

## Total body and regional bone mineral content in hemodialysis patients

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Bone mineral content (BMC) in the total body and lumbar spine was evaluated in 126 hemodialysis patients (60 males, 66 females) by dual photon absorptiometry with the Norland DBD 2600. Measurements of: 1) total body BMC divided by lean body mass ( $BMC_{TB}/LBM$ ), 2) bone mineral density (BMD) of total body, 3) BMD of four regional sections (head, trunk, pelvis, and legs), and 4) BMD of lumbar spine, generally showed a significant decrease in the hemodialysis patients compared to the reference population. However, arm BMD did not show a significant difference between patients and control populations. The z-score of  $BMC_{TB}/LBM$  declined significantly throughout the duration of hemodialysis, although that of the lumbar spine BMD did not. It should be noted that the degree of decrease in BMC was more prominent in the total body measurement than in the lumbar spine measurement. There was preferential osteopenia of the total body in the hemodialysis patients. Although the lumbar spine BMD showed a lower value than the control population, the lumbar spine is not the recommended region to monitor the BMD change in hemodialysis patients.

**Key words:** bone mineral content (BMC), bone mineral density (BMD), dual photon absorptiometry (DPA), hemodialysis, total body, lumbar spine

### INTRODUCTION

SINCE RENAL OSTEODYSTROPHY is a well-known systemic complication of hemodialysis, its effect is often monitored by bone mineral measurement. Single photon absorptiometry (SPA), and quantitative computed tomography (QCT) have been widely used for these patients for many years.<sup>1,2</sup> These techniques, however, are useful only for the evaluation of regional bone mineral content. The results differed from method to method.<sup>1-3</sup> Neutron activation analysis (NAA) has been utilized to evaluate the total body or radial mineral measurement in hemodialysis patients.<sup>4,5</sup> Other than the study by Meema,<sup>5</sup> NAA studies predominantly evaluated the longitudinal effect on calcium content.<sup>6,7</sup> These longitudinal studies did not contain a control population. Although the study by Meema contained a control population and renal

failure group, the authors did not compare mineral content between these two groups.<sup>5</sup> Few reports are available for the comparison of the bone mineral content (BMC) of total body ( $BMC_{TB}$ ) between hemodialysis patients and a control population.<sup>8</sup> Although Mazess reported 20% lower values in the hemodialysis (HD) patients compared to a control group, they only included 17 patients with relatively small control subjects, and the background of these patients was not described. Currently, dual photon absorptiometry (DPA) is used for the measurement of bone mineral in the total body as well as that in any specific body region.<sup>9,10</sup> This type of analysis measures regional and total body BMC in HD patients, and a reference population, cross-sectionally, to evaluate which site should be measured to detect bone loss in screening these patients.

### MATERIALS AND METHODS

The reference group for our study consisted of 98 men with a mean age of 49.9 years (range 20 to 76), and 161 women with a mean age of 48.5 years (range 21 to 78).<sup>11</sup> The hemodialysis group included 60 men with a mean age

