PHOTON ABSORPTIOMETRY AND SKELETAL MASS IN THE TREATMENT OF OSTEOPOROSIS

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Thirty-six osteoporotic patients who underwent several therapeutic regimes were studied on two occasions by photon absorptiometry and total-body neutron activation analysis (TBNAA). These determinations were made at a mean interval of 8.9 ± 0.8 months. The 8-cm radial site was chosen for the photon absorptiometry which was performed with the Norland-Instruments Densitometer. Mean initial bone mineral content (BMC) was 0.724 ± 0.069 gm/cm and mean bone width was 1.235 ± 0.072 cm. The mean percent change in BMC (%ΔBMC) was 1.02 ± 4.2. The initial total-body calcium (TB-Ca) as determined by TBNAA was reduced when compared with values that would be expected from empirically derived formulas. The mean percent change in TB-Ca (%ΔTB-Ca) was −3.2 ± 4.7. Most patients displayed a change in BMC and TB-Ca that was at least 2 s.d. greater than the precision of the methods used (%ΔTB-Ca > 2). No relationship was found between the ΔBMC and the ΔTB-Ca (r = 0.17). These findings suggest that changes in the radial BMC at the 8-cm site cannot be extrapolated to indicate changes in skeletal mass in response to treatment of osteoporosis. Whether photon absorptiometry at other sites or at multiple sites provides a closer relationship to changes in skeletal mass (TB-Ca) remains to be determined.

Osteoporosis is a major cause of disability in the aged. Various forms of therapy have been proposed including sex steroids, calcitonin, calcium supplements, and fluoride with vitamin D (*1–5*). Despite the availability of a number of these therapeutic agents for many years, their efficacy remains questionable. This is primarily because objective methodology to assess efficacy has not been available until recently. Objective quantitation is particularly important in a disorder such as osteoporosis in which clinical remissions are not uncommon.

Most patients with vertebral crush fractures (an x-ray finding that is characteristic but not pathognomonic of advanced primary osteoporosis) have lost 20% of their skeletal mass (*6*). It is unlikely that any form of therapy will restore this degree of skeletal loss in a short period of time (e.g., 1 year). This further limits interpretation of subjective improvement and makes it unlikely that routine radiography will be helpful in assessing efficacy of therapy.

Several quantitative methods, however, have recently been applied to this problem with the assumption that improvement in an objective measurement demonstrated over a short period (e.g., 6–24 months) would be sustained. These methods include calcium kinetics and balance, histology of bone biopsy samples, photon absorptiometry, and total-body neutron activation analysis (TBNAA).

This study was designed to determine whether changes in the radial bone mineral content following therapy for osteoporosis reflect changes in skeletal mass [total-body calcium (TB-Ca)] as measured by TBNAA.

MATERIALS AND METHODS

Patients. Thirty-six osteoporotic patients (32 women and 4 men) were studied on two occasions with photon absorptiometry and TBNAA. All had radiologic evidence of osteoporosis and severe, disabling back pain. Almost all the patients had multiple vertebral compression fractures of the dorsal spine. The mean age of the patients was 62 ± 6

Received July 25, 1974; revision accepted Oct. 15, 1974.

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years. They were enrolled in several treatment programs including human growth hormone, calcium supplements, sodium fluoride, and sodium fluoride plus salmon calcitonin. Each patient received only one form of therapy during the study period which varied from 3 to 13 months with a mean interval between determinations of 8.9 ± 0.8 months.

TBNAA. The patients were uniformly exposed to a beam of partially moderated fast neutrons. The radiation dose per activation is 0.28 rem. The induced calcium was then measured with the Brookhaven whole-body counter as previously described (*7,8*). The absolute level of total-body calcium (TB-Ca) can be derived from these data with an accuracy of ±5% and a precision of ±1% (s.d.). Thus, a change of 2% in the TB-Ca in the same patient is significant at the 95% confidence level.

Photon absorptiometry. Bone mineral content (BMC) and the width of the radius (BW) were measured by the Cameron-Sorenson technique using the Norland-Cameron absorptiometer equipped with an ^{125}I source. The 8-cm site was selected for these measurements because positioning errors are minimized in the midradius and because this site is frequently used by other investigators (*9,10*). Under the conditions employed in the present study, the accuracy of this technique is ±5% and the precision is about ±2.5% s.d. (*11,12*). Under optimal laboratory conditions the accuracy and precision are 2–4% and 1–2%, respectively (*12*).

RESULTS

Total-body calcium. The initial TB-Ca in each patient (normalized for sex, age, and skeletal size) was >2 s.d. below that for a nonosteoporotic population (*13*). The initial mean TB-Ca was 640 ± 29 gm and this decreased by 22 ± 31 gm on the second determination. The mean percentage change in total-body calcium (% TB-Ca) was −3.2 ± 4.7. Twenty-two of the 36 patients displayed a change in TB-Ca that was significant at the 95% confidence level (i.e., 2%).

Photon absorptiometry. The correlation between TB-Ca, BMC, and BMC/BW has been previously reported (*6*). There was a close correlation between BMC and TB-Ca (r = 0.81). The mean initial BMC was 0.724 ± 0.069 gm/cm whereas mean bone width was 1.235 ± 0.072 cm. The mean change in BMC (ΔBMC) was 0.011 ± 0.037 gm/cm, and the mean %ΔBMC was 1.02 ± 4.2. Twenty-two of the patients had a change in BMC that was significant at the 95% confidence level. The ΔTB-Ca and ΔBMC are compared in Fig. 1 in 34 of the 36 patients (the points for two patients are beyond the limits of the graph). There was no apparent relationship between the two parameters (r = 0.17).

