The Effect of Gender and Body Composition Method on the Apparent Decline in Lean Mass-Adjusted Resting Metabolic Rate With Age

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Background. Declining resting energy expenditure (REE) is a hallmark of normal aging, but the cause of this decline remains controversial. Some, but not all, studies have shown that the decline in REE with age is eliminated after adjustment for fat-free mass (FFM).

Methods. We examined the effect of four body composition methods used to assess FFM (underwater weighing [UWW], bioimpedance analysis [BIA], tritium dilution, and total body potassium [TBK]) on the relationship between REE and age in 30 healthy men and 101 healthy women aged 18 to 87 years.

Results. The decline in REE with age was significant in women (−80.3 kJ/d/y, p < .004) but not in men (−46.9 kJ/d/y, p = .328). After adjustment for FFM, the decline in REE with age persisted when FFM was measured by BIA, UWW, or tritium dilution, but no decline was seen when TBK was used to adjust for FFM. In both women and men, fat mass was significantly associated with REE after adjusting for age and FFM.

Conclusion. It is the decline in cell mass with age, detectable by TBK but not by other methods, rather than any metabolic alteration, that explains the decline in FFM-adjusted REE with age.

One of the effects of age on metabolism is a decline in resting energy expenditure (REE) (1–3). Since metabolic rate accounts for roughly two thirds of total energy expenditure (TEE) in sedentary adults (4), a decline in REE will lead to positive energy balance if it is not offset by an equal decline in energy intake. Because elderly people appear to have more difficulty than young people in appropriately matching their intake to a perturbation in their energy balance, the decline in REE with age may be an important problem in elderly persons (5–7).

The reason for the decline in REE with age is unclear, but two schools of thought exist. The first suggests that the decline in REE is a result of the decline in body cell mass (BCM) with age (8,9) but that there is no intrinsic difference in the metabolic rate of single cells from elderly compared with young adults. If this is true, then adjusting the age-REE relationship for BCM, or the more easily measured fat-free mass (FFM), should eliminate the apparent decline in REE with age. Alternatively, others have suggested that hormonal, immunologic, or other regulatory changes with age affect REE (10–12). If this is the case, adjustment for FFM or BCM should not eliminate the downward slope of the age-REE plot. In this case, the implication is that a cell from an elderly person has a slower metabolic rate than a cell from a younger person.

We hypothesized the reason for the persistence of the decline in REE after adjustment for FFM with age is due to the change in the quality of FFM with age (13). That is, as a result of age-related sarcopenia, less of the FFM in older persons is made up of metabolically active cell mass than in younger adults. This change is caused by the greater decline in cell mass, especially muscle mass, with age than in extracellular FFM. This decline cannot be detected by water-based methods of measuring FFM (e.g., underwater weighing [UWW], bioimpedance analysis [BIA], and tritium dilution [3H2O]), but can only be detected by total body potassium (TBK) analysis. Although several studies have examined the decline in REE in absolute terms and after adjustment for FFM (or BCM), to our knowledge no study has compared multiple methods of measuring body composition directly, and no study has assessed the effect of the various methods on the age-REE relationship. We examined this question in a retrospective analysis of 131 healthy men and women aged 18 to 87 years who had undergone indirect calorimetry and assessment of body composition under identical conditions as part of several research protocols over the past 5 years.

Methods

Subjects
All subjects were volunteers recruited for various studies in the Jean Mayer USDA Human Nutrition Research Center on Aging (HNRCA) between 1992 and 1997. All subjects had to be healthy as ascertained by a screening medical history and physical examination administered by a physician, and subjects had to have normal chest radiograph, electrocardiogram, serum chemistry panel, urinalysis, and complete blood count. Subjects were excluded if they had a history of stroke, pulmonary disease, congestive heart failure,
rheumatoid arthritis, body mass index >30 kg/m², cancer other than nonmelanomatous skin cancer, thyroid stimulating hormone levels outside the normal range, or were taking medications known to affect body composition or metabolic rate (beta blockers, corticosteroids, or appetite suppressants). Patients taking other antihypertensive agents were not excluded. Smokers were asked to refrain from smoking for 12 hours before the calorimetry test. Premenopausal women were studied in the midfollicular phase based on their last menstrual period. Written informed consent was obtained from all subjects. All research protocols were approved by the Human Investigations Review Committee of Tufts University and New England Medical Center.

Calorimetry

Indirect calorimetry was performed using a Deltatrac ventilated hood calorimeter (Sensormedics, Yorba Linda, CA) following the manufacturer’s instructions. The calorimeter was flow-calibrated daily, and alcohol burns were performed monthly to confirm stability of measurements. In protocols involving an intervention, only the baseline study was included in this analysis. The instrument was turned on and warmed up for at least 1 hour before use. Subjects were admitted to the HNRCA the night before the calorimetry was to be performed and awakened between 6 and 7 AM and asked to empty their bladder. After a 30-minute rest period, indirect calorimetry was performed over 20 to 40 minutes under thermoneutral conditions in a semidarkened room while subjects rested quietly in the supine position. The test-retest reliability of this method over a 2-day period in five healthy adults was <2.5% (Hughes VA, unpublished observations, 1997).

