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Reduced bone mineral density is not associated with significantly reduced bone quality in men and women practicing long-term calorie restriction with adequate nutrition

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SUMMARY

Calorie restriction (CR) reduces bone quantity but not bone quality in rodents. Nothing is known regarding the long-term effects of CR with adequate intake of vitamin and minerals on bone quantity and quality in middle-aged lean individuals. In this study, we evaluated body composition, bone mineral density (BMD), and serum markers of bone turnover and inflammation in 32 volunteers who had been eating a CR diet (~35% less calories than controls) for an average of 6.8±5.2 years (mean age 52.7±10.3 years) and 32 age- and sex-matched sedentary controls eating Western diets (WD). In a subgroup of 10 CR and 10 WD volunteers, we also measured trabecular bone (TB) microarchitecture of the distal radius using high-resolution magnetic resonance imaging. We found that the CR volunteers had significantly lower body mass index than the WD volunteers (18.9±1.2 vs. 26.5±2.2 kg/m^2; P=0.0001). BMD of the lumbar spine (0.870±0.11 vs. 1.138±0.12 g/cm^2, P=0.0001) and hip (0.806±0.12 vs. 1.047±0.12 g/cm^2, P=0.0001) was also lower in the CR than in the WD group. Serum C-terminal telopeptide and bone-specific alkaline phosphatase concentration were similar between groups, while serum C-reactive protein (0.19±0.26 vs. 1.46±1.56 mg/L, P=0.0001) was lower in the CR group. TB microarchitecture parameters such as the erosion index (0.916±0.087 vs. 0.877±0.088; P=0.739) and surface-to-curve ratio (10.3±1.4 vs. 12.1±2.1, P=0.440) were not significantly different

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between groups. These findings suggest that markedly reduced bone mineral density is not associated with significantly reduced bone quality in middle-aged men and women practicing long-term calorie restriction with adequate nutrition.

Keywords

calorie restriction; bone mineral density; bone quality; bone turnover; trabecular bone microarchitecture; high-resolution magnetic resonance imaging

INTRODUCTION

Long-term calorie restriction (CR) without malnutrition extends health span and lifespan in rodents and monkeys (Anderson et al 2009). In humans, long-term CR without malnutrition protects against obesity, type 2 diabetes, hypertension and atherosclerosis, which are leading causes of morbidity, disability and mortality (Fontana & Klein 2007). However, low body mass index (BMI) is a well-documented risk factor for future fragility fractures (an important cause of morbidity and mortality among the elderly) in the general population eating typical Western diets (Ravn et al 1999;Slemenda 1995). Whether long-term CR with adequate micronutrient intake affects the risk of developing bone fractures is not known. In particular, we are not aware of any study that has evaluated the effects of long-term CR with adequate nutrition on risk factors for bone fractures (e.g. bone mineral density, bone turnover, and bone quality) in middle-aged lean humans practicing CR.

Data from experimental animal studies indicate that long-term 30-50% CR can have a significant impact on bone metabolism, bone mineral density (BMD), bone microarchitecture and bone strength in rodents, depending on the age when CR is started, the severity and duration of CR, and the micronutrient content of the diet (Kalu et al 1984;Lambert et al 2005;Lamothe et al 2003;McCay et al 1989;Saville & Lieber 1969;Talbott et al 2001;Westerbeek et al 2008). The majority of studies published so far indicate that 30-50% CR reduces BMD in rodents and monkeys, independently of the age when CR is started (Kalu, Hardin, Cockerham, Yu, Norling, & Egan 1984;Lambert, Lamothe, Zernicke, Auer, & Reimer 2005;Lamothe, Hepple, & Zernicke 2003;McCay, Crowell, & Maynard 1989;Saville & Lieber 1969;Talbott, Cifuentes, Dunn, & Shapses 2001;Westerbeek, Hepple, & Zernicke 2008). On the other hand, it has been reported that long-term 40% CR in animals improves bone quality and strength through a reduction of bone turnover and a prevention of secondary hyperparathyroidism (Kalu, Hardin, Cockerham, Yu, Norling, & Egan 1984;Tatsumi et al 2008). Moreover, one study showed that 40% CR preserves trabecular bone mass in the mouse skeleton (Hamrick et al 2008).