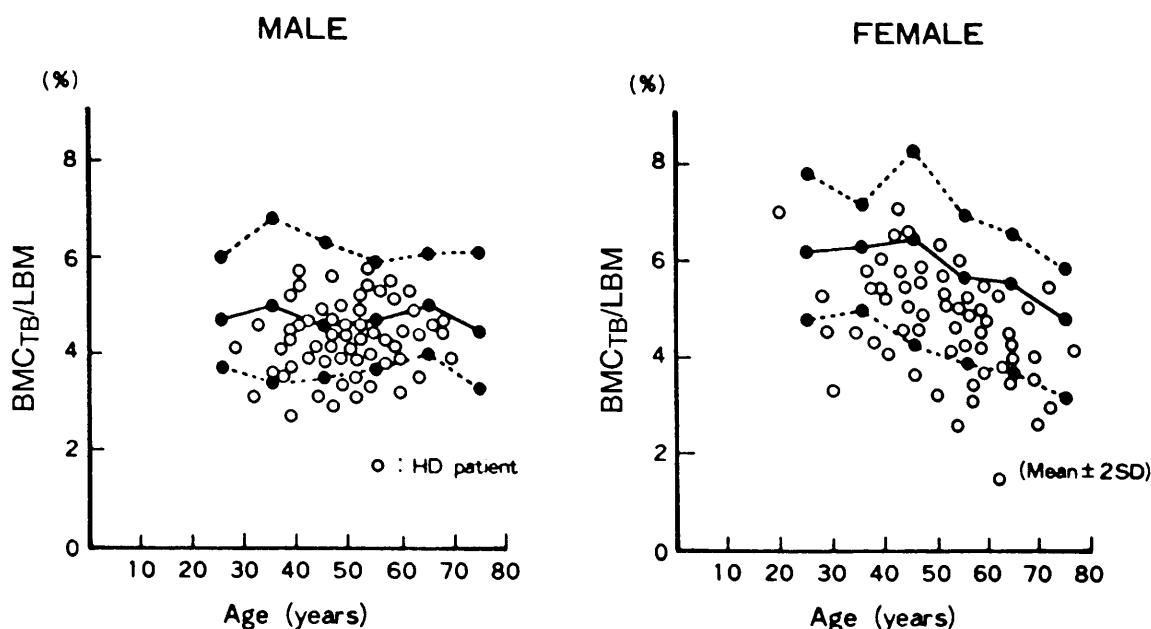
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**Table 1** Subjects

	Male		Female	
	Control group	HD patients	Control group	HD patients
n	98	60	161	66
Age (y)	49.9 ± 14.5	48.7 ± 9.3	48.5 ± 14.5	50.2 ± 12.4
Height (cm)	164.5 ± 7.0	164.5 ± 7.0	153.2 ± 6.9	152.2 ± 5.4
Weight (kg)	62.6 ± 11.1	59.9 ± 7.8	54.4 ± 11.1	49.8 ± 7.2
Lean body mass (kg)	45.9 ± 7.6	44.7 ± 6.3	32.2 ± 4.1	31.4 ± 5.7
% Fat (%)	21.9 ± 10.4	21.3 ± 10.3	37.0 ± 11.8	32.2 ± 12.5
HD duration (y)	—	7.8 ± 5.5	—	7.3 ± 5.0

(Mean ± SD)

