LOSS OF CALCIUM FROM AXIAL AND APPENDICULAR
SKELETON IN PATIENTS WITH CHRONIC RENAL FAILURE*

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The widespread prevalence of bone disease in chronic renal failure both prior to and during hemodialysis is an important aspect of uremia. Loss of bone mineral of the skeleton in renal disease can be measured directly by total-body neutron activation analysis (TBNA). The absorptiometric technique, using monochromatic photons from ^{125}I , applied to the appendicular skeleton (radius) also reflects the loss of bone mineral content (BMC) in renal disease. In the present study the results of these two techniques are compared in 25 patients with renal insufficiency, 53 with end stage renal failure on dialysis, and 24 normal control subjects.

The range in absolute levels of total-body calcium in the renal patients is very large (466-1307 g) (see Table 1). This variability renders an average TBCa value for the group meaningless. However, normalization of the data for sex, age and skeletal size greatly reduce this variability. In order to measure the relative deficit in TECA in individual patients from the absolute Ca measurement, it is necessary to normalize the data for sex, age and skeletal size. For this purpose an empirically derived relationship was used to predict the normal skeletal Ca in each subject, based on weight, height, sex and age (1,2). The measured TBCa divided by the predicted TBCa is referred to as the calcium ratio. This ratio is shown to be useful in expressing the relative deficit of Ca in individual renal patients (see Table 1).

The mean values for the calcium ratios for males and females of Group I were $1.033 \pm 15.4\%$ and $0.901 \pm 12.5\%$, respectively. For males and females of Group II, the corresponding mean ratios were $1.015 \pm 15.6\%$ and $0.970 \pm 16.1\%$ as compared to $0.997 \pm 5.6\%$ and $0.987 \pm 4.6\%$ for normal male and female subjects. The corresponding BMC ratios for ^{Group} I were $1.044 \pm 15.2\%$ and $0.848 \pm 14.4\%$ as compared with the normal ratios of $0.994 \pm 6.4\%$ and $1.011 \pm 5.5\%$.

The calcium ratio is plotted against the BMC ratio for each individual in Groups I and II in Fig. 1. The distribution of Ca ratios in Groups I and II, indicate that about 50% of the patients fall within 2 SD of the normal mean (1.014 ± 0.082). About 20% of the patients in Groups I and II have Ca ratios greater than 2 SD of the mean, while 32% from Group I and 25% from Group II have Ca ratios below 2 SD of the mean. Thus, about half of the patients were in negative or positive balance for sufficient time to alter the total-body calcium. This wide range in Ca ratio reflects the diversity with regard to the extent of osteodystrophy and degree of soft tissue calcification. The heterogeneity with regard to skeletal mass in uremic patients results from variability in dietary calcium intake, duration and extent of uremia, course of treatment, and type of disease.

The bone mineral content, a measure of the linear density of the bone scanned (density per unit length of bone, g/cm) also varies widely, from 0.465 to 1.568 g/cm in the renal patients. The large variation again 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 to 24% (4). To compare BMC in individuals of different sizes, an index of size and age is required (2). A small degree of normalization is effected by dividing the radius BMC by the radius width, (see Table 1), but the correlation of BMC/W with the Ca ratio is poor, and reflects the inability of the width to normalize the data effectively. This result is not surprising since there is poor correlation between radius width and the parameters of height, age and skeletal size. For example, despite cortical thickening, radius width does not change markedly with age (5).

The mean values of the BMC ratios for males in both renal Groups I and II do not differ significantly from the values of the ratios for normal males.

The females of Group I, however, have a mean value lower than that of the controls. In both renal groups, the females have lower mean values of BMC and Ca ratios than those of males. The greater loss of Ca from the body and the radius in uremic females is associated with amenorrhea and depression of ovulatory function. The disturbances of the endocrine factors which contribute to the anovulatory state in uremia may contribute to the more extensive loss of calcified tissue mass in the female uremic patient. Katz (6) and Ritz (7) also reported a significant decrease in BMC associated with increased immunoreactive parathyroid hormone blood levels, as well as a higher prevalence of radiographic abnormalities in the female renal patients on maintenance hemodialysis.

The data indicate a significant correlation between TBCa and BMC in all groups studied. The correlation was the highest (0.944) in the normal contrast group, as would be expected. There is no disturbance in the calcium metabolism in these subjects, and all parts of the skeleton show the same constituent proportions. The correlation coefficient between BMC and TBCa in patients with renal disease (Group I), was 0.919 which is not as high as that for the normal subjects, but equally significant. Even in patients on dialysis, (Group II), with more extensive osteodystrophy, the correlation was still highly significant, although lower than that for the other two groups: 0.892.

The findings suggest that there is a differential rate of loss of Ca from the different parts of the skeleton in renal patients. It is well known that cortical bone and trabecular bone have differing turnover rates. While the 8 cm site on the radius, of course, consists primarily of cortical bone, the total body contains both cortical and trabecular bone. In addition, patients with renal disease have a potential abnormal pool of calcium in sites of soft tissue calcification.

Finally, the question arises on the relative utility of quantitating changes in skeletal Ca by both TBNA and BMC measurements. The correlation coefficient relating the relative change in TBCa ($\Delta\%$) and the change in BMC ($\Delta\%$) in 16 patients following 9-12 months of dialysis was very poor: 0.25.

It is clear from the results that changes in BMC in individual patients do not necessarily relate to changes in TBCa. In like manner, the TBCa measurement alone does not define the distribution of total body Ca between the skeleton and soft tissue in renal patients. However, taken together, the BMC measure along with that of TBCa does suggest possible alterations in the skeletal Ca distribution associated with renal disease.

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Table 1. Total-Body Calcium and Radial Bone Mineral
Content of Patients with Renal Disease

Patient Category	No.	Sex	Total-Body Calcium		Bone Mineral Content			
			$\frac{\text{TBCa}}{\text{g}}$	$\frac{\text{TBCa}}{\text{Ca}_p}$	$\frac{\text{BMC}}{\text{g/cm}}$	$\frac{\text{Width}}{\text{cm}}$	$\frac{\text{BMC/W}}{\text{g/cm}^2}$	$\frac{\text{BMC}}{\text{BMC}_p}$
I Renal (non-dialysis)	15	M	1018 $\pm 14.1^*$	1.033 ± 15.4	1.154 ± 14.7	1.491 ± 8.0	0.766 ± 11.4	1.044 ± 15.2
	10	F	728 ± 13.7	0.901 ± 12.5	0.753 ± 15.9	1.171 ± 10.2	0.652 ± 20.0	0.848 ± 14.4
II Renal (dialysis)	29	M	1048 ± 16.7	1.015 ± 15.6	1.159 ± 16.1	1.525 ± 11.5	0.760 ± 12.5	1.003 ± 16.6
	24	F	753 ± 15.9	0.970 ± 16.1	0.812 ± 19.7	1.249 ± 9.4	0.650 ± 17.1	0.955 ± 19.5
Normal Contrast	12	M	1077 ± 15.7	0.997 ± 5.6	1.192 ± 15.8	1.469 ± 9.7	0.813 ± 13.2	0.994 ± 6.4
	12	F	795 ± 12.2	0.987 ± 4.6	0.893 ± 11.0	1.204 ± 12.7	0.749 ± 9.2	1.011 ± 5.5

* - coefficient of variation (percent)

TBCa = total body calcium

Ca_p = predicted total-body calcium

BMC = bone mineral content of radius

BMC/W = bone mineral content of radius/
width of radius

BMC_p = predicted bone mineral content of
radius

FIGURE 1