

# Influence of Age and Sex on Bone Mineral Density in Dialysis Patients

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*In the present study, we evaluated bone mineral density (BMD) in relation to the age and sex of dialysis patients. The study was performed in 30 patients divided into two groups according to age (older group: 12 patients older than 65 years; younger group: 18 patients 65 years of age or younger) and according to sex (18 women, 12 men). We used dual-energy X-ray absorptiometry to examine BMD in the femoral neck (N) and lumbar spine (L2–L4). We simultaneously evaluated parathyroid hormone, calcium–phosphate balance, blood pH, markers of inflammation and nutrition status, and measurements of body composition by bioimpedance analysis. We found significant differences for BMD measured in N (older group:  $0.709 \pm 0.111$  g/cm<sup>2</sup>; younger group:  $0.884 \pm 0.130$  g/cm<sup>2</sup>), T-score [older group:  $-2.64$  (range:  $-4.06$  to  $-0.17$ ); younger group:  $-0.88$  (range:  $-3.25$  to  $2.37$ )], and BMD as a percentage of peak bone density [older group: 68.0% (54.2% – 97.0%); younger group: 89.5% (range: 61.4% – 135.0%)]. The older patients also had lower serum albumin and higher serum ferritin. After adjustment of the results by sex, the older group also showed lower serum Ca and lean body mass and higher serum glucose. Grouping of the patients by sex revealed significant differences in BMD when results were adjusted for age: men had a higher BMD in N ( $0.85 \pm 0.16$  g/cm<sup>2</sup>) than women did ( $0.79 \pm 0.14$  g/cm<sup>2</sup>). We conclude that older age, which is more frequently associated with protein malnutrition, inflammation, and glucose abnormalities than is younger age, is also the important factor influencing BMD loss in dialysis patients.*

## Key words

Bone mineral density, age, sex

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## Introduction

In the skeletal system, chronic kidney disease changes both the quality and quantity of bone through multifactorial influences on bone metabolism, leading to osteopenia, osteoporosis, and increased risk of fracture. Renal osteodystrophy is one of the most important problems in long-term dialysis treatment. However, uremia is not alone in influencing bone metabolism; factors also seen in populations with healthy kidneys contribute to bone destruction in dialyzed patients. Age-related bone loss has been shown to occur in normal adults at a rate of 1% – 2% per year after age 40, increasing to 2% – 4% for 5 – 8 years after menopause in women (1). The relationship between age and bone mineral density (BMD) in dialyzed patients is controversial (2–6).

Results of our earlier study performed in dialysis patients older than 65 years of age and 65 years of age or younger showed that the older group had a lower serum concentration of intact parathyroid hormone (PTH) and lower serum levels of 1-84 PTH (known as cyclase-activating PTH) and 7-84 PTH (known as cyclase-inactive PTH). Serum osteoprotegerin concentration was higher in the older dialysis group than in the younger one (7). These differences in serum bone markers by age suggested that BMD in our dialyzed patients may be also influenced by age.

The aim of the present study was to evaluate BMD in dialysis patients divided into two groups according to age (using a cut-off point of 65 years) and according to sex. The BMD results were also related to other parameters that may influence bone—among them, intact PTH.

## Patients and methods

The study was performed in 30 dialysis-dependent uremic patients divided into two groups according to age [older group:  $n = 12$ , older than 65 years, mean age  $73.6 \pm 6.2$  years, 7 women, 2 patients on

hemodialysis, 10 patients on peritoneal dialysis, median duration of dialysis treatment 22.7 months (range: 7.9 – 42.8 months); younger group:  $n = 18$ , 65 years of age or younger, mean age  $44.6 \pm 12.6$  years, 11 women, 2 patients on hemodialysis, 16 on peritoneal dialysis, median duration of dialysis treatment 16.3 months (range: 6.3 – 59.6 months)] and according to sex (women:  $n = 18$ , mean age  $53.1 \pm 18.0$  years, 3 patients on hemodialysis, 15 on peritoneal dialysis, mean duration of dialysis treatment  $21.2 \pm 13.9$  months; men:  $n = 12$ , mean age  $60.7 \pm 17.2$  years, 1 patient on hemodialysis, 11 on peritoneal dialysis, mean duration of dialysis treatment  $26.1 \pm 14.3$  months).

We observed no significant differences between the age groups in sex distribution, dialysis modality, or duration of dialysis treatment. The sex groups showed no significant differences in age, dialysis modality, or duration of dialysis treatment.

The underlying disorders leading to end-stage renal failure were chronic tubulointerstitial nephritis (8 cases), diabetic nephropathy (7 cases), chronic glomerulonephritis (5 cases), polycystic kidney disease (4 cases), hypertensive nephropathy (1 case), and obstructive nephropathy (1 case). In 4 cases the reason for end-stage renal disease remained unknown.