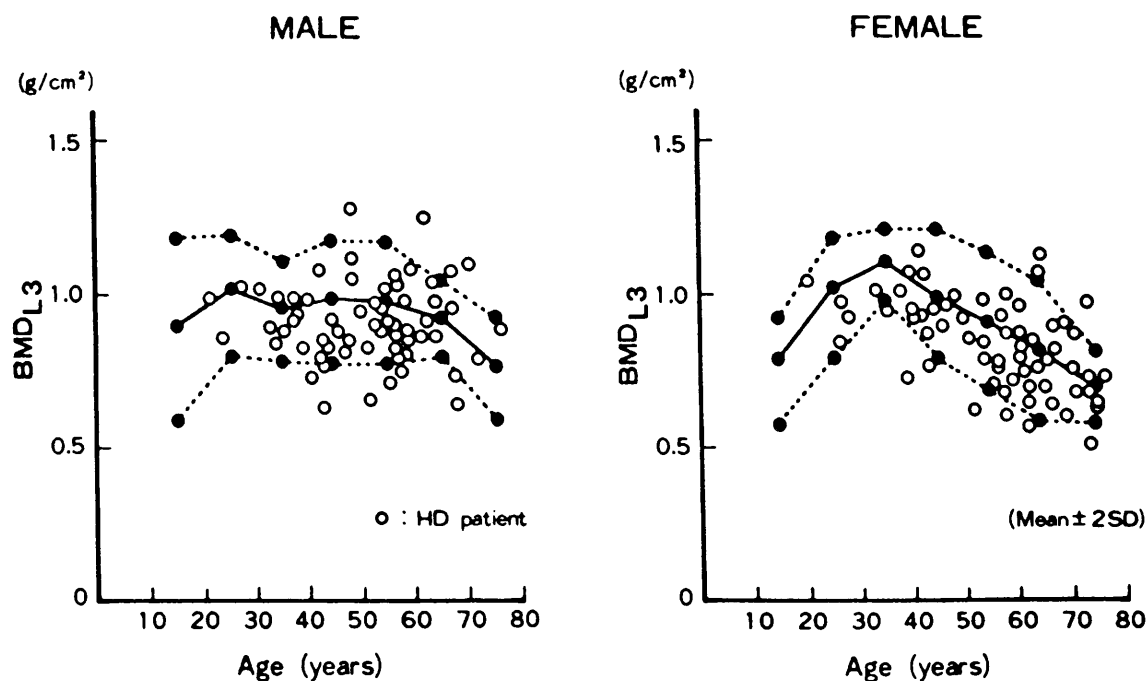


**Fig. 1** Total body bone mineral (BMC<sub>TB</sub>)/lean body mass (LBM) in HD patients (lt: male, rt: female). BMC<sub>TB</sub>/LBM showed significant lower values in HD patients than in the reference groups in both sexes.

of 48.7 years (range 25 to 70) and a mean dialysis history of 7.8 years (range 0.5 to 15 years), and 66 women with a mean age of 50.2 years (range 20 to 76) and a mean dialysis history of 7.3 years (range 0.3 to 17 years). Patients with diabetic nephropathy were excluded from all of these groups. Most patients were dialyzed 3 times per week for 3–5 hours. No subjects had had either a parathyroidectomy or renal transplant. Fifty-eight subjects have received aluminum, 52 have received calcium phosphate, and 108 were currently receiving or had received an active form of vitamin D<sub>3</sub> to maintain their serum calcium level (range: 7.1 to 10.6 mg/dl) and phosphate level (range: 3.5 to 6.9 mg/dl). Both height and weight were measured on the scanning day. There were no significant differences between groups in age, body height, body weight, or lean body mass (Table 1).

A dual-photon bone densitometer (model 2600, Norland Corp., WI, U.S.A.) with a Gadolinium-153 photon source

was used to measure bone mineral content. BMC<sub>TB</sub>, total body bone mineral density (BMD<sub>TB</sub>), lean body mass (LBM) and % fat were obtained from the total body scan. All indices were automatically analyzed. The regional BMC and BMD were obtained at the same time. The regions of interest (ROI) were the head, trunk, pelvis, legs, and arms. The arm BMC consisted of the summation of right and left arm BMC, and the arm BMD consisted of the average of the BMD of both arms. BMD was calculated by means of each individual's BMC divided by the bone area. The BMD of the third lumbar vertebra (BMD<sub>L3</sub>), and the BMC of from the second to fourth lumbar vertebrae (BMC<sub>L2-4</sub>) were evaluated from the lumbar spine scan. Both the total body and the lumbar spine were scanned on the same day. Coefficients of variation for the total body and lumbar spine have been reported previously (BMC: 0.4 [lumbar spine: lumbar spine mode] to 3.6 [pelvis] %, BMD: 0.8 [leg] to 2.8 [pelvis] %).<sup>11,12</sup>



**Fig. 2** Bone mineral density of the third lumbar spine ( $BMD_{L_3}$ ) in HD patients (lt: male, rt: female). Average of  $BMD_{L_3}$  showed significant lower values in HD groups than in reference groups in both sexes.

**Table 2** Comparison of regional BMD between control and HD patients

Region	Male				Female			
	Control group	HD patients	% change	p-value	Control group	HD patients	% change	p-value
Total body	$0.87 \pm 0.12$	$0.72 \pm 0.15$	82.8	$p < 0.01$	$0.84 \pm 0.13$	$0.70 \pm 0.14$	83.3	$p < 0.01$
Head	$1.73 \pm 0.27$	$1.53 \pm 0.29$	88.4	$p < 0.01$	$1.62 \pm 0.29$	$1.46 \pm 0.29$	90.1	$p < 0.01$
Trunk	$0.37 \pm 0.08$	$0.31 \pm 0.07$	83.8	$p < 0.01$	$0.38 \pm 0.09$	$0.31 \pm 0.09$	81.6	$p < 0.01$
Pelvis	$1.47 \pm 0.30$	$1.31 \pm 0.36$	89.1	$p < 0.05$	$1.47 \pm 0.22$	$1.36 \pm 0.37$	92.5	$p < 0.05$
Legs	$1.20 \pm 0.22$	$0.98 \pm 0.23$	81.7	$p < 0.01$	$1.06 \pm 0.20$	$0.91 \pm 0.21$	85.8	$p < 0.01$
Arms	$0.98 \pm 0.22$	$0.82 \pm 0.25$	83.7	$p < 0.01$	$0.88 \pm 0.18$	$0.82 \pm 0.27$	93.2	$p < 0.1$
L3	$0.96 \pm 0.13$	$0.91 \pm 0.13$	94.2	$p < 0.01$	$0.93 \pm 0.17$	$0.84 \pm 0.16$	90.3	$p < 0.01$

