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Resting Energy Expenditure: A Stronger Marker Than Body Weight for BMD in Caucasian Women But Not Men? The Rancho Bernardo Study

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Abstract

Objective—An association between resting energy expenditure (REE) and bone mineral density (BMD) has not been reported in Caucasian adults.

Design—Cross-sectional study.

Setting—Caucasian, middle-class to upper middle-class community-dwelling adults.

Participants—Women (n=996) and men (n=686) aged 36–97 years.

Assessment of Risk Factors—REE calculated using the Harris-Benedict equation.

Main Outcome Measurements—BMD of the lumbar spine (L1–L4), total hip, and total body measured using dual energy x-ray absorptiometry.

Results—REE was lower in women than in men (1220 versus 1566 kcal/day, $p < 0.0001$); women were also thinner based on BMI. After adjusting for lean body mass (LBM), REE was higher in women than men (1407 versus 1296 kcal/kg LBM/day, $p < 0.0001$). In stepwise multiple linear regression models, REE explained 13% of variance in spine BMD in women and 6% in men, 33% of variance in hip BMD in women and 22% in men, and 32% of variance in total body BMD in women and 22% in men. In women, weight explained 10% less of the hip BMD variance and 6% less of the total body BMD variance than REE. In men, weight explained 4% more of the spine BMD variance and 1% more of the total body BMD variance than REE.

Conclusions—REE explained more of the BMD variance than weight in women and the reverse was true in men. These sex differences were largely explained by sex differences in LBM or weight.

Keywords

Harris-Benedict equation; REE; bone mineral density; osteoporosis; weight

INTRODUCTION

Fracture risk is greater in women than men (1–3). In the United States, the estimated lifetime risk of a hip fracture in Caucasians is 17.5% in women and 6% in men; the lifetime risk of a

clinical vertebral fracture is 16% for women and 5% for men; the lifetime risk of forearm fractures is 16% for women and 2.5% for men (2,3). The lifetime risk of any of these three fractures is 40% for women and 13% for men (2,3). These differences have been mostly attributed to postmenopausal hormone loss in women coupled with their smaller bone size. Although many studies have reported positive associations between body size and bone mineral density (BMD), the role of sex differences in body weight and its association with bone density is complex.

Body weight is regulated by the dynamic balance between energy intake and energy expenditure. An individual may become overweight with appropriate energy expenditure if intake is excessive or with an appropriate energy intake if expenditure is low. Since resting energy expenditure (REE) is the largest component of total energy expenditure (4) and a low REE is one factor that predisposes individuals to gain body weight (5), understanding sex differences in REE and its association with BMD may partially explain sex differences in fracture rates. Absolute REE is lower in women (6), but evidence that this difference persists after adjustment for lean body mass (LBM) is contradictory. Some have reported LBM-adjusted REE is lower in women than men (7–9), lower in men than women (10,11), or does not differ by sex (6,12,13).

We previously reported results from a cohort of African-American women (14), in whom REE explained more of the BMD variances in hip, lumbar spine, and total body than did weight, body mass index (BMI), fat mass, or LBM. Whether REE is independently associated with BMD in Caucasian women or men is unknown. The purpose of the present study was to assess the sex-specific independent contributions of LBM-adjusted REE versus weight to BMD at the hip, spine and total body in older Caucasian women and men.

MATERIALS AND METHODS

Study Cohort & Subject Description

The study cohort was established in 1972–74 when 82% of adult community-dwelling residents of Rancho Bernardo, California, enrolled in a heart disease risk factor study. The present study of this cohort was conducted in 1992 – 1996 when a total of 996 postmenopausal Caucasian women (mean age= 72.2 years) and 686 Caucasian men (mean age= 71 years), about 78% of locally dwelling survivors of the original Rancho Bernardo cohort, were enrolled in a new study focused on osteoporosis. Reasons for dropout of the 22% of the original cohort were diverse and included being too busy, traveling, no longer interested, not feeling well, etc. We looked at the association of sex with whether or not they participated and there was no association (chi-square = 0.0636, $p=0.80$). In this study, tests and interviews were performed by specially trained staff in the Rancho Bernardo Study Clinic located in Rancho Bernardo. All participants were ambulatory and gave written informed consent. This study was approved by the Institutional Review Board of the University of California, San Diego.

