ABSOLUTE AND RELATIVE DEFICIT IN TOTAL-SKELETAL CALCIUM AND RADIAL BONE MINERAL IN OSTEOPOROSIS

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There was a marked deficit in the total calcium content of the skeleton in a group of 40 osteoporotic patients as measured by total-body neutron activation analysis (TBNAA). A highly significant correlation (0.826, $p < 0.001$) was found between the bone mineral content of the radius (measured by absorptiometric technique) and total-body calcium (measured by TBNAA). However, the correlation was not as high as in the group of normal subjects (0.973, $p < 0.001$).

In order to measure the relative deficit in total-body calcium in individual patients from the absolute calcium measurement, it was necessary to normalize the data for sex, age, and skeletal size. For this purpose an algorithm was used to predict the normal skeletal calcium in each subject based on lean-body mass, height, sex, and age. In the female osteoporotic group the mean normalized total-body calcium ratio was 0.82 compared with a mean value of 1.00 ± 0.05 (s.d.) in the contrast normal group. For patients with significant loss of height or abnormally low total-body potassium, the calcium ratio is overestimated.

In a similar manner, to facilitate intercomparison of bone mineral content (BMC) measured by absorptiometry, an index of size and age is required. Whereas division of the BMC by the width of the radius (W) tends to reduce the variability in the group, it is not satisfactory as a normalizing factor. In fact, the correlation coefficient of BMC/W with the normalized total-body calcium is low: 0.454, $p < 0.005$.

The large inherent variability in the bone mineral content measurement (of the radius) and the inability to normalize these data often make it unsatisfactory for evaluation of the extent of osteoporosis in an individual. The total-body calcium measurement normalized for sex, age, and skeletal size provides a more accurate technique for evaluating the loss of bone mass and hence is a more useful index for quantitating the degree of osteoporosis in an individual.

A decrease in the total mass of bone, a normal concomitant of the aging process, is apparently accelerated in osteoporotic patients (*1–4*). Loss of calcium from the skeleton is not uniform in osteoporosis. The most striking loss of calcium occurs in trabecular bone of the vertebral bodies but significant losses also occur in the neck of the femur, the upper humerus, and the distal radius (*1,5,6*). Diagnosis of osteoporosis is usually based on radiological evaluation of the vertebral skeleton. A decrease in vertebral density and, more importantly, the occurrence of vertebral compression fractures, are the essential criteria for the diagnosis (*1–4*). When the loss of calcium exceeds the level required for structural integrity, vertebral collapse occurs. Diagnosis of an osteoporotic condition at this stage is reasonably certain.

Unfortunately, prior to the occurrence of compression fractures, it is difficult to distinguish between an osteoporotic person and a normal individual matched for sex and age on the basis of present criteria. A number of studies have been carried out in which an evaluation of the degree of osteoporosis was made based on the measurement of bone mass or bone density in specific sites; efficacy of therapy has also been evaluated on this basis (*6–13*). These studies indicate that a measure of the density at various sites in the appendicular skeleton may be used as an indicator of axial osteoporosis.

It is, of course, more satisfactory to measure skeletal loss in osteoporosis by the measure of the calcium content of the entire skeleton, not merely

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by that of one component. The recent development of the technique of total-body neutron activation analysis (TBNAA) has made possible the measurement of the mineral content of the whole skeleton in vivo. The absolute level of total-body calcium can be directly measured with high accuracy and precision (*14,15*).

For routine purposes it is, of course, simpler to approximate the total-body skeletal calcium by measurement of some part of the appendicular skeleton. The absorptiometric technique, using monochromatic photons from ^{125}I, was selected for this study on the basis of the relative ease with which the measurement can be made and the relatively high degree of precision provided by this technique (*10,11*). The measurements are restricted to certain portions of the appendicular skeleton where the amounts of soft tissue are small compared with amounts normally surrounding the axial skeleton.