Body Composition

Four different body composition methods were used in the various protocols that supplied subjects for this analysis: BIA, UWW, tritium dilution (H2O), and TBK. All subjects underwent all four measurements.

Bioelectrical impedance.—BIA was carried out using an RJL-103 impedance analyzer (RJL, Mt. Clemens, MI) following the manufacturer’s instructions with standard tetrapolar lead placement. The analyzer was calibrated using a 500-ohm resistor as recommended by the manufacturer. Because of the wide age range of the subjects in this study, the equation derived by Lukaski (14) was applied to all subjects. We have previously demonstrated that this equation functions well in elderly populations (15). The coefficient of variation (cv) of repeated measurements of total body water over 5 days in five individuals of various body weights and compositions using this instrument was previously shown to be 1.6% (16).

Underwater weighing.—Hydrostatic weight was measured as previously described (16). Briefly, subjects were fasted and, wearing their own bathing suits, were weighed using a Sauter scale (model K120; Denshore Scale, Holbrook, MA) attached to a computer to read underwater weight. Residual lung volume was determined by nitrogen dilution in 51 subjects (505 Nitraliser, Med Science, Saint Louis, MO), by nitrogen washout (Vmax 2900, Sensormedics) in 47 subjects, or estimated from published norms in 91 subjects (17,18). A maximum of five trials was performed for each subject. The three trials with the least variability and yielding the highest density were averaged to obtain final body density. FFM and fat mass (FM) were calculated using Siri’s equation (19). The cvs in our laboratory for three measurements made on three subjects over a 7-day period were 1.0% for FM and 0.4% for FM (16).

Tritium dilution.—Total body water (TBW) was measured by the dilution of 1.85 MBq of tritiated water after a 3-hour equilibration period. A venous blood sample of 10 ml was used to determine dilution. Water samples were extracted from the plasma by freeze-drying and were measured in a liquid scintillation counter (Beckman Instruments, Los Angeles, CA). The statistical error of scintillation counting was <0.5%, and the cv of TBW measurements with this method was 2.3% for 21 subjects measured three times over a 10-month period (16,20). TBW was converted to FFM by dividing by 0.72, assuming a fixed hydration of FFM. An adjustment of 5% was used to correct for the overestimation of TBW by the tritium space (16).

Total body potassium.—TBK was determined in a whole body counter by measuring the gamma rays resulting from the decay of the naturally occurring potassium isotope ⁴¹⁶K. The cv for TBK at our institution is <3% (13). To allow direct comparison with the other methods, TBK was converted to FFM using the equations of Cohn and colleagues (21).

Statistical Analysis

All data were examined for normality graphically and statistically and were found to be normally distributed. No age-by-sex interaction was seen when predicting REE from age and sex (p = .62). In addition, there were no significant interactions between any of the body composition methods and sex. Therefore, simple linear regression was used to assess the association between total REE and age in the combined sample of both men and women together. Simple linear regression was used to examine this association after adjustment for each body composition method separately in the form of

$$\text{REE} = \text{constant} + \beta_1 \times \text{age} + \beta_2 \times \text{FFM}.$$  

In a subsequent analysis, FM was added to this model for each method as well. Because there is no standard analytic procedure for comparing the regression coefficients for age across many equations (i.e., one from each of the four body composition methods), the differences were examined in 250 bootstrap samples. Associations were considered significant if the two-sided p value was <.05. All data were analyzed using Systat (SPSS, Inc, Chicago, IL). Data are presented as means and standard deviations unless otherwise noted.

Results

Thirty-one men and 101 women met the inclusion criteria for the study. The mean body mass index was 24.8 ± 3.1
kg/m² in the men and 25.4 ± 6.0 kg/m² in the women. The mean (±SD) age was 56.4 ± 22.1 years (range, 18–86.8) and did not differ by sex. The mean resting metabolic rate was 6487 ± 570 kJ/d in the men and 5316 ± 818 kJ/d in the women. Although the mean FM and FFM were not significantly different among the four body composition methods, there were substantial differences in these values by method (Table 1).

There was a small but significant association between total REE and age in the whole study population (β = −75.3 ± 23.4 kJ/d/yr [SE], p < .002), in the women (β = −80.3 ± 26.8 kJ/d/yr, p < .004), but not in the men (β = −46.9 ± 46.9 kJ/d/yr, p = .33, Figure 1). Adjustment for total body weight did not affect this observation in either sex (Table 2). Adjustment of this relationship for FFM led to mixed results, depending on the method. As shown in Table 2, the decline in REE with age persisted after adjustment for FFM using total weight, UWW, BIA, or tritium dilution, but was eliminated after adjustment using TBK.