Body Composition and Bone Mineral Density

Fat mass (kg) and LBM (kg) were obtained using dual-energy x-ray absorptiometry (DXA) of the total body. Bone mineral density (BMD) in grams per unit projected area (g/cm^2) was measured at the lumbar spine (L1–L4), the hip (femoral neck, trochanter, Ward's triangle, and total hip), and total body (average BMD of 9 regions not including the head) using Hologic QDR-1000 (software version 5.73, Hologic Inc., Bedford, MA). All scans were performed by one specially-licensed and certified radiology technician. Quality control was performed daily. The precision error (coefficient of variation for repeated measurements) for this technique is 0.43% for spine, 1.02% for the total hip and 0.46% for the whole body.

Weight, Height, and Anthropometry

Weight and height were measured in subjects wearing light clothing without shoes. Weight was measured in kilograms using a standard regularly calibrated scale and recorded to the nearest 0.1 kg. Height was measured using a stadiometer and recorded to the nearest 0.1 centimeters. BMI was calculated as the ratio of body weight to height squared (kg/m^2).

Waist and hip girth were measured in participants who were wearing light, single-thickness clothing, and standing in an erect position with their feet together. Waist girth was measured at the bending point and using the smallest circumference of the torso. Hip girth was measured at the level of the iliac crest and at the maximum extension of the buttocks posteriorly. Values were recorded to the nearest 0.1 centimeters. In this paper, the smallest waist and largest hip girth were used to calculate the waist-to-hip ratio (WHR) as a measure of central adiposity.

Resting Energy Expenditure

The Harris-Benedict equation for REE was originally derived from a sample of 103 women and 136 men studied over a 10-year period (15). The equations, in which weight is in kg, height is in cm, and age is in years, are:

For women: $\text{REE (kcal/day)} = 655 + (9.56 \times \text{weight}) + (1.85 \times \text{height}) - (4.68 \times \text{age})$

For men: $\text{REE (kcal/day)} = 66 + (13.75 \times \text{weight}) + (5.0 \times \text{height}) - (6.76 \times \text{age})$

This method has been validated as measure of REE (16–18).

Grip Strength

A hand-held grip dynamometer (Therapeutic Instruments Hand Dynamometer, Clifton, NJ) was used to assess strength. Seated subjects were instructed to grip the dynamometer as hard as possible for 3 seconds, and were instructed not to press the instrument against their body or bend their elbow. They were tested twice with each hand, and the best grip strength of each hand was reported in kilograms of force.

Physical Activity

Three questions were used to assess physical activity. One question was related to the intensity of exercise: “Do you regularly engage in strenuous exercise?” A second question was related to the frequency of exercise: “Do you exercise at least three times a week?” A third question related to the frequency of resistance exercise asked: “Have you lifted weights in the past 2 weeks?” The first 2 questions are from the Lipid Research Clinics Questionnaire by Ainsworth and colleagues (19), and were indirectly validated as follows in the Rancho Bernardo cohort: physically active women had significantly lower resting heart rates (61.4 beats/min *versus* 66.5 beats/min) and body mass indexes ($23.4 \text{ kg}/\text{m}^2$ *versus* $26.3 \text{ kg}/\text{m}^2$) (20), and had significantly higher levels of HDL-cholesterol (Barrett-Connor, unpublished, 1983, 1990).

Risk Factors

Information about bone density covariates (cigarette smoking, menopause status, postmenopausal hormone therapy, diuretic use, and current use of osteoporosis medication) was obtained by standard questionnaires. Reported smoking habit was indirectly validated by showing an association between pack years and pulmonary function (21). Current use of postmenopausal hormone therapy, diuretics, and bone specific medications were validated by a specially trained nurse who examined pills and prescriptions brought to the clinic for that purpose.

Statistical Analysis

All analyses were performed using SPSS version 14.0 (SPSS Inc, Chicago, IL), with a type I error set at $p < 0.05$. Spearman correlations were performed to determine the associations between BMD and the covariates. Covariates were selected for entry into separate multiple regression models based on the strength of their correlation with BMD ($p < 0.0001$) at each of the 3 sites (lumbar spine, hip, total body). Stepwise linear regression analysis was used to identify the significant covariates of BMD.