The present study evolves from two questions:

1. To what extent can the total-body calcium be characterized by measures of the density of selected areas of the appendicular skeleton, especially the radius?
2. Can a quantitative assessment of the degree of osteoporosis be made on the basis of the deficit in total-body calcium or on the basis of densitometric measurement of the radius?

METHOD

Patients. Forty osteoporotic patients (36 postmenopausal women and 4 men) were selected on the basis of having had one or more compression fractures of vertebrae or radiological evidence of osteoporosis.

Total-body calcium. Total-body calcium was measured directly by TBNAA. For this measure, the patient was uniformly exposed to a beam of partially moderated fast neutrons which induce the reaction $^{48}Ca(n,\gamma)^{49}Ca$. The induced ^{49}Ca was then measured with a whole-body counter. The Brookhaven whole-body counter provides an absolute measurement of the ^{49}Ca. From these data, absolute levels of total-body calcium were calculated with an accuracy of $\pm 5\%$ and a precision of $\pm 2\%$ (*14,15*). The radiation dose to the patient in this technique is 0.028 rad (or 0.28 rem).

Bone mineral content of radius. The bone mineral content (BMC) and the width of the radius (W) were measured by the Cameron-Sorenson absorptiometric techniques with the Norland-Cameron absorbtiometer (*10*). The accuracy of this technique is $\pm 5\%$ and the precision (reproducibility) is about 2.5% (*7,16,17*).

At the start of the study, measurements of the radius were made at a point one-third the distance from the distal end of the radius (8-cm site) and at the distal end (3-cm site). The principal site for measuring bone mineral used by Cameron and other investigators (*8,10,11*) is the mid-radius. Other investigators have suggested that a measure of trabecular bone (3-cm site) reflects more reliably the loss of trabecular bone of the spine than does the measure of cortical bone (8-cm site). This consideration is modified, however, by the nature of the bone architecture at the distal radius. The irregular cross-section and inhomogeneity of the bone at the 3-cm site increases the error in measurement. On the other hand, the mid-radius has been shown to be essentially uniform near the one-third distal site; thus positioning errors are minimized. Therefore, the 8-cm site was selected as the most practical scanning site for the determination of bone mineral content.

Estimation of stature from tibia length. The normal (preosteoporotic stature for each individual was estimated from the tibia length as described by Trotter (*18,19*). The tibia length of each patient was measured with precision from radiographic films calibrated with a ruler. The length was taken as the distance between the articular surface of the lateral condyle and the inferior articular surface.

The relationships derived by Trotter are as follows:

For white females:

$$\text{stature} = 2.90 \times \text{tibia length} + 61.5 - 0.06 \times (\text{age} - 30)$$

For white males:

$$\text{stature} = 2.52 \times \text{tibia length} + 78.6 - 0.06 \times (\text{age} - 30)$$

where stature and tibia length are measured in centimeters and age is measured in years.

Calculation of relative calcium deficit. In order to determine the relative deficit in total-skeletal calcium from the absolute measurement of calcium, it is necessary to normalize the data for patients with the parameters of sex, age, and skeletal size. Not only is an accurate measure of the skeletal mass required for this determination but, equally important, a reference is needed for comparison. For this purpose, a previously developed algorithm was used to predict the normal body calcium based on the weight (lean-body mass), height, sex, and age of the patient (*20*).

The predicted normal calcium (Ca_P) was calculated from the following relationships:

$$\text{for males:} \quad Ca_P = 54.5\ H(K)^{1/2}$$
$$\text{for females:} \quad Ca_P = 57.0\ H(K)^{1/2}$$

