Association Between Body Composition and Bone Mineral Density in Men on Hemodialysis

Sandra M. S. de A. Marinho, MD, Vivian Wahrlich, PhD and Denise Mafra, PhD

Abstract: Studies have revealed complex interactions between bone and fat, however there are few studies about this crosstalk in patients with chronic kidney disease. This study investigated possible relationship between bone mineral density (BMD) and body composition in patients who underwent hemodialysis. Twenty patients were enrolled in a cross-sectional study (47.0 [42.3–56.8] years, body mass index 26.0 ± 4.2 kg/m^2, dialysis vintage of 48.5 [26.7–95.7] months). Body composition and BMD were assessed by dual-energy X-ray absorptiometry. Leptin and parathormone levels were analyzed using Multiplex kits (R&D System Inc). Low bone mass in the femoral neck was reported in 54.8% of patients. Total BMD and total T-score were positively correlated with lean mass (r = 0.46, P = 0.04; r = 0.47, P = 0.04, respectively), but not with leptin or body fat mass. In conclusion, lean body mass is probably important to maintain bone health in male patients who underwent hemodialysis.

Key Indexing Terms: Hemodialysis; Bone mineral density; Body composition. **[Am J Med Sci 2015;350(4):286–289.]**

Mineral and bone disorders in patients with chronic kidney disease (CKD) are part of the complex metabolic disorders that affects patients in all disease stages, and contributes to morbidity and poor quality of life of these patients. Thus, understanding the complex biology and evaluating the issues related to this framework are very important.[1,2] Recent studies have shown that excess of body weight is related to high bone mass, and the hypothesis is based on the mechanical load because they accrue more bone as a compensatory mechanism to better support their body mass.[3–5] However, the protective effect of obesity on bone mineral density (BMD) in patients with CKD is still unclear.[6]

Obesity can affect bone metabolism directly, because of mechanical stimulation of bone leading to increased osteoblast proliferation,[6] or indirectly by inflammatory cytokines derived from adipocytes such as leptin and adiponectin.[7,8] High leptin levels can be linked to increased bone mass, which is probably related to osteoblast stimulation. However, some authors have reported an inverse association between leptin; bone mass and parathormone in patients who underwent dialysis suggesting that leptin could be responsible for low bone turnover in these patients. Decreased bone mass observed in conditions of high leptin levels can be understood as a situation that reflects increased bone reabsorption, and this situation may lead to homeostatic mechanisms for bone protection.[9]

As it is unclear if obesity can really be protective for bone mass in patients with CKD. The aim of this study was to investigate possible associations between BMD and body composition in male patients who underwent hemodialysis (HD).

SUBJECTS AND METHODS

Patients

This was a cross-sectional study in 20 men on HD who were recruited from the Renal Vida Clinic in Rio de Janeiro, Brazil. Participants were excluded for inflammatory diseases, thyroid disease, cancer, AIDS, severe osteoporosis, deformity of bones, those who had undergone bariatric surgery, smokers and those who were using catabolizing drugs. Patients were included if they were between 40 and 70 years of age and had been on maintenance HD for at least 6 months before the study.

The dialysis sessions ranged between 3.5 and 4.5 hours at a rate of 3 times/week, with a blood flow greater than 300 mL/min, a dialyzate flow of 600 mL/min and a bicarbonate buffer. Study protocol was approved by Ethics Committee of Medicine School of Federal Fluminense University (301/11). Patients were aware of the study and signed an informed consent after reading such document.

Nutritional and BMD Assessment

Anthropometric measurements were obtained on a day of no HD session by a trained staff member with patient wearing light clothes and without shoes. Waist circumference was measured in the midpoint between the last rib and the top iliac crest with an inelastic tape, and readings were made to nearest 0.1 cm. Body mass was measured in electronic scale (Filizola, São Paulo, Brazil) to within 0.1 kg, and stature was obtained in duplicate with a stadiometer to the nearest 0.1 cm. Body mass index was calculated as body mass (kg) divided by square stature (m).

Lean soft tissue (in this study refers to lean body mass), percentage body fat and BMD were assessed by dual X-ray absorptiometry (DXA) (Lunar iDXA–General Electric Healthcare, Madison, WI), with the software Encore 2010—version 13.40. DXA was calibrated according to the standard procedure recommended by manufacturer. Data acquisition was obtained on a day of no HD session with the subject wearing light clothes (with no metal or plastic) in supine position by a trained X-ray technician.

BMD—g/cm^2 for total body, lumbar spine, femoral neck and femur was expressed as T-score, and it was classified according to the World Health Organization (WHO).[10] T-scores within 1 SD (≥−1 to +1 SD) of the young adult mean were accepted as normal, those 1 to 2.5 SD below the young adult mean (<−1 to −2.5 SD) as osteopenia and values 2.5 SD or more below the young adult mean (≤−2.5 SD) as osteoporosis.

From the Graduate Program in Medical Sciences (SMSDAM), Fluminense Federal University, Rio de Janerio, Brazil; Fluminense Federal University Nutritional and Functional Assessment Laboratory (VW), Fluminense Federal University, Rio de Janerio, Brazil; and Graduate Program in Cardiovascular Sciences (DM), Fluminense Federal University, Rio de Janerio, Brazil.

Submitted April 21, 2015; accepted in revised form July 2, 2015.

The authors have no conflicts of interest to disclose.

The authors acknowledge the Support Foundation for Research of the State of Rio de Janeiro (FAPERJ), National Counsel of Technological and Scientific Development (CNPq) and Coordination of Improvement of Superior Education Personnel (CAPES).