RESULTS

Mean and standard deviations of participant characteristics and statistical tests of sex differences are shown in Table 1. Mean age was 72.2 years for women and 71.0 years for men. All women included in this analysis were postmenopausal, with a mean age of menopause of 47.1 years. 63% of women reported natural menopause (no hysterectomy), 26% reported hysterectomy with ovarian conservation, and 11% reported hysterectomy with bilateral oophorectomy. Mean time since menopause was 25.1 (± 12.0) years. As shown in Table 1, women were on average leaner than men, based on BMI. Fifty nine percent of women had BMIs $< 25 \text{ kg/m}^2$; 31% were overweight ($\text{BMI} \geq 25$ to 30 kg/m^2), and 10% were obese ($\text{BMI} > 30 \text{ kg/m}^2$). In contrast, 40 percent of men had a BMI < 25 , 47% percent were overweight ($\text{BMI} \geq 25$ to 30 kg/m^2), and 13% were obese ($\text{BMI} > 30 \text{ kg/m}^2$).

In women the mean LBM from DXA was lower than in men. In women, REE values ranged from 883 kcal/day to 1922 kcal/day with a mean of 1220.5 kcal/day; in men, REE values ranged from 996 kcal/day to 2498 kcal/day with a mean of 1566.1 kcal/day. Also shown in Table 1, women had less grip strength (both hands) than men and lower BMD at all three skeletal sites.

Figure 1 shows sex-specific REEs before and after adjusting for differences in LBM. Women had lower REEs (mean=1220 kcal/day) compared to men (mean=1566 kcal/day) before adjustment for LBM, but they had higher REEs (mean=1407 kcal/kg LBM/day) compared to men (mean=1296 kcal/kg LBM/day) after adjusting for LBM.

Table 2 shows sex-specific Spearman correlations between REE and other variables with BMD at the lumbar spine, hip, and total body. Age was inversely correlated with BMD in both sexes although these correlations were stronger in women than in men. In both sexes, fat mass, lean body mass, weight, height, BMI, waist and hip girth, REE, and grip strength were all positively and significantly associated with hip, spine, and total body BMD. In women, the strongest correlation at all sites was between REE and BMD, with r value of 0.34 at the lumbar spine, 0.56 at the hip, and 0.56 at the total body; these correlations were stronger than those between weight and BMD. Regular strenuous exercise was reported by 17% of women and 30% of men, exercise 3 times/week by 69% of women and 75% of men, and lifting weights in the past 2 weeks by 5% of women and 14% of men. Regular strenuous exercise was positively correlated with hip BMD in women ($r=0.10$, $p < 0.0001$) and men ($r=0.16$, $p < 0.0001$) and with total body BMD in women ($r=0.08$, $p < 0.05$) and men ($r=0.18$, $p < 0.0001$). Exercise 3 times/week correlated only with hip BMD in men ($r=0.11$, $p < 0.05$). Lifting weights in the past 2 weeks, although relatively uncommon (5% of women and 14% of men), was positively correlated to hip BMD in women ($r=0.08$, $p < 0.05$) and men ($r=0.12$, $p < 0.05$) and with total body BMD in women ($r=0.07$, $p < 0.05$) and men ($r=0.11$, $p < 0.05$).

Past smoking was reported by 43% of women and 60% of men, and current smoking by 8% of women and 6% of men. In women, there were no significant associations between ever smoking and BMD; in men, however, ever smoking was inversely correlated with hip BMD ($r=-0.15$, $p \leq 0.001$) and total body BMD ($r=-0.12$, $p < 0.05$). Almost half of women reported ever (past or current) use of postmenopausal estrogen therapy. Most (87%) used oral conjugated

equine estrogen (Premarin, Wyeth-Ayerst Laboratories, Philadelphia, PA) which was started around time of menopause; use was based on their doctor's recommendation. Estrogen therapy was correlated with BMD at the lumbar spine ($r=0.28$, $p<0.0001$), total hip ($r=0.31$, $p<0.0001$), total body ($r=0.33$, $p<0.0001$), and REE ($r=0.13$, $p<0.0001$). Current diuretic use, reported by 20% of women and 13% of men, was not significantly correlated with BMD in either sex but was inversely correlated with REE in women ($r=-0.11$, $p<0.001$) and men ($r=-0.11$, $p<0.005$). Current osteoporosis-specific medication was reported by only 8% of women and 0.05% of men and was inversely correlated with hip BMD in both women ($r=-0.09$, $p<0.05$) and men ($r=-0.10$, $p<0.05$), with total body BMD ($r=-0.09$, $p<0.05$) and with REE ($r=-0.11$, $p<0.001$) in women only.