where Ca_P is predicted normal total-body calcium

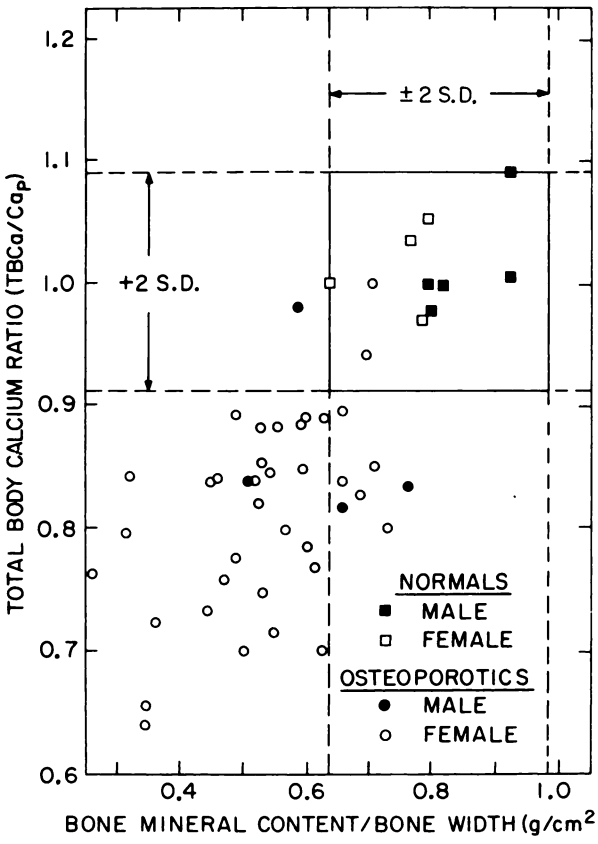

FIG. 1. Total-body calcium ratio is plotted against bone mineral content/width, (BMC/W), of radius in osteoporotic and in normal contrast population.

(gm), H is height (meters), and K is total-body potassium (gm).

The measured total-body calcium (TBCa) expressed in terms of the predicted normal calcium (Ca_P) gives the calcium ratio ($TBCa/Ca_P$) for an individual patient based on the 100% value for his sex, age, body habitus, and size. The percent calcium deficit is then defined as $(1 - TBCa/Ca_P) \times 100$.

In the preceding equations, total-body potassium (K) measured by whole-body counting is an index of lean-body mass (body weight minus the variable fat content) (*21*). Since the total-body potassium decreases with age in a manner similar to calcium, it serves indirectly as a correction factor in the algorithm, reflecting the normal loss of total calcium with age (*22*).

RESULTS

The measured total-body calcium (TBCa), calcium ratio ($TBCa/Ca_P$), bone mineral content (BMC), width of the radius (W), and tibia length are presented in Table 1. The same data for nine normal contrast subjects are included for purposes of comparison.

Absolute levels of total-body calcium in the osteoporotic women range from 344–865 gm, and in men from 658–904 gm. The calcium ratio, however, varies between 1.005 and 0.640 gm in the osteoporotic patients compared with a range of 1.014 ± 0.05 (s.d.) for the normal contrast subjects. The calcium ratio for the patients and control subjects is plotted against the BMC/W (Fig. 1). A calcium ratio of 1.00 indicates that the measured calcium is equal to the predicted calcium value for a person of that age, sex, height, and body size. The square in the figure delineates ±2 s.d. of the normal mean value. It can be seen that all calcium ratio values for the normal contrast subjects fall within 2 s.d. (±10%) of the predicted normal total-body calcium. Five of the osteoporotic women and one osteoporotic male had calcium ratios greater than 0.900, that is, the values were within 2 s.d. of those of the normal subjects. Three of these patients (CAS, HER, and LEV), had very low total-body potassium possibly due to the use of diuretic agents in their therapy. When correction was made for their low potassium values in the calcium prediction equation, their calcium ratios were 0.881, 0.880, and 0.855, respectively. Thus, 37 of the 40 patients studied had calcium ratios differing by more than 2 s.d. of normal. Moreover, one of the three patients whose Ca ratios fell within 2 s.d. of normal (LEH), had an inconclusive diagnosis of osteoporosis. The BMC and stature measures for this patient were normal.

The mean BMC of the female osteoporotic group was 0.646 gm/cm; the contrast normal mean was 0.941 gm/cm. The male osteoporotic group had a mean of 0.877 gm/cm; the contrast normal mean for males was 1.248 gm/cm. The BMC/W (in gm/cm^2) of the osteoporotic females was 0.528 (±22.3%) compared with a normal mean of 0.741 ± 9.7%, and the male osteoporotic group had a mean of 0.625 ± 17.1% compared with the normal mean of 0.847 ± 7.9% gm/cm^2.

