Panel Session: Bone Mass, Bone Loss Measurement

Usefulness of Bone Mass Measurements by Photon Absorptiometry

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Synopsis . . . .

We compared three different methods of measuring bone mass for their diagnostic value and their usefulness in follow-up measurements. The three methods were: measurement of (1) bone mineral content in the distal forearm by single photon (^{125}I) absorptiometry, (2) bone mineral content and bone mineral density of the lumbar spine measured by dual photon (^{153}Gd) absorptiometry, and (3) total body bone mineral and total body bone density also measured by dual photon (^{153}Gd) absorptiometry. The diagnostic validity was evaluated from measurements on healthy premenopausal women, and three groups of postmenopausal osteoporotic women (prior forearm fracture (N = 45), prior spine fracture (N = 46), or prior hip fracture (N = 27)). The forearm measurement separated all three osteoporotic groups from the premenopausal women at least as well as the spine measurement. The value of follow-up procedures was estimated using data from a clinical trial on prevention of postmenopausal bone loss by sex hormones. Fewer participants are needed in clinical trials when a forearm scanner is used instead of a spine scanner, because of the better precision of the former.

The forearm scanner seems to be the best tool of the three for bone mass measurements, in both clinical practice and for research purposes.

MEASUREMENT OF the bone mineral content of the skeleton plays a major role in osteoporosis research. During the last two decades, a variety of techniques have been developed, including simple radiography (1), single (2) and dual (3) photon absorptiometry, quantitative computed tomography (4), neutron activation analysis (5), and ultrasonic attenuation (6). Of these methods, single and dual photon absorptiometry are the most widely used. Bone mineral content of the appendicular skeleton can be measured by single photon absorptiometry (2), while area (7) and total body (3) bone mineral content can be measured by dual photon absorptiometry. We studied the various photon absorptiometric techniques for diagnosing osteoporosis and evaluating changes in bone mass over time, as found in our department during the last 5 years. This paper reports these findings.

Methods

Bone mineral content of the distal part of the forearm (BMC_{arm}) was measured by single photon (^{125}I) absorptiometry as developed in our laboratory (2). Measurements of both arms required 15 minutes.

Bone mineral content (BMC_{spine}) and bone mineral density ($BMD_{spine} = BMC_{spine}$ divided by the projected scan area) in the lumbar spine ($L_2 - L_4$) were measured by dual photon (^{153}Gd) absorptiometry (DP 3 Scanner, Lunar Radiation Corp.). One scan required 45 minutes.

Total body bone mineral (TBBM) and total body bone density (TBBD = TBBM divided by the projected area of the skeleton) were measured by dual photon (^{153}Gd) absorptiometry on a whole body scanner developed in our laboratory (3). One scan of a normal adult required 90 minutes.

For follow-up measurement, BMC values should be used, as calculation of BMD depends on the estimation of the area of interest, and therefore introduces another source of variability. BMD values may be preferable, however, in longitudinal spinal measurements on osteoporotic subjects, since division by the area scanned also corrects for the errors of repositioning, or reselecting the edges and borders of the region. For diagnostic purposes and comparisons

Table 1. Accuracy and precision of photon absorptiometric methods

Parameter	BMC_{arm}	BMC_{spine}	BMD_{spine}	TBBM
Accuracy	0.98[1]	0.97[1]	—	0.99[1]
Precision (coefficient of variation, percent)				
Short-term	0.6[2]	3.0[2]	2.8[2]	1.3[1]
Long-term	1.0[2]	3.4[2]	3.7[2]	2.1[1]

[1] Reference (9).
[2] Reference (8).

Table 2. BMCarm, BMDspine, and TBBD in three groups of osteoporotic patients[1]

Type fracture	N	BMC_{arm}	BMD_{spine}	TBBD
Colles'	45	− 2.6 ± 1.3	− 1.9 ± 1.2	− 2.5 ± 1.3
Spinal	46	− 2.8 ± 1.2	− 2.3 ± 1.0	− 2.8 ± 1.0
Femoral neck	27	− 2.7 ± 1.4	− 2.2 ± 1.2	− 3.4 ± 1.0

[1] The values (mean + SD) are expressed as z scores (deviation in standard deviations from healthy premenopausal mean); z score = (measured value − mean premenopausal value)/premenopausal standard deviation. The data are from Reference (11).

among groups, BMD values may be more useful, as division by the area scanned also corrects for individual variability.