As major species differences between rodents and humans exist in bone composition, bone metabolism, BMD, and bone quality (Aerssens et al 1998), the availability of individuals practicing long-term CR with adequate nutrition (i.e. adequate intake of vitamin D, calcium and other micronutrients that may influence bone health) made it possible for us to investigate bone mass and quality in people on a low calorie diet. In this paper, we report data on BMD, markers of bone turnover and inflammation, in individuals who have been practicing a CR diet for periods ranging from 3 to 20 years. We also report novel data on bone quality, which is an important predictor of bone fractures (Seeman & Delmas 2006), specifically trabecular microarchitecture as measured by high resolution magnetic resonance microimaging.

RESULTS

BODY COMPOSITION AND BONE MINERAL DENSITY

Body weight and BMI were significantly lower in the CR group than in the WD group (Table 1). Total body fat and lean mass were also lower in the CR group than in the WD group (Table 1). The mean BMD and T scores in the CR group were significantly lower than in the WD group at the lumbar spine, total hip, and femoral neck and trochanter sites (Table 1). None of the participants had clinical evidence of bone fractures.

Hr-MRI

Among the simple topological parameters measured using hr-MRI, only trabecular thickness was significantly lower in the CR group compared with the WD group, whereas there were no significant between-group differences across all other parameters (BV/TV fraction, volume, and skeleton density). More importantly, there were no significant group-differences in the composite topological parameters of TB microarchitecture, surface-to-curve ratio and erosion index (the sample sizes required for significant differences are equal to 137 and 687, respectively), indicating intact trabecular network (Table 3).

MARKERS OF BONE TURNOVER AND INFLAMMATION

The serum CTX- and BSAP concentrations in the CR group were not significantly different from those of the WD group (the sample sizes required for significant differences are equal to 124 and 1699, respectively) (Table 1 and 2). Serum high sensitive CRP concentration was markedly lower in the CR group than in the WD group (Table 1).

NUTRIENT INTAKE

Calorie and nutrient intakes differed significantly between the CR and WD groups. The CR practitioners designed their diets in order to reduce the caloric intake by eliminating the consumption of energy-dense foods and increasing the intake of a wide variety of nutrient-dense foods that supply more than 100 percent of the Recommended Daily Intake (RDI) for all the essential nutrients. The total caloric intake of the CR group was ~ 35 % lower than the caloric intake of the WD group (1758±369 kcal/d vs. 2699±459 kcal/d, respectively). The CR practitioners eat a wide variety of vegetables, fruits, nuts, low-fat dairy products, egg whites, wheat and soy proteins, fish and meat (~23.7% calories from protein, ~28.5% from fat, ~48% from complex carbohydrates and ~1% from alcohol). All of the participants in the CR group strictly avoided refined and processed foods containing trans-fatty acids and high glycemic foods (e.g. refined carbohydrates, potato, white bread, white rice, sweets and soft drinks). Their mean daily dietary intakes of calcium and vitamin D were 1339±366 mg/day and 1036±516 U/day, respectively. The WD group ate typical Western diets containing ~16.5% calories from protein, ~34.7% from fat, ~49% from carbohydrates and ~3.6% from alcohol. Their mean daily dietary intakes of calcium and vitamin D were 1082±382 mg/day and 358±186 U/day, respectively. Accordingly, in a subgroup of CR (n = 18) and WD subjects (n = 18), the serum vitamin D levels were 85.4 ± 36.3 nmol/L and 41.8 ± 28.5 nmol/L, respectively ($P < .05$).

