Differences in skeletal and muscle mass with aging in black and white women

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Aloia, John F., Ashok Vaswani, Martin Feuerman, Mageda Mikhail, and Ruimei Ma. Differences in skeletal and muscle mass with aging in black and white women. Am J Physiol Endocrinol Metab 278: E1153–E1157, 2000.—Previous cross-sectional studies using delayed gamma neutron activation analysis and whole body counting suggested that the relationship of total body calcium (TBCa) to total body potassium (TBK) (muscle mass, body cell mass) remained constant with age. This led to the hypothesis that the muscle mass and skeletal mass compartments are integrated in their response to aging. It had also been hypothesized that loss of skeletal and muscle mass was similar between races. In the current study, delayed gamma neutron activation analysis and whole body counting were performed on 90 black and 143 white women 20–69 yr of age. Black women had higher TBCa and TBK values than white women, even when the data were adjusted for age, height, and weight. TBCa was correlated with height and TBK with weight. The estimated decline of skeletal mass (TBCa) from 20 to 70 yr was 18% in black women and 19% in white women. However, the lifetime decline of TBK was only 8% for black women, compared with 22% for white women. Black women may lose TBK more slowly than TBCa with aging, compared with white women. In particular, correlation of TBCa and age was similar for blacks and whites (r = −0.44 and r = −0.54, respectively). However, for TBK these correlations were r = −0.14 and r = −0.42. These data confirm a higher musculoskeletal mass in black women and suggest that the loss of muscle mass with age may be lower in black than in white women. These ethnic differences do not support the hypothesis of an integrated musculoskeletal system, so that these two components should be considered separately. A prospective study is needed to confirm these findings.

Body composition; osteoporosis

Body composition in a healthy population is influenced by gender, ethnicity, and age (2, 3, 9, 10, 18, 19). There are common genetic and environmental influences on the skeletal and muscle compartments. These compartments may be viewed as integrated (i.e., one component influences the other or both components are influenced by the same variables). One concept of involutional loss of skeletal mass is that bone loss results from a decline in mechanical stress due to a decline in skeletal muscle mass. The mechanostat theory proposes that the skeleton responds to the mechanical load placed upon it, increasing or decreasing proportionately to the load (20).

Previous studies of the loss of skeletal and muscle mass with age have targeted white women (2, 6, 15–17). There are few available data on the pattern of loss in these two components of the musculoskeletal system in black women (3, 10). Both cross-sectional and longitudinal studies support an accelerated rate of loss of both skeletal and muscle mass after menopause in white women, further supporting the concept of an integrated response of the musculoskeletal system to hormonal changes. However, in a group of women given hormonal replacement at the menopause, loss of bone mass was prevented, whereas loss of muscle mass (as measured by dual-energy X-ray absorptiometry) was not prevented (4). This finding of discordant response in a longitudinal study is inconsistent with previous reports from cross-sectional studies and led us to question the hypothesis of integration of the muscle and skeletal components.

Measurement of skeletal and muscle mass may be accomplished in vivo by neutron activation analysis and whole body counting. Total body calcium (TBCa) measures skeletal mass because 99% of the body calcium resides in bone. Total body potassium (TBK) is primarily intracellular, so that it reflects body cell mass, including skeletal muscle. The upgraded neutron activation facility at Brookhaven National Laboratory (BNL) was used to measure TBCa in black (n = 90) and white (n = 143) women. The specific question we hoped to examine was whether the pattern or quantity of involutional changes in skeletal and muscle mass is different between races.

MATERIALS AND METHODS

Subjects. There were 233 participants who had volunteered for studies at BNL (5) and were part of a larger study of body composition in black and white women. Women were excluded if body mass index (BMI) was <18 or >32. A cut-off on 32 was chosen because of the influence of body thickness on elemental analyses and because BMI misclassifies 12% of black women as obese (3). The age range was 20–69 yr. Exclusion characteristics consisted of any chronic illness, including hypertension, hysterectomy, diabetes, and obesity, or any past history of illness or medication known to affect bone metabolism or skeletal muscle mass, and any use of oral contraceptives, diuretics, or hormonal replacement therapy.
After telephone screening, women were further rejected on the basis of abnormal blood chemistries (multichannel chemistries, complete blood count, urinalysis, free thyroxine, thyroid-stimulating hormone), or abnormal physical findings. The study was approved by the Institutional Review Board of Winthrop-University Hospital, and written informed consent was obtained from each participant. A detailed history and physical examination was completed with the assistance of a nurse clinical research coordinator and physician. A recall activity questionnaire for each decade of life was completed, and the Compendium of Physical Activity was used to evaluate habitual physical activity (1).