Diagnostic Values

All three methods have a relatively low accuracy error (table 1), and the local bone mass measurements correlate with TBBM (10). The standard error of the estimate of the correlation between the BMC_{arm} and the BMC_{spine} is more than 10 percent (10). This has led some researchers to conclude that the spinal measurement is better than the forearm measurement for diagnosing spinal osteoporosis. It is, however, not important to know how well the forearm measurement predicts spinal osteopenia, documented by a local spinal measurement, which itself is imprecise. The important issue is the diagnostic ability to predict an osteoporotic fracture.

The ability of the diagnostic values of the three measurements (BMC_{arm}, BMD_{spine}, and TBBD) to distinguish three groups of osteoporotic women from healthy premenopausal women is reported in table 2. The osteoporotic groups were defined by a history of Colles', spinal, or femoral neck fractures. Although

discrimination among healthy premenopausal women and osteoporotic postmenopausal women has little clinical relevance, the diagnostic ability in this situation probably has implications for the general diagnostic ability of the measurements. The overlap between normal premenopausal and osteoporotic postmenopausal values was largest for the BMD_{spine} measurement for all three fracture types. Therefore, even for a spinal fracture, the forearm measurement seems to be at least as good a diagnostic tool as the spinal measurement.

None of these measurements is, however, able to discriminate effectively between age-matched postmenopausal women, with and without osteoporotic fractures (12). Diagnosis of manifest osteoporosis has, however, only limited clinical value as yet, since therapy for this disorder is still in the experimental stages. The diagnostic value of these measurements lies, therefore, primarily in its usefulness as a research tool, and for determination of peak bone mass at menopause. For these purposes, forearm measurements seem to be at least as useful as spinal measurements.

Follow-up Measurements

Of the three methods reported here, the forearm measurement has the greatest precision (table 1). The practical relevance of precision is illustrated in figure 1. The minimum detectable significant (95 percent confidence limit) difference between two measurements in a single subject is 2.8 percent if the measurement precision is 1 percent, and 14 percent if the measurement precision is 5 percent (figure 1, left). A bone loss of 2 percent per year, corresponding to that in a normal early postmenopausal woman (13), would therefore take 1.4 years to detect with an apparatus with 1 percent precision, and 7.1 years using one with a 5 percent precision if only two measurements were made. For research purposes, groups of patients are often studied. If the biological variability is ignored (figure 1, right), and a difference at 0.5 percent on a group basis is to be detected from two measurements on each subject, then a 1 percent precision demands 32 subjects, while a 5 percent precision demands 800 subjects. Although the biological variation will increase both these numbers, and the 32 relatively more than the 800, this example clearly demonstrates that research resources can be spared by using the measurement with the greatest precision.

The value of BMC_{arm}, BMD_{spine}, and TBBM in longitudinal studies is illustrated in figure 2, which shows the results from a double-blind, placebo-controlled study on the prevention of early

postmenopausal bone loss by combined estrogen-progestogen therapy *(14)*. The mean difference in response between the treated and the placebo group was the same for all three measurements, but the variability in the measured response was much larger for the BMD_{spine} than for the BMC_{arm}. Compared with BMC_{arm}, the use of BMD_{spine} therefore resulted in considerably larger risks of type 1 error. This means that more subjects are needed in prevention studies when a spine scanner is used instead of a forearm scanner if the conclusions are to be considered valid.

The lower long-term precision of the spine scanner compared with the forearm scanner is probably due to the well-known instability of the former during source replacement, and source decay *(8)*. Furthermore, even the short-term precision is lower for the spine scanner, indicating problems with baseline determination and edge detection.

Conclusions

The diagnostic ability of the forearm scanner seemed to be at least as good as that of the spine scanner, even for predicting the risk of spinal fractures. The precision of the forearm scanner was, however, considerably better than the precision of the spine scanner. On the basis of these facts, and the time needed for one scan, the forearm scanner seems to be the best tool for bone mass measurements, both in clinical practice and research purposes. This is primarily due to the higher ratio of changes to precision for this method. The spine scanner might, however, be superior to the forearm scanner in rare situations where the events in the spine are not related to the events in the forearm. If the precision of the BMC_{spine} were in the same range as that of the BMC_{arm}, then the spine scanner would probably be the best instrument for bone mass measurements.

Proven therapy for established osteoporosis does not yet exist. Prevention of bone loss by hormone replacement therapy begun soon after menopause is, therefore, the best possible approach for the management of osteoporosis today.