DISCUSSION

In this study, we compared BMD, TB bone microarchitecture, and markers of bone turnover in healthy weight-stable lean men and women, who were consuming a self-imposed CR-diet, containing more than 100% of the RDI for all essential nutrients (including calcium and vitamin D), for 3 to 20 years, with age- and sex- matched sedentary individuals, who were consuming Western diets. Our data show that BMD at the lumbar spine and hip sites was significantly lower in the CR group than in the WD group. However, serum CTX-1 and

BSAP, two well accepted markers of bone resorption and formation (Johnell et al 2002;Ross et al 2000), respectively, were not significantly different between the two groups, which suggest that long-term CR with adequate micronutrient intake does not significantly increase the rate of bone turnover. In addition, one of the key and novel findings from this study was that TB microarchitecture of the distal radius, as indicated by surface-to-curve ratio and erosion index assessed by hr-MRI, was not significantly different between the CR and WD groups, despite markedly low BMD.

Nutrition has a unique role in the maintenance of bone health. Dietary macro- and micronutrients affect bone metabolism, bone density and strength through changes in body weight, hormonal and inflammatory status (Ilich & Kerstetter 2000;Muhlbauer & Li 1999;Ravn, Cizza, Bjarnason, Thompson, Daley, Wasnich, McClung, Hosking, Yates, & Christiansen 1999). In general, data from epidemiological studies conducted in Europe and North America indicate that a low body weight is associated with low bone mass and an increased risk of fragility fractures (Ravn, Cizza, Bjarnason, Thompson, Daley, Wasnich, McClung, Hosking, Yates, & Christiansen 1999;Slemenda 1995). However, correlation is not the same as causation, and cross-national analysis have shown that the age-adjusted incidence rates of hip fracture among Asian populations seems to be 30–70% of those observed among Caucasians, despite lower BMI and BMD values, suggesting that other factors may be involved (Blaum et al 2005;Ross et al 1991;Silverman & Madison 1988). In our study, body weight, body fat and BMD of the spine and hip were markedly low in both men and women in the CR group, but markers of bone turnover and TB microarchitecure were not significantly different between the CR and the WD groups.

Evidence that bone turnover and bone quality play a key role in determining fracture risk is provided by the finding that in osteoporotic patients, bisphosphonate therapy results in a rapid reduction in markers of bone turnover and bone remodelling, and in a 30-40% reduction in fracture risk, even in the absence of any change in bone mass (Bjarnason et al 2001;Cummings et al 2002;Sarkar et al 2002). Moreover, type 2 diabetics with a high BMI have increased bone fracture risk, despite a high bone mass, probably because of poorer bone quality (Reddy et al 2001;Schwartz 2003;Verhaeghe et al 1994). Our findings of not significantly altered rates of bone turnover and TB microarchitecture despite markedly low BMD in CR subjects reinforce these previous findings (Bjarnason, Sarkar, Duong, Mitlak, Delmas, & Christiansen 2001;Cummings, Karpf, Harris, Genant, Ensrud, LaCroix, & Black 2002;Reddy, Stehno-Bittel, Hamade, & Enwemeka 2001;Sarkar, Mitlak, Wong, Stock, Black, & Harper 2002;Schwartz 2003;Verhaeghe, Suiker, Einhorn, Geusens, Visser, Van, Van, Magitsky, & Bouillon 1994) of the lack of concordance between BMD and bone quality. In addition, these findings appear consistent with the known effects of CR in suppressing inflammation, reducing protein glycosylation and other metabolic/hormonal changes that may reduce the slope of decline of age-related bone loss (Fontana & Klein 2007;Tatsumi, Ito, Asaba, Tsutsumi, & Ikeda 2008). Indeed, long-term CR in humans results in very low levels of markers of systemic inflammation (e.g. CRP and TNF-alpha), and because inflammatory cytokines are potent bone resorptive agents, (Bertolini et al 1986;Schett et al 2006) our data suggest that a low state of inflammation in the bone microenvironment may partially mediate the lack of increased bone turnover in individuals practicing long-term CR. We measured CRP in the present study because it is a sensitive marker of systemic inflammation, and is an inexpensive and simple test that has been used to assess the risk for atherosclerosis (Cesari et al 2003). Numerous studies have found a negative association between CRP and BMD (Ding et al 2008; Koh et al 2005) and bone fracture (Ma et al 1996), and bone turnover (Oelzner et al 1999). However, is not known whether CRP is a direct mediator of bone loss, or whether it is surrogate marker for other factors directly associated with osteoporosis. CRP is predominantly produced in the liver, and IL-1, IL-6 and TNF-alpa have been identified as regulators of CRP production. It is

