Panel Session: Bone Mass, Bone Loss Measurement

Bone Mass Measurement, Fracture Risk, and Screening for Osteoporosis

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Synopsis

There is a positive relationship between bone mass and resistance to breaking. Measurements of the spine made by quantitative computed tomography (QCT) and dual photon absorptiometry (DPA) appear to allow a determination of the risk of vertebral compression fracture, although some important confirmatory studies remain to be done. Measurements made in the extremities generally do not allow prediction of vertebral fracture risk.

Prediction of hip fracture risk is difficult because of the complex geometry of the femur. The few data which are available suggest that DPA may be useful to predict the risk of femoral neck fracture. If these data can be confirmed, cost-benefit analysis indicates that mass screening for osteoporosis may be a viable strategy.

Physicians and patients using bone mass measurement techniques should be aware that these tests can be misleading, and that scrupulous attention to detail is required. Close supervision of the tests by a physician is necessary to ensure that meaningful data are obtained.

EXPERIMENTAL STUDIES HAVE CONFIRMED the association of low bone mass with decreased bone strength. For compressive forces, bone strength is proportional to the square of bone density *(1)*. In the clinical setting, the relationship between bone density and fracture risk is more complex. Fractures partly result from lack of bone strength; fractures also result from the interplay among the nature, direction, and violence of traumatic forces, and the protective effect of muscles and soft tissues. Further, the decrease in bone strength that occurs with age is greater than the decrease in density. Certain fractures generally do not occur until bone mass is significantly decreased below young adult values.

The most common osteopenia-related fractures are those of the hip, spine, and distal radius. Attention has been directed toward spinal fractures because of their frequency, and toward hip fractures because of their serious consequences.

Does knowledge of bone mass allow determination of fracture risk? This question has two parts: *(a)* Is knowledge of bone mass at a given site predictive of fracture risk at that site, or do other factors supervene? and *(b)* Do measurements made in one part of the skeleton accurately reflect the condition elsewhere?

Measurements of the appendicular skeleton generally have not been useful for prediction of fracture of the spine or hip *(2–4)*. Recently, absorptiometry of the calcaneus has been reported to be an exception to this rule *(5)*, but experience with this technique is limited. Two methods for assessing axial bone mass are widely available: dual photon absorptiometry (DPA) and quantitative computed tomography (QCT).

Both DPA and QCT of the spine are capable of distinguishing between patients with and without vertebral compression fractures *(6–9)*. There appears to be a level of bone mass below which fractures occur, regardless of patient age. This has led to the concept of "fracture threshold." Patients whose density values are above the fracture threshold seldom have spontaneous vertebral fractures. For QCT, the fracture threshold varies from approximately 90 milligrams (mg) K_2HPO_4 per cubic centimeter (cc) to 110 mg K_2HPO_4 per cc *(10,11)*. For DPA, the fracture threshold is approximately 1.0 gram per square centimeter *(12)*. Since mean bone

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mass declines with age, by 75 years most women are below the fracture threshold. Nonetheless, clinical studies continue to show that fractures are most prevalent in those patients with the lowest density measurements *(13)*.

Unfortunately, the definition of fracture threshold is based on cross-sectional data and on prevalent, rather than incident, cases. The concept of fracture threshold is, therefore, of limited value in determining future fracture risk. To accurately estimate fracture risk, prospective studies of fracture occurrence and bone mass must be conducted. This type of information may soon become available since both DPA and QCT have been in use for a long time.

The precision (reproducibility) and accuracy of QCT have been studied in detail. Short-term precision in patients has been reported to be 1–3 percent *(4)*, but in our experience the precision error does not depend upon density. If the error is expressed as a percentage, it will appear to be higher in more osteopenic individuals *(10)*. We believe that the average density of four lumbar levels (L1–L4) has a mean precision error of 5 mg per cc, regardless of density. QCT tends to underestimate mineral content because of the effect of marrow fat. This effect is approximately 1 mg mineral for every 10 mg fat, and may be partially corrected for by using a dual energy QCT technique *(11)*.