Delayed gamma neutron activation. Early studies at BNL used 14 MeV neutrons generated from a neutron generator (11). In the 1970s the first delayed gamma neutron activation (DGNA) facility, including a whole body counter (WBC) and a whole body neutron irradiation facility, was built to measure total body levels of Ca, Na, Cl, and P in vivo (24). The original calibration was done on an anthropomorphic hollow phantom filled with solutions containing predetermined amounts of calcium based on the results of whole body gamma counting and measurements of thermal neutron flux. In 1987, the WBC underwent a major upgrade to improve the counting efficiency (9, 12, 14). The DGNA facility was upgraded in 1993, and a new phantom was designed to calibrate the system (23). The precision of repeated TBCa measurements of the phantom, containing $\pm 1,000$ g of calcium in an artificial skeleton, is 1.5% (24).

TBCa. TBK is measured by whole body counting of the radioactive isotope $^{40}$K. The Brookhaven WBC was built in the late 1960s and was upgraded in 1987. It consists of 32 rectangular NaI (T1) detectors (10.2 cm $\times$ 10.2 cm $\times$ 45.7 cm); 16 detectors are positioned above and 16 below the subject (9). Repeated measurements of TBK in vivo give a coefficient of variation (CV) of <1.0% (R. Ma, personal communication).

Statistical analysis. Because the dependent variables (TBCa and TBK) were normally distributed, differences between blacks and whites were assessed by the unpaired t-test. However, age, height, weight, BMI, and physical activity depart from normality, so a rank-sum test was utilized instead of a t-test. Spearman correlations of the dependent variable vs. age were used (instead of Pearson correlation) because of the skewness of age. In summary, univariate analyses included the use of unpaired t-tests, rank-sum tests, and the Spearman correlation.

To investigate the covariate relationships of age, race, height, weight, and the dependent variables were regressed against (age minus its mean), (age minus its mean)$^2$, height, weight, race, and age $\times$ race, using stepwise multiple regression with $P < 0.05$ as a cut-off. This technique of regressing age minus its mean is known as “centering.” When one regresses the dependent variable against age and age$^2$, computational difficulties may arise from the fact that age and age$^2$ can be highly correlated (collinear). Such difficulties can usually be overcome by redefining age and age$^2$ as deviations from their means. Conclusions of significance of curvature were made using the centered regression equation and the equation to plot the curve. The equations listed with each figure use age directly, instead of deviations from the mean, for simplicity of understanding. The age $\times$ race interaction term in our models was used to determine whether the declines in the dependent variables with age were significantly different between blacks and whites. If the age $\times$ race interaction was significant, we performed separate regressions by race. The quadratic component of age$^2$ was used to investigate potential nonlinear relationships (e.g., effect of menopause and/or peak mass). We also utilized spline (segmented) regression models, in which two straight lines are fitted to join at a common point; with our data we chose age = 50 yr (average age at menopause) as the common point or “knot” of the spline. This technique is discussed in detail in SAS (TM) System for Regression (2nd ed.), Cary, NC: SAS Institute, 1991, p. 158–163. The spline model would illustrate the sharp effect of menopause and was used as a comparison with the quadratic model.

In summary, with our multiple regression models (quadratic, linear, and spline), we were basically interested in controlling for weight and height and in determining how TBCa and TBK are dependent on age, race, and the interaction of age and race.

All analyses were done using SAS (TM), Version 6.12 (Cary, NC). Statistical significance was set at $P < 0.05$ by use of a two-sided $P$ value.

### RESULTS

Subjects. Of the 233 participants, 90 were black and 136 were premenopausal. The percentage of blacks that were premenopausal (60%) was essentially the same as whites (57%). The clinical characteristics are given in Table 1. The black women were slightly younger and heavier than the white women. The calculation of physical activity did not reveal any inter racial difference in any decade of life, or any significant correlations with TBCa and TBK (separately by race and for both races combined).