possible that inflammatory processes can upregulate these cytokines, which strongly stimulate CRP production from the liver as well as induce bone resorption, and increased bone resorption may result in increased bone turnover and decreased BMD. The discovery of the importance of osteoprotegerin and the RANK ligand in modulating osteoclast formation and activity provides further support for the important role that inflammation plays in determining the rate of bone turnover and quality (Kong et al 1999;Takayanagi 2007;Theill et al 2002).

Trabecular bone microarchitecture is also a major determinant of bone strength and a good predictor of the risk of developing fragile fracture (Dempster 2003;Seeman & Delmas 2006). A number of studies have shown that patients with fragility fractures have poorer TB microarchitectural integrity than age-, sex- and BMD-matched nonfractured control subjects (Aaron et al 2000;Homminga et al 2002;Kleerekoper et al 1985;Legrand et al 2000). Interestingly, aging is associated with a conversion from a honeycomb-like TB microarchitectural structure to a network of interconnected rods with higher structural and mechanical anisotropy (Dempster 2003;Seeman & Delmas 2006). Studies using high-resolution peripheral quantitative computed tomography have shown that by age 30, TB architecture starts to deteriorate with a similar pattern at the femur neck, distal radius, and distal tibia in both men and women (Riggs et al 2004). However, vital information on TB microarchitecture is not routinely available because normally it requires invasive bone biopsy or exposure to a high dose of X-ray radiation. In this study, we used the technique of hr-MRI to determine whether the trabecular architecture of individuals practicing long-term CR with adequate vitamin D and calcium intake differs from that of age- and sex-matched individuals eating a typical WD diet. This novel and non-invasive technique allowed us to calculate the degree to which trabecular plates have deteriorated to become rods in the distal radius (Wehrli 2007;Wehrli et al 2002). We found that parameters such as the erosion index and the ratio of surface voxels to curve voxels were not significantly different between groups, indicating that the low BMD in CR subjects is accompanied by preserved TB microachitecture, consistent with normal rates of bone turnover, and suppressed inflammation. It has been shown that hr-MRI parameters differentiate subjects who have vertebral fractures from those who do not better than bone densitometry (Wehrli 2007;Wehrli et al 2001). Therefore, given the markedly decreased BMD in the CR subjects (T score ~-2.0), we would have expected that they would have even worse TB microarchitecture as evaluated by the sensitive hr-MRI technique but clearly this was not the case (e.g. no significant differences in erosion index and surface-curve ratios from the WD subjects with normal BMD). Some limitations in our study must be acknowledged. One is the fact that the CR volunteers are a heterogeneous group, and therefore differences in macro- or micronutrient content of their diets may be responsible, at least in part, for the differences in BMD, independently of caloric intake. Although we think it is likely that the low bone mass is due to bone loss after institution of CR diet, because this is a cross-sectional study we cannot completely exclude the possibility that this could also be due to low peak bone mass. Finally, our sample size was small; therefore, larger studies are needed to confirm our preliminary findings that low BMD may not be associated with reduced bone quality in men and women practicing long-term CR.

In conclusion, the results of this cross-sectional study on 32 individuals practicing severe CR without malnutrition provide preliminary evidence that a CR diet is associated with low bone mass at clinically important skeletal regions but without evidence of significant increase in bone turnover, and impaired bone quality. Clearly, it will be necessary to follow a large number of people practicing severe CR with adequate nutrition for a sufficiently long period. Long-term follow up is necessary to determine whether or not people practicing CR have an increased risk of developing fractures.