DISCUSSION

Total-body calcium. The range in absolute levels of total-body calcium is very large reflecting not only degree of osteoporosis but also body habitus, age, and sex. This variability in TBCa renders an average for the group meaningless. In order that changes occurring in an individual be made evident, it is essential that calcium levels be compared with "normal" values for that individual. It is for this reason that the absolute TBCa values were normalized for sex, age, and skeletal size. When the data are normalized by means of the use of the calcium ratio, ($TBCa/Ca_P$), the variability in the osteoporotic group is reduced considerably. The variability

TABLE 1. TOTAL-BODY CALCIUM AND RADIAL BONE MINERAL CONTENT OF OSTEOPOROTIC AND NORMAL SUBJECTS

Patient	Age (yr)	Weight (lb)	Height (cm)	Tibia length (cm)	Height (est.) (cm)	Δ %	BMC gm/cm	Width (cm)	BMC/W gm/cm²	TBCa (gm)	TBCa Ca_P
Osteoporotic Females											
ABR	81	115	148.7	34.2	157.6	5.6	0.625	1.042	0.600	636	0.942
CAS	50	86	154.5	33.5	157.5	1.9	0.545	1.035	0.526	606	0.943
COH	63	141	152.4	32.6	154.0	1.1	0.630	1.012	0.622	524	0.701
DAN	78	117	152.5	31.6	150.2	0	0.452	1.428	0.317	590	0.841
DIR	53	97	153.7	33.6	157.5	2.4	0.595	1.225	0.486	564	0.776
FAL	70	141	154.6	33.1	155.1	0.3	0.760	1.293	0.588	632	0.885
FIS	73	151	156.4	33.3	155.5	0	0.558	1.152	0.484	691	0.895
GRE	55	123	156.0	33.2	156.2	0.2	0.710	1.088	0.653	674	0.899
GRO	63	104	157.5	34.9	159.7	2.0	0.595	1.168	0.510	621	0.838
GUN	65	113	156.7	36.8	166.1	5.6	0.550	1.242	0.443	480	0.733
HAL	67	120	149.5	32.7	154.1	3.0	0.740	1.252	0.591	608	0.848
HER	81	197	161.3	33.3	155.0	0	1.003	1.840	0.562	798	0.944
HUF	77	117	145.6				0.540	1.228	0.440	561	0.838
IRW	70	144	142.8	30.1	146.4	2.5	0.582	1.062	0.548	479	0.715
ISA	69	174	157.8	34.8	160.1	1.4	0.680	1.302	0.522	665	0.820
JAC	51	158	153.5	33.8	158.2	3.0	0.830	1.220	0.680	685	0.828
JAR	68	111	144.0	30.3	147.1	2.1	0.598	1.132	0.528	500	0.747
JEN	88	80	124.8	27.2	136.9	8.8	0.375	1.445	0.260	344	0.763
KOH	74	126	152.9	35.4	161.6	5.4	0.470	1.308	0.359	582	0.723
LAU	56	217	173.3				1.028	1.415	0.726	787	0.800
LEH	66	164	164.5	35.5	162.2	0	0.868	1.240	0.700	865	1.005
LEV	44	120	162.4				0.762	1.090	0.700	711	0.913
MIL	79	88	150.5	33.7	156.3	3.7	0.450	1.440	0.312	502	0.795
MUL	66	134	162.2	36.2	164.3	1.3	0.795	1.270	0.626	695	0.890
OLS	63	129	159.5	35.0	161.0	1.0	0.738	1.232	0.598	584	0.785
ROB	65	114	154.0	33.8	157.4	2.2	0.583	1.260	0.463	573	0.840
ROM	68	137	154.9	33.0	154.9	0	0.630	1.262	0.499	523	0.700
ROS	74	119	144.0	32.3	152.6	5.6	0.618	1.178	0.524	563	0.854
SHA	64	101	144.8	31.3	150.3	3.7	0.542	1.152	0.471	486	0.757
SHP	74	117	146.7	33.1	154.9	5.3	0.712	1.165	0.611	507	0.768
SHO	58	148	159.7	33.4	156.7	0	0.474	1.368	0.346	503	0.655
SIE	59	100	145.5	33.0	155.5	6.4	0.648	1.198	0.541	516	0.845
SIN	60	106	151.3	32.0	152.5	0.8	0.648	1.148	0.564	526	0.797
TAL	65	117	162.7	36.9	166.4	2.2	0.828	1.266	0.654	628	0.839
VAA	71	86	151.1	33.6	156.4	3.4	0.362	1.050	0.345	391	0.640
WAR	36	90	156.3				0.718	1.212	0.592	634	0.883
Avg.				33.4		2.5	0.646	1.234	0.528	590	0.818
Osteoporotic Males											
DEN	76	128	166.3	36.3	167.3	0.6	0.788	1.350	0.583	832	0.979
GOS	65	124	162.7	37.5	171.0	4.8	0.760	1.502	0.506	658	0.838
NIC	46	133	169.5	37.5	172.1	1.5	0.855	1.310	0.653	788	0.817
TOD	58	188	178.3	40.9	180.0	0.9	1.105	1.460	0.757	904	0.834
Avg.				38.1		2.0	0.877	1.406	0.625	796	0.867
Normal Females											
ORL	54	197	158.7				1.005	1.585	0.634	857	0.999
KON	39	116	156.4				0.840	1.105	0.760	783	1.035
FIL	36	144	161.4				0.892	1.142	0.781	833	0.971
STE	51	173	172.0				1.025	1.302	0.787	1018	1.053
Avg.							0.941	1.284	0.741	873	1.014
Normal Males											
CAR	39	159	159.8				1.180	1.282	0.920	1036	1.091
COH	51	170	179.8				1.274	1.616	0.788	1161	0.997
FAI	36	198	185.5				1.580	1.718	0.920	1366	1.005
PRI	49	155	175.0				1.198	1.475	0.812	1042	0.998
SHU	30	132	164.0				1.010	1.270	0.795	876	0.978
Avg.							1.248	1.472	0.847	1096	1.014