To examine BMD, we used dual-energy X-ray absorptiometry, which is a reference method for measuring bone mass and assessing fracture risk in various skeletal sites (8). Assessment of bone mass was performed at two sites: femoral neck (N) and lumbar spine from the second to the fourth lumbar vertebra (L2–L4). We simultaneously evaluated serum concentration of intact PTH, total Ca and inorganic phosphates, serum activity of alkaline phosphatase, blood pH, serum markers of inflammation [C-reactive protein (CRP), ferritin], records of body composition measured by bioimpedance analysis, and serum and anthropometric markers of nutrition status. Laboratory markers were determined using standard methods.

Results are expressed as mean and 1 standard deviation or as median and range. Analysis of covariance methodology was used to compare the results by group, with adjustments for sex, age, dialysis modality, and dialysis duration. A  $p$  value below 0.05 was considered to be statistically significant.

## Results

### *Data by age group*

Within the age groups, subgroups were created based on T-score values. These groups were small, but the results suggested that, for N, the worst values occurred more frequently in the older group (Table I). In the younger group, a T-score better than  $-1.0$  predominated. The T-score for L2–L4 was similar in both groups.

We observed significant differences between the older group and the younger one for BMD measured in N (older group:  $0.709 \pm 0.111$  g/cm<sup>2</sup>; younger group:  $0.884 \pm 0.130$  g/cm<sup>2</sup>;  $p = 0.003$ ), T-score [older group: median (range),  $-2.64$  ( $-4.06$  to  $-0.17$ ); younger group: median (range),  $-0.88$  ( $-3.25$  to  $2.37$ );  $p = 0.003$ ], and BMD expressed as a percentage of peak bone density [older group: median (range),  $68.0\%$  ( $54.2\%$  –  $97.0\%$ ); younger group: median (range),  $89.5\%$  ( $61.4\%$  –  $135.0\%$ );  $p = 0.028$ ]. The BMD parameters in L2–L4 were not significantly different between the age groups.

When BMD measured in N was compared with BMD assessed in L2–L4, the older group was seen to have a higher BMD in L2–L4 than in N ( $1.098 \pm 0.286$  g/cm<sup>2</sup> vs.  $0.709 \pm 0.111$  g/cm<sup>2</sup> respectively,  $p = 0.000$ ), a higher T-score [median (range):  $-1.06$  ( $-3.13$  to  $4.07$ ) vs.  $-2.64$  ( $-0.17$  to  $-4.06$ ) respectively,  $p = 0.001$ ], and a higher BMD as a percentage of peak bone mass [median (range):  $90.0\%$  ( $62.8\%$  –  $139.0\%$ ) vs.  $68.0$  ( $54.25$  –  $97.0\%$ ) respectively,  $p = 0.000$ ]. In the younger group, only BMD expressed in grams per square centimeter (and not T-score or BMD expressed as a percentage of peak bone mass) was significantly different between the two sites ( $1.059 \pm 0.250$  g/cm<sup>2</sup> vs.  $0.884 \pm 0.881$  g/cm<sup>2</sup> respectively,  $p = 0.004$ ).

The older patients had a lower serum albumin concentration ( $3.30 \pm 0.37$  g/dL vs.  $3.73 \pm 0.45$  g/dL,  $p = 0.013$ ) and a higher serum ferritin level ( $447 \pm 278$  ng/mL vs.  $328 \pm 193$  ng/mL,  $p = 0.034$ ).

After adjustment of results for sex, the differences in BMD between the age groups were maintained, and lower serum Ca levels were then also observed in the older group ( $8.67 \pm 0.77$  mg/dL vs.  $9.11 \pm 0.92$  mg/dL,  $p = 0.039$ ). This adjustment for sex also revealed the additional feature of worse protein nutrition in the older group. Lean body mass (LBM:  $48.6 \pm 9.6$  kg vs.  $50.9 \pm 10.9$  kg,  $p = 0.000$ ) and LBM as percentage of total body mass ( $66.5\% \pm 7.3\%$  vs.

TABLE I Results of grouping dialyzed patients by T-score

T-score	Femoral neck [n (%)]		Lumbar spine [n (%)]	
	Older group	Younger group	Older group	Younger group
> -1.0 (normal bone)	1 (8.3)	11 (61.1)	6 (50.0)	8 (44.4)
> -2.5 < -1.0 (osteopenia)	5 (41.7)	6 (33.3)	4 (33.3)	8 (44.4)
< -2.5 (osteoporosis)	6 (50.0)	1 (5.6)	2 (16.7)	2 (11.1)

72.2%  $\pm$  8.9%,  $p = 0.003$ ) were lower in the older group despite their higher total body mass (73.0  $\pm$  10.7 kg vs. 71.7  $\pm$  13.1 kg,  $p = 0.039$ ). After adjustment of the results for sex, the older group showed a higher glucose level in a fasting blood sample (125  $\pm$  60 mg/dL vs. 108  $\pm$  36 mg/dL,  $p = 0.043$ ).