EXPERIMENTAL PROCEDURES

STUDY PARTICIPANTS

Thirty-two individuals who strictly adhere to a CR diet were recruited through the Calorie Restriction Society. They had been practicing CR with adequate nutrition for an average of 6.8±5.2 years (range 3-20 yrs). None of the CR group was physically trained; ~50% of them do 30 to 45 min of weight training or interval training per week to try to maintain muscle mass. They do not exercise more because this would necessitate increasing their calorie intake. Thirty-two sedentary (regular exercise <1 h per week) individuals eating typical Western diets matched with the CR group in terms of age, sex and height, served as a sedentary comparison group. The characteristics of the study participants are shown in Table 1. None of the subjects had a history or clinical evidence of bone fractures or any other chronic disease (including cardiovascular, lung, gastrointestinal and autoimmune disease, type 2 diabetes, and cancer) based on medical history, complete physical exam, routine biochemistries, hematological evaluation and urinalysis. They were all non-smokers. All of the women in the CR and WD groups were postmenopausal. None of the participants in this study were taking drugs that affect bone metabolism (e.g. biphosphonates, hormone replacement, steroids), or other medications that could affect the variables that were measured. All of the study participants were weight stable, i.e. less than 2 kg weight change in the preceding 6 months. Informed consent was obtained from all subjects. This study was approved by the Human Studies Committee of Washington University School of Medicine.

ANTHROPOMETRIC, BODY COMPOSITION, AND BONE DENSITY MEASUREMENT

Height was measured without shoes to the nearest 0.1 cm. Body weight was obtained on a balance scale in the morning after a 12-hour fast. Body mass index (BMI) was calculated by dividing body weight (in kilograms) by the square of height (in meters). Bone mineral density (BMD) of the total body, lumbar spine (L1-L4), and proximal femur, were measured by dual-energy X-ray absorptiometry (DXA) using a Hologic QDR 4500 (Hologic Inc, Waltham, MA). Assessments of test-retest reliability of BMD measurements yielded intraclass correlation coefficients that were greater than 0.98 for all sites of interest. Regarding precision, the coefficients of variation for BMD were all less than 1.5%. DXA was also used to estimate body composition using v5.71 of the enhanced whole body analysis software. The precision of measuring total mass, fat mass, bone mineral mass, and non-bone fat- free mass (lean mass) was 0.96 ± 4%, 1.66 ± 0%, 0.86 ± 3%, and 1.86 ± 9%, respectively.

BONE QUALITY MEASUREMENT WITH HIGH RESOLUTION MRI IN VIVO

High resolution magnetic resonance imaging (hr-MRI) was performed in a subgroup of 10 subjects in the CR group and 10 subjects in the WD group. Hr-MRI utilizes a patented algorithm that converts data into a highly detailed three dimensional (3-D) model of trabecular bone (TB) microstructure as previously described (Wehrli et al 1998). Briefly, the components of the hr-MRI are the 1) radiofrequency (RF) pulse sequence software, 2) the imaging RF coil and immobilization device, and 3) the post processing software algorithm. We used the fast large-angle spin echo (FLASE) pulse sequence, which is specifically designed for structural imaging of trabeculae and provides artifact-free images of signal to noise ratio adequate for the processing algorithms to operate reliably (Ma, Wehrli, & Song 1996). A custom designed receive only RF phased array surface coil was used to assess the distal radius using the Siemens Sonata 1.5 Tesla Scanner (Siemens, Iselin, NJ). The distal radius was used because signal-to-noise limitations dictate the use of a peripheral site and because the presence of distinct anatomic landmarks facilitates the precise location of the scan and analysis volume (Wehrli 2007). Analyses of the scans were done by MicroMRI Inc (Langhorne, PA) in a blinded manner using software algorithms that include processing the

