Panel Session: Bone Mass, Bone Loss Measurement

Panel Summary

VIRGINIA M. PAPPAS, CAE

Ms. Pappas is Deputy Executive Director, Society of Nuclear Medicine, New York, NY. Ms. Pappas served as the Moderator of the panel "Bone Mass, Bone Loss Measurement" at the FDA Special Topic Conference on Osteoporosis, sponsored by the Food and Drug Administration, held at Bethesda, MD, October 30, 1987. This article is a summary of the panelists' presentations.

SEVERAL ASPECTS of the topic were discussed during the panel on "Bone Mass, Bone Loss Measurement." First, since estrogen can prevent postmenopausal bone loss, and fast bone losers respond to therapy, fast bone losers must be identified early so that treatment can begin. Second, in a comparison of various methods to measure bone mineral content, dual photon absorptiometry (DPA) and dual energy radiography (DER) were rated as the most important clinical procedures. Third, the usefulness of quantitative computed tomography (QCT) was discussed for predicting fracture risk.

Dr. Claus Christiansen, in his talk entitled "Usefulness of Bone Mass, Measurements by Photon Absorptiometry," stated that estrogen therapy can prevent postmenopausal bone loss, stop bone loss, or increase bone mineral retention a few percent; optimal doses of estrogen for prevention of osteoporosis are known; and it is not safe to use estrogen therapy on all women. Therefore, finding the women who are at the highest risk to develop osteoporosis just after menopause is important, so that treatment can be given to that group.

The procedures that Dr. Christiansen recommended are a bone mass measurement at menopause, combined with an estimate of bone loss after menopause. Dr. Christiansen recommended measurement of the forearm by single photon absorptiometry (SPA), along with blood and urine tests to determine levels of serum alkaline phosphatase and urinary hydroxyproline to distinguish among slow, normal, and fast bone losers. The borderline, or normal, group would then be evaluated based on risk factors, the slow bone losers would not be treated, and the fast bone losers would be treated with estrogen therapy. A study of various doses of estrogen and placebo showed that the best results were obtained with low and mid-level estrogen doses in the fast bone losers.

Dr. Heinz Wahner, in his talk on "Technical Aspects and Clinical Interpretation of Bone Mineral Measurements," reviewed the various methods for estimating bone mineral content. They are: SPA, with the radius and calcaneus being the sites of greatest interest; dual photon absorptiometry (DPA), with spine, hip, and total skeletal measurements; DEXA or x-ray absorption, a new procedure designed as a technical improvement of DPA; and QCT for trabecular bone. Dr. Wahner gave details of the procedures he considered clinically most attractive, which were DPA and DEXA, with much more emphasis on DEXA.

In DPA, the spine, hip, or the entire patient is scanned with a dual energy photon beam. Two absorption curves are obtained, from which bone mineral content is calculated. Measurements can be performed with a precision of 2–3 percent coefficient of variation (CV), for spine, femur neck, and trochanter, and 4–6 percent for Ward's triangle. The method has a similar accuracy when tested on ashed bone, and is relatively insensitive to variation in body composition. Extremes in body thickness require special consideration.

DEXA is a new method, similar to DPA in its concept and performance, but based on dual energy x-rays rather than on an isotope source. The use of x-rays results in a stable, incident-radiating intensity (no decay as with an isotope source), a smaller beam results in bone mineral images of higher resolution, and, most importantly, the precision is better, about 1.0 percent (CV). The data output and display are similar to those from a single photon instrument. When the results from DPA and DEXA instruments are compared, they are highly correlated over the entire range of bone mineral content seen in patients. Bone mineral density measurements by DEXA are 4–6 percent lower because of more accurate assessment of bone area. As in DPA, the position of the bone in the radiation beam is critical, and patient thickness has some influence on the results. These problems are well known from using DPA, and can be compensated for.