The independent contributions of body weight, BMI, fat mass, and LBM to BMD were determined by stepwise multiple regression analyses (Table 3). The correlations observed between these variables and REE were very high: body weight with REE ($r=0.91$ in women, $r=0.92$ in men), BMI with REE ($r=0.70$ in women, $r=0.69$ in men), fat mass with REE ($r=0.79$ in women, $r=0.65$ in men), and LBM with REE ($r=0.76$ in women, $r=0.91$ in men). Therefore, to avoid problems of multicollinearity, REE was taken out of the regression models and instead, body weight, BMI, fat mass, and LBM were each separately entered into different models. In women, when total body weight replaced REE in the models, weight became the strongest covariate of BMD, but it explained less of the variance than REE. Weight explained 13% of the variance in spine BMD, 23% of the variance in hip and 26% of the variance in total body BMD. When BMI, fat mass, or LBM replaced REE in the models, compared to REE, they also explained less of the variance.

In men, when total body weight replaced REE in the models, weight became the strongest covariate of BMD and explained more of the variance than REE. Weight explained 10% of the variance in spine BMD, 22% of the variance in hip and 23% of the variance in total body BMD in men. When BMI, fat mass, or LBM replaced REE in the models, compared to REE or to body weight, they explained less of the variances in spine, hip, or total body BMD.

To determine whether age at menopause had an influence on the main findings of this study, we divided the women into three groups: women with early menopause (EM: menopause age ≤ 44 , $n=259$), women with average age at menopause (AM: menopause age between 45 and 52, $n=577$), and women with late menopause (LM: menopause age ≥ 53 , $n=157$). We then reexamined the independent contributions of REE, weight, and estrogen therapy to spine, hip, and total body BMD. As shown in Table 4, the stronger role of REE than weight on BMD did not differ by age at menopause. In all 3 groups, REE was a better covariate of hip and total body BMD compared to weight; the contributions of REE and weight to the variance in spine BMD were about equal. As expected, estrogen therapy had the greatest contribution to the variances in spine, hip, and total body BMD in early menopausal women, who had the longest continuous use and the best BMD (22).

To further explore the combined influence of weight and REE on BMD, weight and REE were divided into tertiles (women weight < 57.73 , $57.73 - 66.36$, and > 66.36 ; REE < 1150.1 , $1150.1 - 1273.5$, and > 1273.5); men weight < 74.09 , $74.09 - 84.55$, and > 84.55 ; REE < 1449.1 , $1449.1 - 1658.5$, and > 1658.5). Within each weight group, spine, hip, and total body BMD increased with increasing REE in both women (Figures 2a, 2b, 2c) and men (Figures 3a, 3b, 3c).

DISCUSSION

Abundant evidence suggests that variation in REE among individuals is determined primarily by differences in body size and LBM (7,11,23,24), the latter possibly accounting for 65–90%

of the variance (12,23). Therefore, it is difficult but necessary to study the independent body size association of REE with BMD. Sex differences in REE have been reported previously with contradictory findings (6–13); these different findings may reflect differences in sample size, participant age, and/or failure to adjust for LBM.

The present investigation included 1,682 Caucasians, making it the largest study examining sex differences in REE in older adults, and the first to report the independent association of REE with BMD in Caucasians. In this study, age, body composition, weight, height, BMI, waist girth, hip girth, REE, physical activity, grip strength, and estrogen therapy (in women) were each significantly associated with BMD in both sexes. As expected, men had better BMD than women. Results from the present study clearly show the importance of considering sex differences in body mass index, LBM and fat mass in the REE analyses. The absolute or unadjusted REE was lower in women than men (Figure 1), but, because men had higher BMIs and more LBM than women, adjusting for LBM, reversed the association such that men now had lower REE than women.