image, enhancing the resolution, and providing visualizations and quantitative metrics regarding 3-D trabecular bone architecture. The technique permits quantification of the degree to which trabecular plates (surfaces) have deteriorated to become rods (curves), a change that highlights osteoporosis (Wehrli, Gomberg, Saha, Song, Hwang, & Snyder 2001). The hr-MRI indices include: (a) simple topological parameters, such as the bone volume to total volume ratio (BV/TV), trabecular thickness, skeleton density, and volume; and (b) two composite parameters that have been found to be very sensitive to bone loss (Wehrli, Gomberg, Saha, Song, Hwang, & Snyder 2001) and response to treatment (Benito et al 2005;Greenspan et al 2010), such as the surface-to-curve ratio where higher values indicate a more intact trabecular network and lower values indicate a network that has deteriorated; and an erosion index, a ratio of parameters expected to increase when bone trabeculae deteriorate, where higher values indicate greater deterioration. The average coefficient of variation of hr-MRI-based parameters of TB architecture in the distal radius are 4.6%, 10.0%, and 6.9% for BV/TV, surface-to-curve ratio, and erosion index, respectively (Gomberg et al 2004). The validity of hr-MRI has been established by performing hr-MRI on TB obtained from autopsy specimens at "gold standard" *in vitro* resolution (39 μm), and then the images were resampled to yield images of in vivo resolution (156 μm) (Wehrli, Gomberg, Saha, Song, Hwang, & Snyder 2001). In all parameters of trabecular architecture, the results at the two resolutions highly correlated with each other (r=.684 to .928). Moreover, hr-MRI parameters of TB architecture have been shown to differentiate women who have vertebral fractures from those who do not better than bone densitometry (i.e. subjects with fractures had lower surface-curve ratios (P<.001) and higher erosion index (P=.001) than subjects without fractures, whereas BMD did not show significant differences between groups (all P>.05) (Wehrli 2007;Wehrli, Gomberg, Saha, Song, Hwang, & Snyder 2001).

BLOOD ANALYSES

A venous blood sample was taken after subjects had fasted for at least 12 hours. Commercial ELISA kits were used to measure serum C-terminal cross linking telopeptide of type-I collagen (CTX-1) (Nordic Bioscience Diagnostics, Herlev, Denmark), bone-specific alkaline phosphatase (BSAP) (Quidel Corporation, San Diego, CA), and high sensitivity C-reactive protein (ALPCO Diagnostics, Windham, NH) concentrations. Serum hsCRP concentrations from 28 of 32 CR volunteers were reported previously.(Fontana et al 2008). Serum vitamin D level was measured using commercial enzyme-linked immunosorbent assay kits (Immunodiagnostic Systems Limited, Boldon, England).

DIETARY ASSESSMENT

The study participants were instructed by a research dietician to record for 7 consecutive days all foods and beverages consumed, preparation methods, and approximate portion sizes in food diaries at the time of consumption. To assist with portion size determinations, measuring spoon and cup sets were provided to all participants, and all food diaries had a ruler imprinted on the back cover. The food record was analysed using the NDS-R program (version 4.03_31), which is the Nutrition Data System for research from the Nutrition Coordinating Center at the University of Minnesota. The database has 117 nutrients. The nutrients of interest are calories, total fat, total carbohydrate, total protein, animal protein, vegetable protein, calcium, vitamin D, soluble fiber, insoluble fiber, folate, all of the amino acids, and phytic acid.

STATISTICAL ANALYSIS

The unpaired Student's *t*-test was used for normally distributed variables with approximately equal SD. For variables not normally distributed or with unequal SD the Wilcoxon two-samples test was used. Statistical significance was set at $P \leq 0.05$. Data were analyzed by

using SPSS FOR WINDOWS software, version 17.0 (SPSS Inc, Chicago). Values are expressed as means ± SD.

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Table. 1

Subject characteristics, body composition, bone mineral density, and markers of bone turnover and inflammation

