient management. If the BMD has decreased beyond the LSC there is cause for concern and reevaluation of diagnosis and treatment are warranted.[4]

RECOMMENDATIONS FROM OTHERS

Guidelines on monitoring the clinical response to osteoporosis therapy with DEXA are available from numerous groups (**Table**). In clinical practice, it is common for a BMD difference of 3% to 5% at the spine or 4% to 6 % at the hip to be considered clinically significant.[13]

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CLINICAL COMMENTARY

If follow-up is needed, rescan in 2 to 3 years

Rates of vertebral and hip fractures are significantly reduced by alendronate and risedronate, making them important in the prevention and treatment of osteoporosis. Despite controversies over the timing and necessity of monitoring bisphosphonate therapy with DEXA scans, they may be useful clinically if their limitations are recognized. It is necessary to wait 2 to 3 years to repeat the DEXA after initiating therapy to account for the slow rate of change of bone density and compensate for the regression-to-the-mean phenomenon seen in clinical trials.

If after 2 or 3 years the bone density remains stable or has increased, reassurance can be given that fracture risk has decreased. If bone density has decreased more than the LSC, consider the following questions. Is the medicine is being taken first thing in the morning on an empty stomach? Is weight-bearing exercise performed routinely, tobacco avoided, and caffeine limited? Is the patient continuing adequate calcium and vitamin D supplements? The physician should also consider secondary causes of osteoporosis, such as hyperthyroidism and hyperparathyroidism.

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