Based on WHO (25) BMI definitions for overweight and obesity, 47% and 13% of the 686 male participants were overweight or obese, respectively, compared to 31% and 10% of the 996 female participants. There were strong and similar correlations between REE and BMI in women ($r=0.70$, $p<0.0001$) and men ($r=0.69$, $p<0.0001$). There were also differences in reported physical activity, which was more common in men than women, but declined in both sexes with age. These results are compatible with other studies (26) showing a linear decrease in physical activity with age. Controlling for physical activity, which was mainly walking in this cohort, did not materially change the REE-BMD association.

The etiology of sex differences in skeletal mass is incompletely understood, but age and body size are major determinants, as observed here. In the present study, all body size measures, REE, physical activity, grip strength, and estrogen therapy (in women) were each significantly associated with BMD in both sexes (Table 2). In women, REE explained 9% more of the variance in hip BMD and 6% more of the variance in total body BMD than weight or any other measures of body size or composition (Table 3). In contrast, in men, REE explained 1% less of the variance in total body BMD than weight or other measures of body size or composition (Table 3). Collectively, these findings confirm that REE (14), body size and obesity (27,28) protect against osteoporosis and likely explain part of the lower fracture rates in men compared to women (3).

Some of the sex differences with regard to the contribution of REE *versus* weight to the variances of spine, hip, and total body BMD may reflect an interaction of age and height with these variables. It is noteworthy that age, weight, and height are each part of the Harris-Benedict equation used to calculate REE. While the correlations between weight and BMD at the three sites was comparable in women and men (Table 2), the associations between age and hip BMD, between age and total body BMD, and between height and BMD at all three sites were significantly stronger in women than in men (Table 2). Similarly, while age and spine BMD were significantly and inversely correlated in women ($r=-0.16$, $p<0.0001$), the correlation was non-significant in men (Table 2). For these reasons, we suggest that the combined influences of weight, height, and age, making up REE as a whole, have a stronger role on BMD in women than in men, while weight alone seems to be the best contributor to the variances. Thus when REE was replaced with BMI and age in the regression models, with BMD as the dependent variable, the combined variances of BMI and age were still not as strong as REE in women and weight in men and these differences remained statistically significant.

This study has several strengths, including the large sample of community-dwelling seniors, axial and appendicular BMD by DXA, and a large number of potential confounders. The

limitation is that large epidemiologic studies are rarely suitable for direct measurements of REE under inpatient laboratory conditions using indirect calorimetry (29). For this reason, simple anthropometric measurements are used in predictive equations. The Harris-Benedict equation used here to estimate REE has acceptable accuracy for groups of individuals (30), and several studies (11,16–18) have shown that the Harris-Benedict equation accurately predicts REE. Taaffe and colleagues (18) concluded that the Harris-Benedict equation was one of the three most accurate equations (of eight different equations) used to predict REE. De Lorenzo and co-investigators (17) determined that the Harris-Benedict equation provides a valid estimate of REE in both average-weight and overweight adults. In so far as indirect calorimetry is a better measure of REE, the misclassification of REE represents a conservative bias which is expected to underestimate the strengths of observed associations.

In conclusion, REE showed a small but significantly stronger association with hip and total body BMD than other body size measures in postmenopausal Caucasian women but not men. Because REE requires the calculation of an equation and weight does not, it is not likely to replace body size in clinical estimations of BMD or fracture risk. The sex differences in REE and BMD are nevertheless interesting because they may help to explain part of the sex differences in bone health in old age.

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Figure 1. Absolute versus adjusted (for LBM) REE. The height of each bar represents the mean $\pm$ SD.

Figure 2.

(a) Levels of spine BMD in relation to tertiles of weight and REE in women. There were no women with weight in the 1st tertile and REE in the 3rd tertile; therefore, there is a bar missing in this figure.

(b) Levels of hip BMD in relation to tertiles of weight and REE in women. There were no women with weight in the 1st tertile and REE in the 3rd tertile; therefore, there is a bar missing in this figure.

(c) Levels of total body BMD in relation to tertiles of weight and REE in women. There were no women with weight in the 1st tertile and REE in the 3rd tertile; therefore, there is a bar missing in this figure.

Figure 3.

- (a) Levels of spine BMD in relation to tertiles of weight and REE in men.
- (b) Levels of hip BMD in relation to tertiles of weight and REE in men. There was only one man with weight in the 3rd tertile and REE in the 1st tertile and no hip scan was obtained on this participant. Therefore, there is a bar missing in this figure.
- (c) Levels of total body BMD in relation to tertiles of weight and REE in men.