Error in precision can be minimized by scrupulous attention to detail. In QCT scanning, some of the factors that we have found to be significant are close contact between the patient's back and the mineral phantom, and consistency of repositioning, including centering within the gantry, selection of slice position, angulation, and choice of the region of interest *(12)*. Repeat scans should be performed on the same scanner, preferably by the same technician, and supervised by the same physician. The characteristics which make a quantitative scan reliable are not the same as those which produce good images, and consequently we have found that few technicians adapt easily. In our institution, close and constant physician supervision is necessary, despite the fact that our technicians have been performing this procedure for 8 years.

The greatest asset of QCT as a measurement modality is its sensitivity to change. It is the only available technique that can evaluate trabecular bone separately from cortical bone. Since the turnover rate of trabecular bone is approximately 6–7 times greater than that of cortical bone, this is a significant advantage in detection of early disease, and early response to therapy. In a study of women treated with estrogen after removal of the ovaries, QCT scans showed significant bone loss in untreated women, and a protective benefit from estrogen replacement earlier than all other modalities *(13)*. In our studies of parathyroid hormone treatment of osteoporosis *(14)*, QCT revealed marked increases in trabecular bone, while cortical measurements were unaffected.

Limited data are available on the relationship between spinal bone mass and hip fractures. Although measurements taken on the hips of hip fracture patients are consistently lower than those taken in nonfracture patients, differences in spinal measurements between the two groups are small and inconsistent *(15)*. Low spinal values are found, but they are not necessarily below the limits of age- and sex-matched normals, and, in fact, not necessarily below the threshold for spinal fracture *(16)*. Thus, neither QCT nor DPA of the spine appears to be a suitable tool for identifying patients at specific risk for hip fracture. Development of direct application of QCT to the hip has been slow, probably because of the anatomical complexity of that region. Recently, applications of 3-D techniques have been rewarding *(17)*, but the technique is not ready for widespread clinical use. DPA of the hip has proven to be difficult. We have found that it is subject to large precision errors, owing to repositioning difficulties. Studies at the Mayo Clinic *(18)* have attempted to quantify the relationship between DPA measurements of the hip and fracture risk. Those results indicated that this technique may allow prediction of hip fracture risk. If these data can be confirmed prospectively, they will have a great impact on the debate about screening *(19)*. Although it may be possible to demonstrate that large-scale screening is cost-effective in identifying persons at risk of hip fracture, screening for vertebral fracture risk probably would not be cost-effective.

Maximum benefit from screening for skeletal mass can be obtained if these procedures are used in the perimenopausal and early postmenopausal years. Since estrogen therapy appears to be effective in preventing or slowing bone loss, but does not lead to substantial recovery of lost mineral *(2)*, greatest benefit can be obtained if therapy is instituted before substantial bone mineral is lost. The time between re-

examinations should be based upon estimates of the rate of loss of bone, and the precision error inherent in the technique. The average rate of bone loss in postmenopausal women is about 2 percent per year *(2)*, although in some patients a much greater rate of decline, about 7–9 percent, occurs during the early postmenopausal years *(13)*. Given the precision error of both QCT scanning and DPA, after a 1-year interval in a single patient, the results of re-evaluation would probably be equal. Multiple measurements are necessary to accurately assess individual rates of bone loss.

In conclusion, it is important to recall that screening populations is only one application of quantitative bone mass measurements. Screening is controversial because of its public health and economic importance. Other applications, such as evaluation of the high-risk patient, or following the effects of therapy, are much less contentious.

Conclusions

- Bone mass measurements are effective for identifying patients with osteoporosis of the spine, and possibly effective for the hip, but more research is needed for confirmation of the latter.
- 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 role in screening for osteoporosis.
- Prospective patients should be aware that the modalities are complex, and subject to many potential sources of error. Only experienced centers with close physician supervision should be selected for performing measurements.
- The net economic cost of screening programs to detect osteoporosis must be thoroughly evaluated, and weighed against the net health benefits achieved under each program, before policy recommendations regarding screening can be responsibly made.

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