Height (Est) = Height estimated from tibia length.
Δ% = Difference in measured and estimated height.
BMC = Bone mineral content of radius.
BMC/W = Bone mineral content/width of radius.
TBCa = Total-body calcium.
Ca_P = Predicted total-body calcium.

in the contrast population is reduced to about 4% by this normalization procedure. Once the data of the osteoporotic group are normalized, the remaining variability reflects the extent and duration of the disease.

The mean calcium ratio for female osteoporotics is 0.818 and for male osteoporotics 0.867. Thus, the corresponding mean percent calcium deficits (1 — TBCa/Ca_P) × 100, are 18 and 13%, respectively. Reported losses of skeletal calcium (estimated by a variety of other techniques based either on localized measurements in the appendicular skeleton or on biopsies) range from 20–30% (*1–4,6*). Inasmuch as differentials in rates of loss may exist within regions of the skeletal system, it is possible that the percent loss of calcium in localized areas differs from the percent loss from the whole skeleton. It should be pointed out that in those osteoporotic patients with either marked loss of height or with kyphosis, the measured height is underestimated. Thus, for these patients the expressed calcium ratios (TBCa/Ca_P), which are based in part on measured height, tend to be overestimates.

The value of the preosteoporotic height was derived from the length of the tibia in this study (Table 1). Loss of height varied widely in the female osteoporotic patients with a maximum of 10 cm (6.4%). Male osteoporotic patients lost, on the average, 3.4 cm (2.0%) whereas the average loss of height in the female osteoporotic patients was 3.9 ± 3.5 cm (2.5%). On the basis of these figures, correction for loss of height (where necessary) would lower the mean calcium deficit by an average of 2.5%.