TABLE 1. Mean values for clinical characteristics, skeletal mass, and body cell mass

<table>
<thead>
<tr>
<th></th>
<th>Blacks (n = 90)</th>
<th>Whites (n = 143)</th>
<th>Black vs. White P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age yr</td>
<td>44.1 ± 11.9</td>
<td>46.6 ± 12.5</td>
<td>&lt;0.011</td>
</tr>
<tr>
<td>Age at menopause yr</td>
<td>49.8 ± 2.2</td>
<td>51.3 ± 2.7</td>
<td>&lt;0.02</td>
</tr>
<tr>
<td>Height cm</td>
<td>163.4 ± 6.1</td>
<td>164.3 ± 6.0</td>
<td>NS (P = 0.18)</td>
</tr>
<tr>
<td>Weight kg</td>
<td>60.0 ± 10.2</td>
<td>64.3 ± 9.2</td>
<td>&lt;0.0004</td>
</tr>
<tr>
<td>BMI, kg/m$^2$</td>
<td>25.9 ± 3.6</td>
<td>23.8 ± 3.3</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>TBCa, kg</td>
<td>0.776 ± 0.083</td>
<td>0.720 ± 0.095</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>TBK, kg</td>
<td>0.103 ± 0.014</td>
<td>0.096 ± 0.013</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Physical activity kcal</td>
<td>6709.0 ± 6279.7</td>
<td>7807.9 ± 8052.4</td>
<td>NS (P = 0.79)</td>
</tr>
</tbody>
</table>

Values are means ± SD; n, no. in group; BMI, body mass index; TBCa, total body calcium, or skeletal mass; TBK, total body potassium, or body cell mass; NS, not significant.
that predict TBCa, in decreasing order of importance, are height, age, and race. Weight and age \times race are insignificant and do not enter the stepwise model. Therefore, race is still a predictor, even after we have controlled for weight and age. The inferred lifetime (20–69 yr of age) decline in TBCa was 18% in black women and 19% for white women (see Fig. 1). The black women had a higher initial bone mass; the inferred lifetime absolute decline for black and white women was 139 and 138 g, respectively. The quadratic component in the regression is small ($R^2 = 0.03$) for age but of physiological significance because of the influence of menopause on skeletal mass. Thus, when the data were examined in pre- and postmenopausal women by use of a spline model, with age 50 as the average age at menopause, there was a significant change in slope from pre- to postmenopausal ($P < 0.0002$). The spline model, which is virtually equivalent to the quadratic model in terms of total $R^2$ squared ($R^2 = 0.58$ and SEE = 0.062 kg), illustrates more clearly the sharp effect of menopause on TBCa (Fig. 2). The quadratic model also suggests gaining of calcium during the third decade of life, with age of peak calcium estimated from Fig. 1 at 31.5 yr.

TBK. Values for TBK were also normally distributed. The average TBK of black women was significantly higher (8%), on average, than that of white women ($P < 0.0001$). When analyzed separately for each race, the correlation of TBK with age was not significant ($r = -0.14, P = 0.18$) for black women but was significant for white women ($r = -0.42, P < 0.0001$). Thus TBK is inversely correlated with age for white women but not significantly correlated with age for black women.

A stepwise multiple regression analysis with TBK as the dependent variable resulted in the following $R^2$ values for weight, age $\times$ race, height, race, and age: $0.43 (P < 0.0001), 0.16 (P < 0.0004), 0.05 (P < 0.0001), 0.02 (P < 0.0047), and 0.008 (P < 0.03)$, respectively. Therefore, as with TBCa, race is still a predictor of TBK, even after we have controlled for weight and age. For this model, total $R^2 = 0.67$ and SEE = 0.008 kg. Addition of dietary variables to our model does not change the SEE value. There was no evidence for a quadratic component for age ($P = 0.89$). Because the interaction between age and race was significant, separate analyses were done for the black and white populations. These are given in Table 2.

The lifetime absolute TBK loss for black and white women was 8.2 and 23.6 g, respectively. The inferred %loss of TBK from age 20 to 69 yr was calculated at 8% for black women and 22% for white women (see Fig. 3). From Table 2, the inferred loss of TBK with age in black women was barely significant ($P < 0.04$). The regression of TBK against age for white and black women is given in Fig. 3. Weight is the most important variable.

### Table 2. Stepwise multiple regression of TBK in black and white women

<table>
<thead>
<tr>
<th>Step</th>
<th>Black $R^2$</th>
<th>P</th>
<th>White $R^2$</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Weight</td>
<td>0.51</td>
<td>0.0001</td>
<td>Weight</td>
</tr>
<tr>
<td>2</td>
<td>Height</td>
<td>0.09</td>
<td>0.0002</td>
<td>Age</td>
</tr>
<tr>
<td>3</td>
<td>Age</td>
<td>0.02</td>
<td>&lt;0.04</td>
<td>Height</td>
</tr>
</tbody>
</table>
for predicting TBK in both races. Once weight is in the model, height has a smaller role (6–9%). Age clearly has a much greater influence in predicting TBK in whites compared with blacks. The equations describing these relationships are given in the legend for Fig. 3.