Correspondence: Sandra M. S. de A. Marinho, MD, Estrada do Muriqui, 273—Vila Progresso, Niterói-RJ 24322520, Graduate Program in Medical Sciences Fluminense Federal University (UFF), Niterói-RJ, Brazil. (E-mail: sandramaramarinho@hotmail.com).

Biochemical Variables

Blood samples were obtained from an arterial line before the start of the HD session after the patients had fasted overnight, and serum was immediately frozen at −80°C until analysis. Serum albumin (bromocresol green method), calcium and phosphate were measured using standard laboratory methods. Leptin and parathormone levels were analyzed using Multiplex kits (R&D System Inc, Minneapolis, MN).

Statistical Analysis

The Kolmgorov-Smirnov or Shapiro-Wilk normality test was used to characterize the data distribution. Results were expressed as mean ± SD or median (interquartile range), as applicable. Pearson's or Spearman's correlation coefficient was calculated for univariate analyses. Statistical significance level of 5% was accepted. The statistical analyses were performed through SPSS 19.0 software (Chicago, IL).

RESULTS

The study included 20 patients whose biochemical, body composition and anthropometric data are summarized in Table 1. The average age of participants was 49.6 ± 8.7 years, and dialysis vintage was 60.5 ± 42.7 months. The main causes of CKD were hypertensive nephrosclerosis (61.3%) followed by chronic glomerulonephritis (9.7%), diabetes (9.7%) and other diseases or unknown causes (19.4%). According to body mass index, 60% of patients presented overweight or obesity. Table 2 shows BMD and T-score values in the patients. Low bone mass in the femoral neck was reported in 54.8% of patients. Total BMD (Figure 1) and total T-score were positively correlated with lean mass, but not with leptin or body fat mass.

Femoral neck and lumbar spine BMD and T-score did not correlate with serum leptin levels or body composition parameters. Besides, the BMD-evaluated parameters did not correlate with dialysis vintage.

DISCUSSION

This study provides information about the relationship between body composition (lean and fat tissue) and BMD of various skeletal sites in men on HD. The results showed significant positive relationship between BMD and lean body mass, but not with fat mass or leptin.

TABLE 1. Anthropometric and biochemical data in HD patients

Parameters	Values
Age (yrs)	47.0 (42.3–56.8)
Waist circumference (cm)	94.0 ± 11.6
BMI (kg/m^2)	26.0 ± 4.2
Lean mass (kg)	49.5 ± 6.8
Body fat (%)	30.3 ± 8.8
Calcium (mg/dL)	6.3 (4.9–9.2)
Phosphate (mg/dL)	4.7 ± 0.9
Albumin (g/dL)	4.1 (3.8–4.4)
PTH (pg/mL)	574.6 ± 238
Leptin (ng/mL)	8.0 (3.2–14.2)

Parametric variables displayed as mean ± SD and nonparametric variables displayed as median and interquartile range.
PTH, parathormone.

TABLE 2. BMD and T-scores values in HD patients

Parameters	BMD (g/cm^2)	T-Score
Total	1.091 ± 0.142	−1.01 ± 1.30[a]
Femoral neck	0.859 ± 0.143	−1.58 ± 1.07[a]
Femur	0.918 ± 0.153	−1.26 ± 1.04[a]
Lumbar spine	1.098 ± 0.156	−1.11 ± 1.20[a]

[a] WHO (1994): osteopenia = SD between −1.0 and −2.5.
BMD, Bone mineral density.

Previous studies have described the crosstalk between bone and adipose tissue, besides the increased leptin levels and decreased adiponectin levels present in obesity that seem to be complex and exert both positive and negative metabolic effects on bone, which the action depends on the signaling pathway.[7,8,11–15] However, recently, adiposity has been negatively associated with BMD, and its mechanism is multifaceted. Leptin through sympathetic nervous system may adversely affect bone mass; and in addition, the adipokines may exert a detrimental influence on BMD.[16–18]

Ob/ob mice, a natural mutant strain where the leptin gene is inactivated, exhibited elevated bone mass, and this provided strong evidence that leptin uses the central pathway to control bone mass because leptin intracerebral ventricular infusion normalized the high bone mass caused by leptin deficiency.[19] However, there is a lack of studies on the possible effects of body fat mass on bone in patients who underwent HD.

Despite potential positive effects of mechanical loading conferred by increased body weight with obesity on bone, accumulating data point to another direction, suggesting that obesity is detrimental to bone health.[6] Evidence has shown that there is an inverse reciprocal relation between fat mass and bone mass. Subjects with higher percentage body fat independent of body weight, physical activity and age present higher risk of osteoporosis and low bone mass. Thus, fat mass has a negative effect on bone mass in contrast with the positive effect of weight bearing itself.[20] In obesity, impaired bone quality can occur because in this condition, the well balance between adipocyte and osteoblast differentiation in bone marrow may be gradually affected.[21]

In fact, both lean mass and fat mass possibly are important determinants of BMD.[22] However, lean mass seems to be the dominant positive predictor BMD, and maintaining lean mass is critical for maintaining bone mass.[23] A recent study showed that athletes (high lean mass) when compared with controls presented a strong correlation between lean mass and bone geometry.[24] There are few studies about this relationship in patients with CKD. Body composition of patients who underwent HD has been assessed using DXA, and the results showed positive correlation between BMD and weight.[25,26] With similar findings, Negri et al[27] also observed that lean body mass was the most important component that determines total bone mineral content in patients who underwent peritoneal dialysis particularly in men and postmenopausal women.

The bone mass may be primarily determined by the dynamic loads from muscle force.[28] Although both lean mass and fat mass are pointed as determinants of BMD, because fat tissue is metabolically active, its action on the skeleton may be influenced not only by the weight bearing but also by others effects.[20,22] In fact, positive association between lean mass and BMD was found in several studies.[20,22,29–31]