The calcium ratio will also be overestimated when the total-body potassium is abnormally low. The need for a correction in this case is minimized, however, by the use of $(K)^{1/2}$ in the algorithm. It should be emphasized that the data presented in Table 1 have not been corrected for loss of height in an individual or for abnormally low body potassium.

Bone mineral content (BMC) of the radius. The bone mineral content, a measure of the linear density of the bone scanned (density per unit length of bone, gm/cm), varies widely, from 0.362 to 1.105 gm/cm, in the osteoporotic group (Table 1). The large variation is again due in part to the degree of osteoporosis but also reflects sex, age, and size of the individual. For example, even in a large normal population the coefficient of variation in BMC (at the 8-cm site) in various age groups ranged from 6–24% (*7*).

Clearly, in order to facilitate intercomparison of BMC in individuals of different sizes, an index of size and age is required. The width of the radius (measured from the scan) is a parameter of the cross-

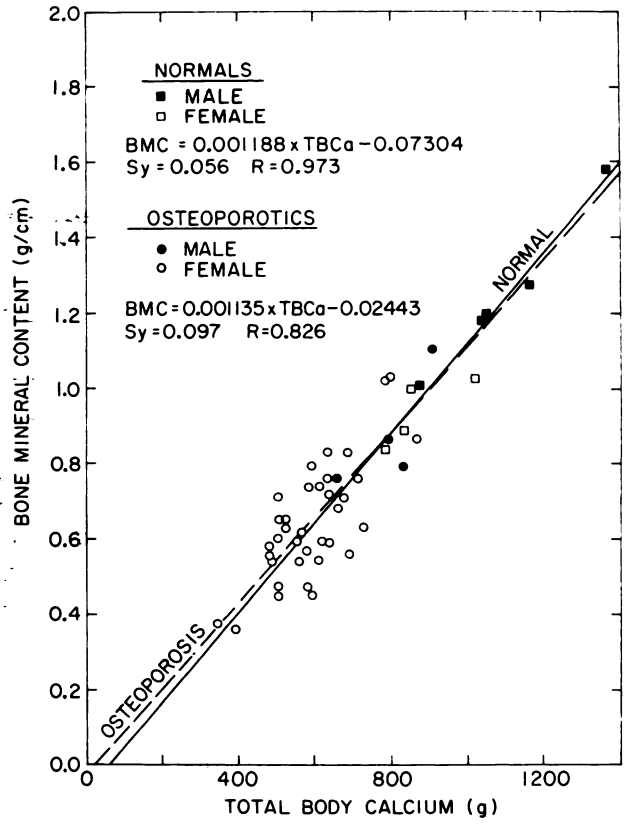

FIG. 2. Total-body calcium is plotted against bone mineral content (BMC) in osteoporotic patients and in normal contrast population.

sectional area (particularly at the 8-cm site) and has been used for normalization (*7*). Division of the BMC value by the width of the radius reduced the mean coefficient of variation (at the 8-cm site) of all age groups from 16 to 11% (*7*). Smith (*9*) adjusted the BMC to an arbitrary radius width (12 mm for cortical bone and 18 mm for trabecular bone). This procedure reduced the coefficient of variation of cortical bone in the normal population from 14 to 9%; it had minimal effect on trabecular bone measurements.

It was found in the present study that although the BMC value correlated well with the TBCa value, the correlation between the "normalized" values (BMC/W versus TBCa/Ca_P) was poor. Clearly, the "normalization" provided in the two cases differs markedly. No correlation with respect to size and age appears between the radius width and the parameters height, age, skeletal size, or degree of osteoporosis. BMC/W had a correlation with the normalized Ca ratio (TBCa/Ca_P) of 0.454, $p < 0.005$ in osteoporotics, and 0.409, $p < 0.003$ in normal subjects (Fig. 1). This poor correlation reflects the inadequacy of using the radius width to normalize the BMC measurement for size and age. This is not

surprising since it has been reported that the radius width does not change with age despite evidence of cortical thickening (*9*). This lack of correlation of radius width with parameters of habitus, sex, and age and diagnosis of osteoporosis was corroborated in the present study. Further, the mean width of the radius of the osteoporotic male and female groups was almost identical with that of the corresponding contrast control population.