Even though the usefulness of bone mass measurements is still debated, Dr. Wahner stated that they are potentially useful in clinical practice in two different approaches: *(1)* as regional bone mineral measurements for fracture risk assessment and *(2)* as

repeated bone mineral measurements for estimating the integrated rate of bone loss over periods of 1–2 years.

While the debate continues, Dr. Wahner feels that one should not overlook the meaningful clinical information on diagnosis and management of osteoporosis and diseases or conditions associated with bone loss that can be obtained with bone mineral measurements. The rate of loss has been difficult to estimate in the past with usefully short intervals, but with new techniques such as DEXA more confidence can be placed on these measurements, and the time interval can be shortened to more meaningful time limits. The new DER-based fast scans should allow patient cost reduction because of shorter scanning time, and no need to buy new isotope sources, as with DPA. Accuracy and precision will be improved, and the rate of loss measurements and fracture risk predictions in the hip should be more valid. Improvements in region of interest selection in the hip have also made this site more attractive for hip fracture risk prediction in clinical practice. Greater insight can be expected within the near future. Dr. Wahner warned that consumers who choose to have a bone mineral measurement without interpretation by a physician who is familiar with their health condition risk getting little more than a number, with a high chance for misinterpretation due to the complexity of the techniques.

Dr. Daniel Rosenthal's talk, entitled "Bone Mass Measurement, Fracture Risk, and Screening for Osteoporosis," focused on the question: Does the knowledge of bone mass allow determination of fracture risk? Dr. Rosenthal stated that two tests are widely available for axial bone mass determination: DPA and QCT. His talk focused on QCT.

Both procedures, when used on the spine, are capable of distinguishing between patients with and without vertebral compression fractures. There appears to be a level of bone mass below which fractures occur, regardless of patient age. This has led to the concept of the "fracture threshold." Patients whose bone density values are above the fracture threshold are seldom found to have sustained spontaneous vertebral fractures. Clinical studies continue to show that fractures are most prevalent in those patients with the lowest bone density measurements. Since the definition of fracture threshold is based on cross-sectional data and on prevalent, rather than incident, cases, the concept of fracture threshold is of limited value in determining future fracture risk. To accurately estimate fracture risk prospectively, studies of fracture occurrence and bone mass must be conducted.

The precision and accuracy of QCT have been thoroughly studied; precision error can be minimized by scrupulous attention to detail. Repeat scans should be performed on the same scanner, preferably by the same technician, and supervised by the same physician. The greatest asset of QCT as a measurement modality is its sensitivity to change. It is the only available technique which can evaluate trabecular bone separately from cortical bone.

Limited data are available on the relationship between spinal bone mass and hip fractures. Although bone mass measurements taken in the hip of hip fracture patients are consistently lower than those taken in nonfracture patients, differences in spinal measurements among the two groups are small and inconsistent. Thus, neither QCT nor DPA of the spine appears to be a suitable tool for identifying patients at specific risk for hip fracture. Direct application of QCT to the hip has been slow to develop, probably because of the anatomical complexity of that region. Studies at the Mayo Clinic have attempted to quantify the relationship between DPA measurements in the hip and fracture risk. The results indicate that this technique may allow prediction of hip fracture risk. If these data can be confirmed prospectively, they will have a large impact on the screening debate.

In closing, Dr. Rosenthal concluded:

1. Bone mass measurements are effective for identifying patients with osteoporosis of the spine, and possibly effective in the hip, but more research is needed for confirmation of the latter.
2. Measurements of bone mass in the extremities may be useful when it is necessary to know the extent of cortical bone loss, but have no place in screening for osteoporosis.
3. Prospective patients should be aware that the modalities are complex, and subject to many potential sources of error. Only experienced medical centers with close physician supervision should be selected to perform measurements.
4. The net economic cost of screening programs to detect osteoporosis must be thoroughly evaluated, and weighed against the health benefits achieved under each program, before policy recommendations regarding screening can be responsibly made.