The risk of developing osteoporosis probably depends partly on peak bone mass, and partly on rate of bone loss. Peak bone mass may be estimated by relating it to body size *(15)*, and rapid bone loss may be predicted by analyzing one blood sample, one urine sample, and measuring body height and weight *(16)*. Bone mass measurements have, therefore, only limited value today in the management of the individual patient. If treatment of osteoporosis becomes possible in the future, and the precision of spine scanners is improved to about 2 percent, then this

Figure 1. Theoretical considerations of photon absorptiometric measurements.
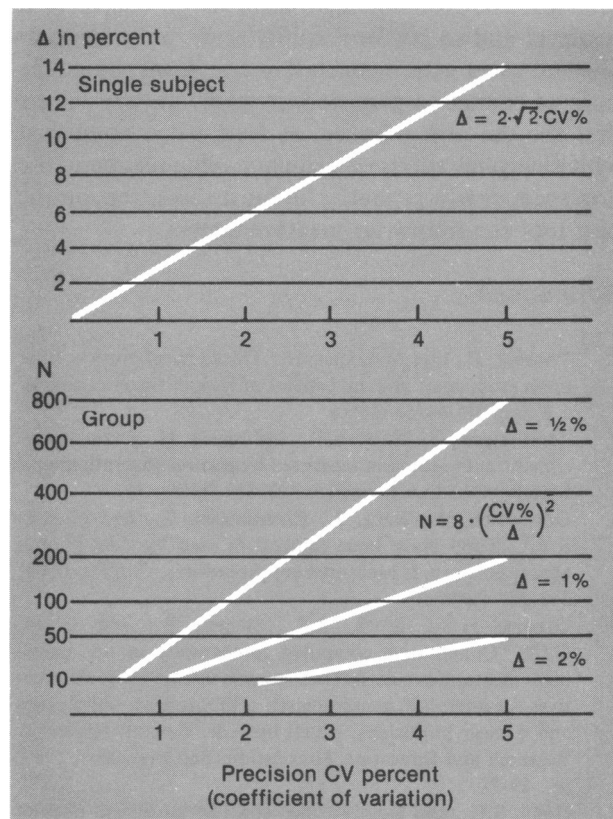
Top: The relationship between precision of the method and the minimal detectable (confidence interval + 95 percent) difference (Δ) between two measurements in one subject.

Bottom: The relationship between precision of the method and the necessary number of subjects in a group to detect (confidence interval 95 percent) a change of 0.5, 1, or 2 percent. Note that the ordinate is quadratic.

Figure 2. Bone Mineral Density (spine), Total Body Bone Density, and Bone Mineral Content (arm) after 2 years of therapy with either estrogen/progestogen (o) or placebo (•) in early postmenopausal women
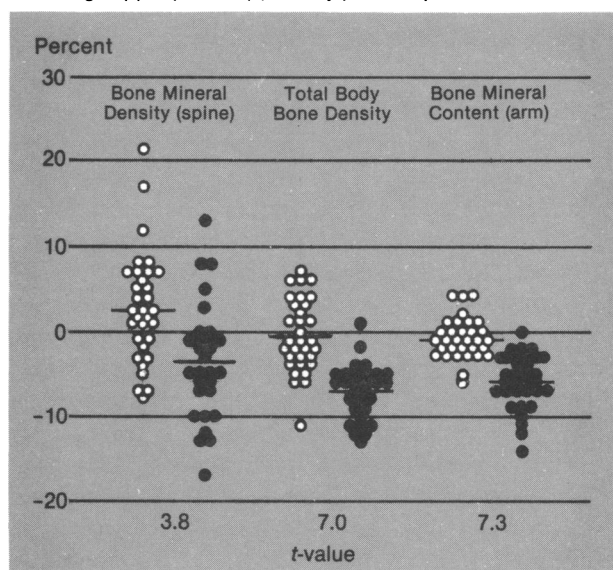
Note: Values are given as percentages of initial levels. Data from Reference *(14)*; *t*-values were obtained from unpaired Student's *t*-test.

scanner might have a well-deserved place in clinical practice. The protocol might be to screen with an arm scanner, and to perform spinal scans only on complicated cases with inconclusive arm scans. Since the ratio of change to precision probably always will be best for the arm scanner, at least when compared with new generations of ordinary spine scanners, the arm scanner will probably, in most cases, remain the best tool for follow-up measurements.

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