% change: % difference of HD vs. controls

( $g/cm^2$ , Mean  $\pm$  SD)

A least squares regression analysis was used to examine correlations. Unpaired *t*-tests were used to compare pairs of independent means. Correlations and differences were considered to be significant when *p*-values were less than 0.05.

## RESULTS

Figure 1 shows the distribution of  $BMC_{TB}/LBM$  in the HD patients. The means of  $BMC_{TB}/LBM$  in the HD group were  $4.27 \pm 0.70$  (SD), and  $4.61 \pm 1.17\%$  in the male and female groups, respectively, which was significantly lower ( $p < 0.01$ ) than that in the reference groups of  $4.79 \pm 0.62$ , and  $5.67 \pm 1.16\%$ , respectively. The  $BMC_{TB}/LBM$  index was not influenced by body height or weight.<sup>11</sup>  $BMD_{L_3}$  in the HD patients are shown in Figure 2. The means of  $BMD_{L_3}$  for HD patients of both sexes (male:  $0.909 \pm$

$0.131$ , female:  $0.837 \pm 0.159$   $g/cm^2$ ) were also significantly lower ( $p < 0.01$ ) than those for the reference groups (male:  $0.964 \pm 0.133$ , female:  $0.929 \pm 0.172$   $g/cm^2$ ). However, most of the BMD values stayed within the normal range. Significant differences ( $p < 0.005$ ) between these two groups were seen in  $BMD_{TB}$  (Fig. 3) and other regional BMD. However, the female arm BMD only showed a tendency to a lower BMD than in the reference group (Table 2). Evaluating the  $BMC_{L_{2-4}}/BMC_{TB}$  ratio between the HD patients and the reference groups showed significant differences for both sexes (Fig. 4). As for other regional BMC, no regional BMC/BMC<sub>TB</sub> ratio showed a significant difference between HD patients and the reference groups. Figure 5 shows the relationship between  $BMC_{TB}/LBM$  and HD duration (male:  $r = -0.394$ ,  $p < 0.01$ , female:  $r = -0.385$ ,  $p < 0.01$ ). A significant decline in  $BMC_{TB}/LBM$  throughout HD duration could be