	CR group (n=32)	WD group (n=32)	P value
Age (years)	52.7 ± 10.3	53.4 ± 9.4	0.761
Sex (M/F)	28/4	28/4	
BODY COMPOSITION			
Body weight (kg)	57.5 ± 5.3	84.8 ±11.4	0.0001
Body mass index (kg/m^2)	18.9 ± 1.2	26.5 ± 2.2	0.0001
Body composition			
Fat mass (%)	10.6 ±6.6	25. 4 ± 7.7	0.0001
Lean mass (kg)	49.2 ± 7.3	60.0 ± 9.3	0.0001
BONE MINERAL DENSITY			
Lumbar spine (g/cm^2)	0.870 ± .111	1.138 ± .120	0.0001
T score	−2.1 ± 1.0	0.36 ± 1.0	0.0001
Total hip (g/cm^2)	0.806 ± .118	1.047 ± .118	0.0001
T score	−1.47 ± 0.78	0.12 ± 0.73	0.0001
Femoral neck (g/cm^2)	0.677 ± .110	0.856 ± 0.118	0.0001
T score	−1.8 ± 0.8	−0.53 ± 0.83	0.0001
Trochanter (g/cm^2)	0.611 ± .102	0.809 ± 0.123	0.0001
T score	−1.3 ± 0.80	0.26 ± 0.90	0.0001
MARKERS OF BONE TURNOVER AND INFLAMATION			
S-CTX (ng/mL)	0.595 ± .288	0.508 ± .179	0.152
S-BSAP (U/L)	17.6 ± 5.8	18.1 ± 4.5	0.691
HsCRP (mg/L)	0.19 ± 0.26	1.46 ± 1.56	0.0001

Values are mean ± SD. S-CTX = serum C-terminal telopeptide; S-BSAP = serum bone-specific alkaline phosphatase, HsCRP = high sensitivity C-reactive protein

Table. 2

Subject characteristics, body composition, bone mineral density, and markers of bone turnover and inflammation in the subgroup of subjects who underwent Hr-MRI analyses

	CR group (n=10)	WD group (n=10)	P value
Age (years)	57.1 ± 9.8	57.7 ± 7.2	.878
Sex (M/F)	7/3	7/3	
BODY COMPOSITION			
Body weight (kg)	56.8 ± 7.4	83.1 ± 17.2	<.001
Body mass index (kg/m^2)	19.3 ± 0.8	28.1 ± 5.1	<.001
Body composition			
Fat mass (kg)	9.6 ± 3.2	25. 4 ± 1.3	.002
Fat-free mass (kg)	47. 2 ± 8.4	57.8 ± 12.2	.037
BONE MINERAL DENSITY			
Lumbar spine (g/cm^2)	0.820 ± .113	1.186 ± .138	<.001
T score	−2.4 ± 0.9	1.0 ± 1.2	<.001
Total hip (g/cm^2)	0.724 ± .118	1.007 ± .138	<.001
T score	−2.0 ± 0.7	0.0 ± 0.6	<.001
Femoral neck (g/cm^2)	0.599 ± .083	0.834 ± 0.104	<.001
T score	−2.4 ± 0.6	−0.6 ± 0.7	<.001
Trochanter g/cm^2)	0.558 ± .070	0.780 ± .112	<.001
T-score	−1.7 ± 0.5	0.2 ± 0.8	<.001
Ultra distal radius (g/cm^2)	0.397 ± .021	0.483 ± .064	.009
T- score	−1.5 ± 0.8	−0.1 ± 0.8	<.001
MARKERS OF BONE TURNOVER			
S-CTX (ng/mL)	0.702 ± .285	0.507 ± .192	.423
S-BSAP (U/L)	22.6 ± 5.7	23.1 ± 4.7	.837
HsCRP (mg/L)	0.3 ± 0.1	3.2 ± 1.3	.047

Values are mean ± SD. S-CTX = serum C-terminal telopeptide; S-BSAP = serum bone-specific alkaline phosphatase, HsCRP = high sensitivity C-reactive protein

Table. 3

Hr-MRI Parameters

	CR group (n=10)	WD group (n=10)	P value
BV/TV	0.092 ± .019	0.102 ± .022	.318
Trabecular thickness (mm)	0.089 ± .007	0.097 ± .008	.023
Volume (cc)	1.706 ± .314	1.877 ± .424	.320
Skeleton density	0.051 ± .011	0.056 ± .012	.353
Surface-to-curve ratio	10.3 ± 4.3	12.2 ± 6.7	.440
Erosion index	0.917 ± 0.276	0.876 ± 0.278	.739

Values are mean ± SD. BV/TV = Bone volume to total volume ratio