**DISCUSSION**

The pattern of involutional change in skeletal mass was similar in the black and white women in the current study. However, the involutional change in muscle mass (TBK) differed between ethnic groups, with a greater decline in white women. Thus we observed discordant involutional changes in muscle mass but not in skeletal mass between races. The muscle and skeletal mass components of body composition should be considered separately in studies of different ethnic populations.

Nutritional and hormonal influences are likely to have varying effects on muscle and skeletal mass as well. Dietary calcium insufficiency and disorders of the calcitropic hormones would be expected to primarily affect the skeleton, although reports on measurement of muscle mass in these disorders are sparse. In a study of hormonal replacement therapy on prevention of postmenopausal loss of skeletal and muscle mass, we found an influence on skeletal but not on muscle mass (4). Whether there are differential effects of gonadal hormone withdrawal at menopause on muscle and skeletal mass is uncertain. It is established, however, that skeletal mass is lost at an accelerated rate after menopause (and that the loss may be prevented by hormone replacement therapy and reduced by pharmacological and nutritional intervention).

There is a paucity of reports on the influences of age on TBK in black women. In one study, a significant decline in TBK appeared after the age of 60 yr in white but not in black females, which is consistent with our findings in black women (27). Another study that included 80 black and 68 white women found similar patterns of decrease of TBK with age in both races (18). The latter study may reflect population differences, because height accounted for 28–42% of the variance in TBK, whereas weight generally has a greater influence in most populations studied, including our own.

Discovery of the factors responsible for preservation of muscle mass in black women may provide strategies that can be applied to the whole population. For example, we and others (4, 21) have found higher levels of serum testosterone in black compared with white women and have speculated on the role of androgens in preventing involutional changes in body composition. We considered the possibility of higher physical activity in the black women as a cause of a lesser decline in muscle mass with age, but we could find no evidence to support this suggestion. Of course, because of cohort effects in a cross-sectional study, the racial differences in reduction of muscle mass with age must be confirmed by longitudinal measurements. Such studies should be designed to examine nutritional, ethnic, and hormonal influences on involutional loss of muscle mass.

In the current cross-sectional study, we found no evidence for an effect of menopause on TBK in either race. Although there are numerous cross-sectional studies that use a WBC to measure TBK in white women, these studies have not adequately addressed the question of whether there is an accelerated loss of muscle mass at menopause (16, 17, 27, 28, 30). In some instances a quadratic fit was not attempted, and in others there was no correction for body weight. Detection of perimenopausal change in body composition in a cross-sectional study requires statistical adjustment of confounding variables and a very large sample size. A recent longitudinal study in 61 white women found that the rate of loss of TBK did not achieve statistical significance until the age of 60 yr, although it had become negative in the previous decade (16). In our own earlier cross-sectional and longitudinal studies in white women with a large sample size, we found a loss of TBK of 5.5%/yr in white women between 6 mo and 6 yr after a natural menopause (4). It appears likely to us that there is accelerated loss of muscle mass after menopause.

Our findings support a model in which the higher skeletal mass of the black compared with white women is attributed to development of a higher peak bone mass (7, 9, 22, 26). This may be attributed to skeletal resistance to parathyroid hormone and a longer mineralization period in black women (13, 29). The pattern of change in skeletal mass with increasing age was similar in black and white women in the current study. The inferred loss of bone mass in postmenopausal women appeared similar. This finding is consistent with other studies suggesting that the rate of bone loss is similar in black and white postmenopausal women (22). Differ-
ences in bone density between black and white girls are noted early in life (7). This advantage in peak skeletal mass is thought to be the major explanation for the lesser risk for osteoporotic fractures in black compared with white women.

In summary, we present evidence that muscle mass is similar in black and white women in early adulthood but declines to a greater extent with age in white women. Studies of nutritional, hormonal, and genetic influences on these discordant responses to aging should be carried out. Skeletal mass, on the other hand, is higher in black women than in white women in early adulthood but appears to decline after menopause at a similar rate. The models proposed here must be confirmed by a longitudinal study of loss of skeletal muscle mass in different populations. Skeletal mass and muscle mass should be considered separately when involutional changes in body composition are examined.

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