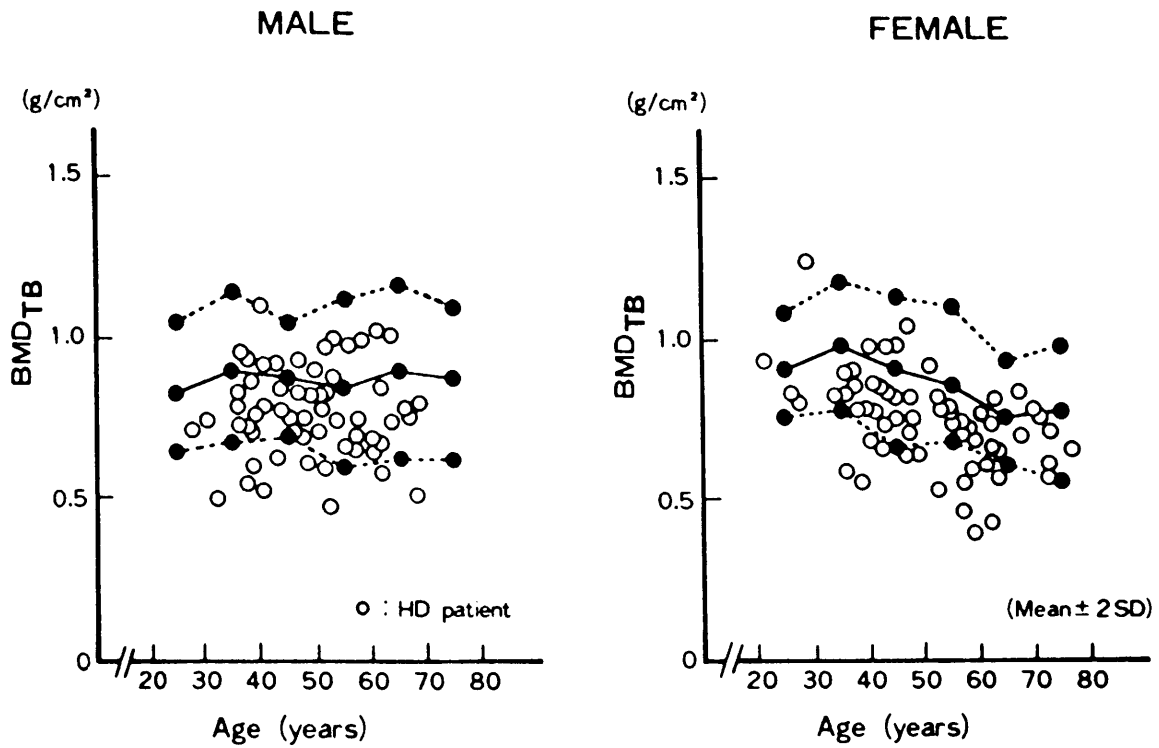


Fig. 3 Bone mineral density of total body ( $BMD_{TB}$ ) in HD patients (lt: male, rt: female).  $BMD_{TB}$  showed significant lower values in HD groups than in reference groups in both sexes.