In accord with previously reported studies, the mean radial BMC or BMC/W in the osteoporotic group was significantly less than that of a normal population.

Correlation of bone mineral content of the radius with the total-body calcium. It would certainly simplify the procedure for the analysis of the degree of osteoporosis if the bone mass could be ascertained by the relatively simple absorptiometric measurement of the radius rather than by TBNAA. It appears from the data that to a significant degree this procedure is feasible. The correlation between BMC and TBCa in osteoporotic patients is high: 0.826, $p < 0.001$ (Fig. 2). The correlation between BMC and TBCa is not as high in the osteoporotic patients as in the normal contrast group (0.973), a finding which is not surprising in light of the possible differential rates of loss in osteoporotic patients. One would, of course, expect that in normal subjects with no disturbance of Ca metabolism all dimensions of the skeleton would be proportional to each other (*18,19*).

The correlation between absorptiometric measurement of BMC and total-body calcium reported here is in good agreement with that previously reported on a group of 14 osteoporotic patients (*23*). Chesnut reported a correlation of 0.94, $p < 0.001$, between total-body calcium (measured by activation analysis in osteoporotic patients) and the measurement of BMC (measured by the absorptiometric technique applied to the distal radius). The same correlation measured at different sites (i.e., mid-radius, ulna, humerus) produced values of the correlation coefficient ranging from 0.93–0.83 (*23*). The correlation was somewhat higher for BMC measurements made on trabecular bone than for those made on cortical bone. The degree of osteoporosis exhibited by these patients was not reported and may have been less marked than in the present study. (Clearly, the less severe the osteoporosis, the higher the correlation between TBCa and BMC).

Diagnosis of osteoporosis based on BMC and total-body calcium. The basic assumption underlying all the measurements of bone mass whether by TBNAA or photon absorptiometry is that there is a relationship between the loss of mineral and the occurrence of spontaneous fractures, characteristic of osteoporosis. It is well established that there is a progressive deterioration of the skeletal structural integrity associated with the loss of bone calcium with age and in osteoporosis (*2–4*). Further, although the loss of Ca occurs initially and primarily in the trabecular bone of the spine, there is invariably some simultaneous loss of mineral in the peripheral skeleton (*5–9*).

Wilson (*24*) has shown directly with human skeletons that the strength of bones and thus the risk of fractures is related to the amount of bone in specific areas. The BMC of the thoracic vertebrae was estimated from the BMC of the radius with a standard error of about 17% (*24*). Further, maximum compressive strength of vertebral bone could be estimated from radial BMC, age, and size.

Bone mineral content of radius: The large statistical variability in the BMC of the peripheral skeleton in normal populations of from 6 to 18% (*7,9*) and the current inability to normalize these data for sex, age, and skeletal size of the individual make it unsatisfactory to use radial BMC as the sole criterion in diagnosing osteoporosis in an individual. However, there is no question that BMC measurement can be used to distinguish an osteoporotic population from an age- and sex-matched normal population (*9*).

Smith and Cameron have attempted to define osteoporosis by comparison of radial BMC in osteoporotic patients with the radial BMC of a large normal population of white females. They have made broad groupings of the statistical probabilities of osteoporosis by means of a fracture index chart, illustrated in Fig. 3 (*25*). An individual is considered to have a high probability of sustaining a spontaneous compression fracture (characteristic of osteoporosis) if the BMC value is less than 0.68 gm/cm (*25*). For comparative purposes the BMC and BMC/W of the present study were plotted on the fracture index chart of Smith and Cameron. These data (normal and osteoporotic) can be compared with the solid line which represents the mean values obtained from the Wisconsin Mineral Laboratory population. The lower dashed line indicates levels 2 s.d. below this mean value. The values in the hatched area, according to Smith and Cameron, represent those individuals who have adequate bone mineral. Those patients whose BMC values fall below 0.68 gm/cm are considered to have a high probability of developing spontaneous fractures.