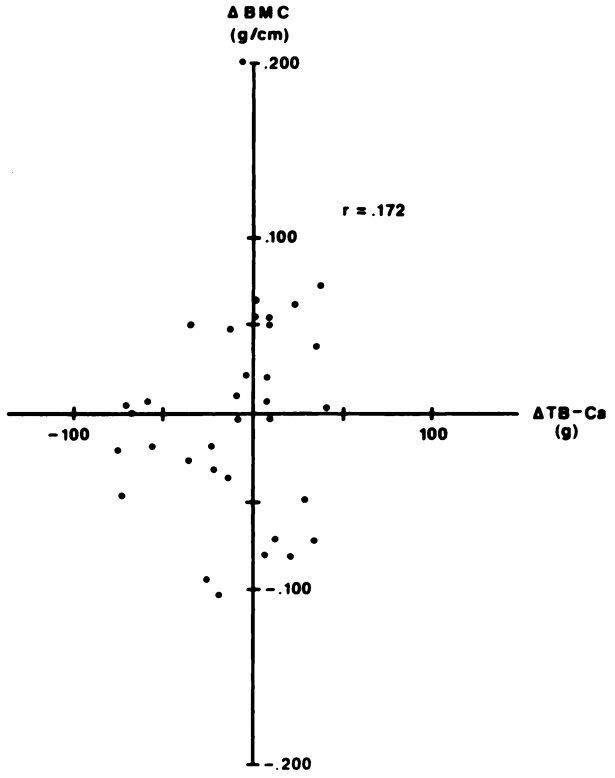

FIG. 1. Comparison between ΔBMC and ΔTB-Ca in 34 patients.

DISCUSSION

Photon absorptiometry of the radius at the 8-cm site varies widely among osteoporotic individuals (*6*). This variation is not only a result of the degree of osteopenia but also is a manifestation of the variables of sex, age, and skeletal size. Bone width (BW) does not provide a meaningful correction (BMC/BW) for these variables (*6*). Accordingly, formulas have been developed by which BMC can be estimated for a given sex, age, and size, thereby providing a means of normalizing the BMC (*13*). Nonetheless, the TB-Ca normalized for sex, age, and skeletal size is statistically more reliable than the BMC for quantitation of the degree of osteopenia in an individual patient (*13*). Although photon absorptiometry separates normal from osteoporotic groups quite well, it is less useful when applied to an individual patient (*13*).

Measurement of TB-Ca is of course more desirable since this measurement normally reflects skeletal mass (99% of TB-Ca resides in the skeleton). Since osteoporosis is conceptually visualized as a disorder of diminished bone per unit volume, TB-Ca should be an accurate reflection of skeletal mass in this disorder.

Because the facilities for TBNAA are costly and technically complicated, it was hoped that photon

absorptiometry could serve as an accurate index of changes in skeletal mass. Indeed, there is a close correlation ($r = 0.826$, $p < 0.001$ between the mean BMC and TB-Ca values in osteoporotic patients (*6*).

In order to extrapolate the mass per unit length derived from absorptiometry at one site of the radius to an estimate of the total skeletal mass, it must be assumed that all areas of the skeleton are proportional to each other. There is convincing evidence that this is so in normal subjects (*14,15*). It can readily be understood, however, that this may not always be the case in metabolic bone disorders, particularly when there is differential remodeling in cortical and trabecular bone. Thus, whereas the correlation between TB-Ca and BMC is high in osteoporosis, it is not as high as in normal subjects (*6*). The correlation between appendicular bone density and skeletal mass results not from the disease process but from a lifetime of normal skeletal growth and development.

The finding in the present study that the ΔBMC of the radius (8-cm site) cannot be interpreted as indicative of changes in skeletal mass in the treatment of osteoporosis is therefore not surprising. The changes in total skeletal mass produced with various forms of therapeutic maneuvers or by the normal attrition of bone over a short period of time (1–2 years) are small and might not be detected in a single bone.

It is quite possible that differential rates of remodeling occur with therapy in various skeletal sites. It is conceivable, therefore, that an increment in BMC of the radius could actually be accompanied by a decrement in total skeletal mass (TB-Ca). The 8-cm site consists predominantly of cortical bone. Since trabecular bone is primarily affected in osteoporosis, a better correlation between ΔBMC and ΔTB-Ca might have been obtained at the 3-cm site which reflects trabecular bone more reliably. This site was not utilized because of its increased error in measurement (due to irregular cross section and inhomogeneity of bone at 3 cm).

Statistically significant changes in the BMC had not occurred in 14 of the 36 patients. It is quite possible that when these patients are followed for a longer period of time, significant differences will develop in the BMC and a better correlation between the ΔBMC and ΔTB-Ca may be obtained. Nonetheless, the tentative conclusion from the present study must be that changes in photon absorptiometry at the radial 8-cm site cannot be extrapolated to indicate changes in skeletal mass. A similar conclusion was reached by Catto, et al (*16*) in their comparison of neutron activation analysis of the hand with photon absorptiometry. These investigators attributed the difference in part to a greater specificity of the neutron activation methods, i.e., photon absorptiometry measures mineral content but is not specific for calcium.

Measurement of TB-Ca does indicate differential changes in bone mass, i.e., trabecular as opposed to cortical bone. Photon absorptiometry may be useful in indicating whether a change in skeletal mass resulted from a change in cortical or trabecular bone or both. Moreover, it is possible that under some conditions (e.g., acromegaly) there may be a differential shift in bone mass (i.e., an increase in cortical bone with a decrease in trabecular bone) while total skeletal mass may remain unchanged (*17*).

ACKNOWLEDGMENT

The research for this paper was supported by the Atomic Energy Commission.

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