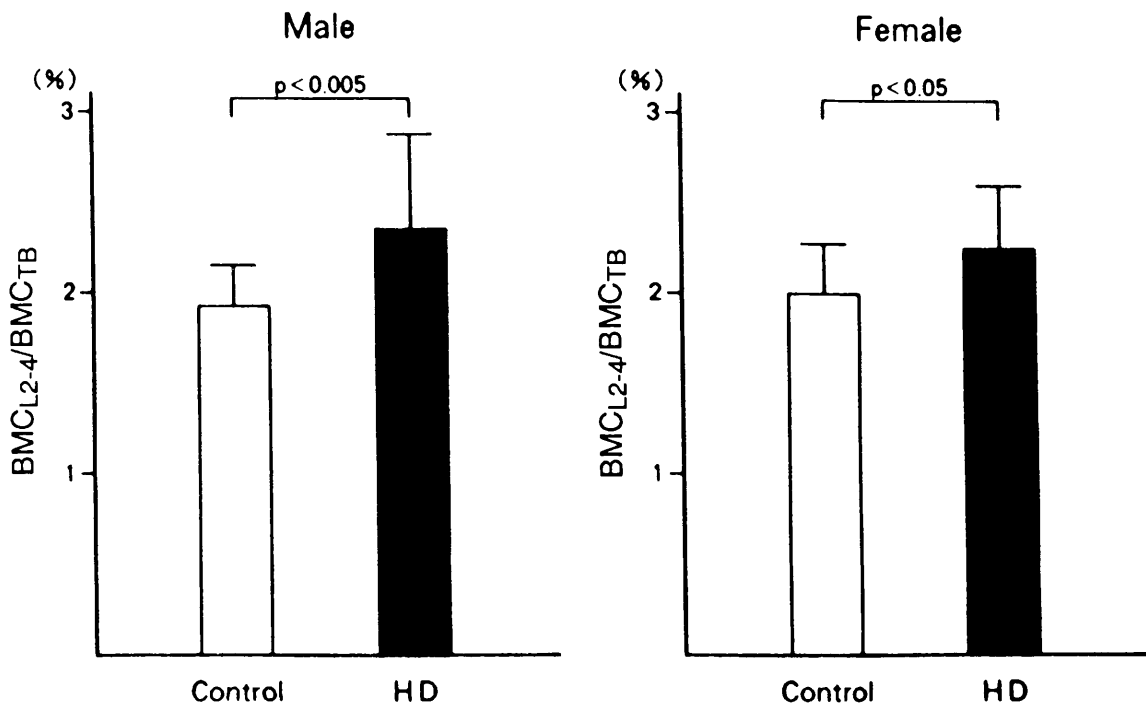
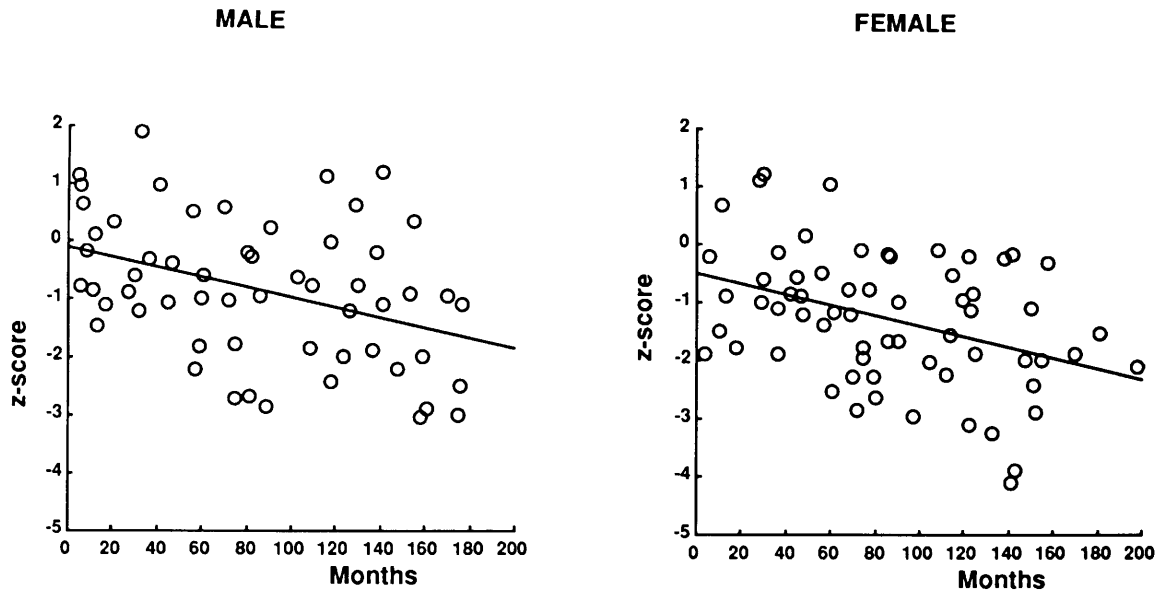


Fig. 4 The ratio of bone mineral content from second to fourth lumbar spine ( $BMC_{L2-4}$ )/total body bone mineral ( $BMC_{TB}$ ) (lt: male, rt: female). The ratio of  $BMC_{L2-4}/BMC_{TB}$  in HD group was significantly higher than in reference group in both sexes. (Male:  $2.35 \pm 0.52\%$  for HD group vs.  $1.91 \pm 0.23\%$  for reference group, Female:  $2.26 \pm 0.36\%$  for HD group vs.  $1.99 \pm 0.14\%$  for reference group)



**Fig. 5** The relationship between z-score of  $BMC_{TB}/LBM$  and HD duration (lt: male, rt: female). The z-score significantly declined with HD duration in both sexes (Male:  $r = -0.3394$ ,  $p < 0.01$ , Female:  $r = -0.385$ ,  $p < 0.01$ ).

found in both groups. However, no significant correlations could be obtained between  $BMD_{L3}$  and HD duration (male:  $r = -0.108$ , female:  $r = 0.092$ ).