Differences in serum levels of intact PTH did not reach significance in this study, although the median concentration of intact PTH in the older group [148.0 pg/mL (range: 14.9 – 429.7 pg/mL)] was lower than that seen in the younger group [214.0 pg/mL (range: 12.3 – 1967.0 pg/mL)]. Serum activity of total alkaline phosphatase, serum concentration of inorganic phosphates, and blood pH were similar in the two groups. Serum level of CRP, blood count, and body composition from bioimpedance records were not significantly different between the groups.

#### Data by sex group

Grouping of the patients by sex did not reveal significant differences in BMD parameters until the results were adjusted for age. After that adjustment, the group of men showed a significantly ( $p = 0.019$ ) higher BMD in N (0.849  $\pm$  0.160 g/cm<sup>2</sup>) than that seen in the group of women (0.790  $\pm$  0.140 g/cm<sup>2</sup>), but no significant differences were observed between the groups in the neck T-score and the BMD as a percentage of peak bone mass.

When BMD measured in N was compared with BMD measured in L2–L4, we observed that BMD was higher in L2–L4 than in N (men: 1.156  $\pm$  0.306 g/cm<sup>2</sup> vs. 0.849  $\pm$  0.160 g/cm<sup>2</sup> respectively,  $p = 0.003$ ; women: 1.020  $\pm$  0.218 g/cm<sup>2</sup> vs. 0.790  $\pm$  0.140 g/cm<sup>2</sup> respectively,  $p = 0.000$ ). No significant differences were noted between the measurement sites with regard to T-score or BMD expressed as a percentage of peak bone density.

Adjustment of the data for age did not reveal significant sex-dependent differences in BMD for L2–

L4, calcium–phosphate balance, blood pH, CRP, or ferritin. Blood count and serum concentrations of albumin and cholesterol were also similar in both groups. In the men, LBM (58.5  $\pm$  8.0 kg vs. 44.3  $\pm$  7.4 kg) and total cell water (44.7  $\pm$  5.5 L vs. 34.0  $\pm$  5.4 L) were, as expected, significantly higher than they were in the women.

#### Discussion

The present study shows that, in dialysis patients, age and sex influence BMD.

In clinical practice, T-score values (measured BMD – young adult BMD / young adult standard deviation) are frequently used to represent severity of bone loss, with a BMD below –2.5 indicating osteoporosis, and a BMD between –1.0 and –2.5 indicating osteopenia (9). As compared with the younger dialyzed patients, the older dialyzed patients in the present study showed greater bone loss, but that loss was significant only in N. Assessment of BMD in L2–L4 was not able to show age-dependent bone loss. Our previous studies (10) also revealed that osteopenia and osteoporosis are more frequently observed in N than in L1–L4. In the present study, BMD measured in L2–L4 was higher than that assessed in N in every study group. This finding probably reflects the presence of spinal osteophytes and aortic calcification, which may spuriously elevate lumbar BMD measurements (11).

Many factors influence bone remodeling and impair bone structure and quality in patients with chronic renal failure. Hyperparathyroidism and hypoparathyroidism, reduced calcium and increased phosphate serum concentrations, uremic toxins, deteriorated cytokine and growth factor function, acidosis, and vitamin D deficiency or excess connected with treatment, malnourishment, immobilization, influences of glucocorticosteroids and heparin, current gastric acid suppression therapy, ethnicity, various genetic factors, and underlying diseases all contribute to development

of various types of uremic bone disease (2,12–14). In the present study, greater bone loss in the older dialyzed patients was shown to be concomitant with lower serum albumin concentration and lower LBM, but serum levels of ferritin and glucose were higher in the older group than in the younger one. Higher total body mass was not a sufficient protective factor against bone loss in the older dialyzed group. In a normal population, weight and BMD are positively correlated (15).

Data presented by Negri *et al.* (16) showed that in patients on peritoneal dialysis, sex is not a predominant factor in the occurrence of osteopenia or osteoporosis. In our investigations, which were performed in uremic patients with a mean dialysis duration of more than 20 months, differences in BMD between the sexes were also nonsignificant in N and L2–L4. We previously found the same results in our patients dialyzed for no more than 1 year (10). However, after adjustment of the present results for age, the men showed a significantly higher BMD in N than the women did. Men dialyzed for less than 1 year also showed a higher BMD in the ultradistal part of the forearm, in the 33% distal part of the forearm, and in total body (10). These results indicate that BMD is better preserved in male dialyzed patients than in female dialyzed patients.

### Conclusions

Older age, which is more frequently associated with protein malnutrition, inflammation, and glucose abnormalities than is younger age, is also an important factor influencing loss of BMD in dialysis patients. Male sex is protective against bone loss in dialysis patients.

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