As can be seen, the Brookhaven National Laboratory (BNL) data are quite consistent with the proposed fracture index chart of Smith and Cameron. The mean BMC in our female osteoporotic population (most with evidence of spontaneous frac-

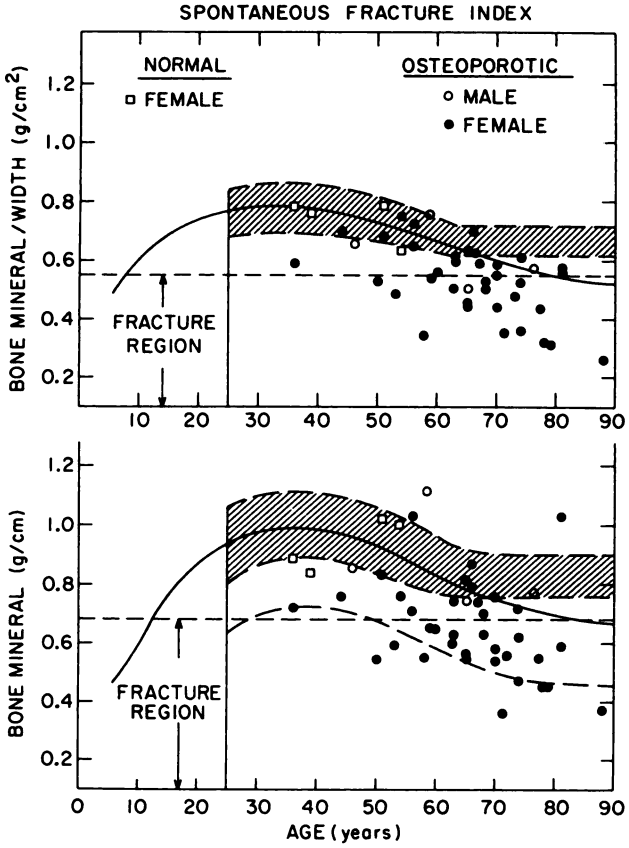

FIG. 3. Spontaneous fracture index chart of Smith and Cameron (25) is plotted along with bone mineral content data in present study. Solid curve represents mean of Wisconsin Mineral Laboratory population. Lower dashed line indicates level 2 s.d. below mean value. In upper figure BMC/W is plotted as function of age. In lower figure BMC is similarly plotted.

ture) was 0.65 gm/cm. However, 13 out of the 36 female osteoporotics had a BMC greater than 0.68 gm/cm. The same relationship holds for the BMC/W shown in the upper curve of Fig. 3 but the variability is again less than in the plot of BMC data. The fracture threshold here is 0.55 gm/cm² compared with the BNL mean of 0.53 gm/cm². Nine of the 36 osteoporotic females had a BMC/W of greater than 0.55 gm/cm². Whereas this analysis is suitable for a general statistical study of a large population, i.e., a demographic study, it is clearly unsatisfactory for individual diagnoses due to the very large overlap noted.

Total-body calcium: An effort to relate quantitatively the calcium ratio to radiographic indices of the degree of osteoporosis was not completely successful. This may be due in part to the inadequacy of techniques for quantifying the radiographic indices. However, patients with the lowest calcium generally had the most severe clinical and radiographic evidence of osteoporosis. The visual rating of the degree of osteoporosis is, of course, only roughly quantitative in nature.

The mean of the skeletal mass (total calcium) of an osteoporotic population differs significantly from an age- and sex-matched normal population. Further, the degree of osteoporosis in an individual appears to be highly correlated with the calcium ratio ($TBCa/Ca_P$) as measured by TBNAA. Thirty-four patients out of 40 exhibited calcium ratios differing in excess of 2 s.d. of normal (<0.900). This figure increased to 37 of the 40 when correction was made for abnormally low total-body potassium values. Thus, the total-body calcium normalized for sex, age, and skeletal size appears to be statistically more reliable than bone mineral content of the radius as an index for quantitating the degree of osteoporosis in an individual.

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