### DISCUSSION

The results of previous cross-sectional studies of BMC in HD patients have varied according to the methods used for BMC measurement. These studies mostly evaluated regional BMC, not that of the total body. SPA has generally shown HD patients to have significantly lower BMC than that which is seen in the reference population.<sup>1,2</sup> In contrast, in the case of vertebral QCT and DPA, measurement values in HD patients have been controversial. Some studies showed a lower value, and others showed a value equivalent to or greater than the value found in the reference population.<sup>2,8,13,14</sup> BMD of the forearm, where cortical bone is dominant, did not correlate with the trabecular bone volume on biopsy.<sup>15</sup> Mazess reported 20% bone loss in  $BMC_{TB}$  and 14% bone loss in the spinal BMD in renal osteodystrophy patients who were tested by DPA.<sup>8</sup> Longitudinal NAA studies show significant BMC decreases in the total body and in the radius over the observation period.<sup>6,16</sup>

DPA can analyze any regional BMC where previous methods failed to quantify. Of interest is evaluation to determine what part of the body shows a significant decrease in the HD patients compared with the normal population. In this study, the evaluation of predominantly cortical bone sites, such as total body or head BMD consistently showed greater difference from reference values than was seen in the trabecular sites of the lumbar spine. The arm BMD in females subjects did not show a

significant difference, although there was a tendency toward lower BMD. The reason for this is unclear. The ratio of  $BMC_{L2-4}$  to  $BMC_{TB}$  was significantly greater in the HD group than in the reference subjects. Gava has reported a 15% lower value for the forearm or cortical BMC, which is closer to the value in  $BMC_{TB}$ .<sup>17</sup> However, "rugger jersey" spine, which can often be seen in HD patients, might influence the results of lumbar spine BMD. The influence of these factors will be evaluated with the lateral scan of the lumbar spine. However, both previous and present studies support the established concept that HD patients preferentially lose bone in cortical regions compared to trabecular regions. This is an indication that the total body measurement would be more practical for the detection of bone loss than the lumbar spine measurement in HD patients. It should be noted that osteosclerosis and ectopic calcification may also be important features to monitor. This study evaluated the ratio of lumbar spine BMC to  $BMC_{TB}$ , by means of scan modes different from each other: lumbar spine BMC from the lumbar spine scan, and  $BMC_{TB}$  from the whole body scan. It is not practical to choose the ROI of the lumbar spine area over the whole body scan since the scan resolution is so poor. Similarly, it is not precise enough to evaluate the ratio of the region of trunk BMC to  $BMC_{TB}$  as an index for the thoracic spine, because the trunk region includes the sternum, scapulas, claviculars, and ribs, which contribute to measurement values.

We found a significant decline in  $BMC_{TB}/LBM$  throughout the duration of hemodialysis. This result is compatible to the study with NAA.<sup>17</sup> No data indicating a significant decline in  $BMD_{L3}$  to HD duration could be obtained. One longitudinal study with DPA showed that lumbar spine

BMC rose significantly over a 3-year follow-up.<sup>14</sup> This was not influenced by whether the patients received vitamin D or not. These results also indicate that the lumbar spine is not always the best region to monitor a change in bone mineral in HD patients. An additional consideration is which body region best predicts fractures. Since this paper is a cross-sectional study and no fractures could be seen in the lumbar spine, it was inappropriate to include fracture risk. A longitudinal study would be necessary for this.

One additional way to evaluate the metabolic state of the bones in HD patients is a bone scintigram.<sup>18,19</sup> Quantification of bone change from bone scintigrams has been challenged by De Graaf.<sup>18</sup> High radioisotope uptake in the head can usually be seen in HD patients, compared with other body regions.<sup>19</sup> Bone scintigrams reflect only the present metabolic state, and therefore, it is difficult to evaluate fracture risks or bone strength. Thus, in this study, we were unable to detect site specific bone loss throughout the entire body compared with the reference group. Although the improvement in BMC after parathyroidectomy in the patients with severe secondary hyperparathyroidism has been most prominent in the head (data in preparation), the decrease in head BMD has not been predominant in HD patients. The reason for this discrepancy is unclear.

This study concludes that HD patients had general bone loss when compared to the reference group. It may be easier to detect bone loss by measuring the total body than to measure the lumbar spine with DPA. However, clinicians should note that BMC<sub>TB</sub> may be falsely increased in HD patients due to extensive ectopic calcifications, therefore, cortical bone dominant regions should be measured in HD patients.

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