In addition, there was a significant relationship between REE and FM after adjusting for FFM and age regardless of method used (data not shown). When both FFM and FM were included in the model, REE declined with age using BIA (−9.4 kJ/d/yr, p < .044) and tritium dilution (−10.7 kJ/d/yr, p < .02), showed a trend toward decline using UWW (−8.2 kJ/d/yr, p < .08), and did not decline using TBK (+3.3 kJ/d/yr, p < .55). Because there was no significant effect of sex or a sex-by-method interaction, these models included both men and women together.

It would be useful to determine whether the differences in sex-, FM-, and FFM-adjusted age coefficients are statistically significant. Unfortunately, we are aware of no formal statistical method that addresses this question. An informal approach was employed by comparing the adjusted regression coefficients in a set of bootstrap samples. The TBK-adjusted age coefficient was the largest (least negative) in every sample. Differences between methods not including TBK included zero between their 2.5th and 97.5th percentiles, while differences between TBK and the other methods did not.

**DISCUSSION**

This study is an analysis of a group of healthy adults aged 18 to 87 years, all studied under the same conditions using a large variety of body composition methods. To our knowledge, this is the largest study to assess the relationship between body composition, REE, and age using more than one method of measuring body composition. The results of this study confirm the cross-sectional inverse association between REE and age previously reported by several authors (8,22,23). However, it should be noted that the unadjusted association between age and REE was rather weak. Nevertheless, since weight gain over many years only requires a small energy imbalance on a daily basis, such a small decline may be biologically, as well as statistically, significant.

The current study confirmed the expected decline in absolute REE with age in women but not in men. This may have been due to the smaller sample size of men in our study or a real difference in this phenomenon between the sexes. Further elucidation of this question will require analysis with a larger sample size. Nevertheless, the change in REE with age persisted after adjusting for FFM by BIA, UWW, and tritium dilution but not by TBK. This finding confirms our hypothesis that loss of cell mass can explain away the decline in FFM-adjusted REE with age. By using TBK to calculate FFM, we may have underestimated the ability of TBK to neutralize the decline in REE with age, because TBK is a less precise estimate of FFM than BCM (21). However, we did this to facilitate comparison with the other methods.

Most previous studies of the change in REE with age have shown the decline in absolute REE that we found as well (8,22,23). After adjustment for FFM, REE was no longer lower in the older subjects studied by Tzankoff and Norris (8) using creatinine excretion, Poehlman and colleagues (10) using UWW, Mifflin and colleagues (24) using anthropometry, or Roubenoff and colleagues (25) using TBK. However, both Kleiber (26) and Cunningham (27) reanalyzed the data collected by Harris and Benedict (22) and

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**Table 1. Fat-Free Mass (FFM) and Fat Mass by the Four Methods Applied to the Study Population**

<table>
<thead>
<tr>
<th>Method</th>
<th>Men (FM) (kg)</th>
<th>Women (FFM) (kg)</th>
<th>Men (FM) (kg)</th>
<th>Women (FFM) (kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bioimpedance analysis</td>
<td>54.5 (4.5)</td>
<td>20.7 (6.8)</td>
<td>63.1 (11.7)</td>
<td>25.4 (4.5)</td>
</tr>
<tr>
<td>Underwater weighing</td>
<td>54.6 (6.5)</td>
<td>20.7 (7.5)</td>
<td>63.4 (11.8)</td>
<td>25.5 (4.4)</td>
</tr>
<tr>
<td>Tritium dilution</td>
<td>50.4 (11.7)</td>
<td>24.9 (11.0)</td>
<td>61.2 (11.9)</td>
<td>25.2 (4.4)</td>
</tr>
<tr>
<td>Total body potassium</td>
<td>47.7 (6.4)</td>
<td>27.5 (9.4)</td>
<td>63.3 (11.8)</td>
<td>25.3 (4.4)</td>
</tr>
</tbody>
</table>

**Note:** Data are mean (SD).

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**Table 2. Effect of Adjustment for Fat-Free Mass (FFM) by Various Methods on the REE-Age Relationship**

<table>
<thead>
<tr>
<th>Adjustor</th>
<th>β (age), kJ/d/yr</th>
<th>SE (β), kJ/d/yr</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>−75.3</td>
<td>23.4</td>
<td>.002</td>
</tr>
<tr>
<td>Weight</td>
<td>−56.1</td>
<td>14.2</td>
<td>.0001</td>
</tr>
<tr>
<td>Bioimpedance analysis</td>
<td>−39.3</td>
<td>19.2</td>
<td>.044</td>
</tr>
<tr>
<td>Tritium dilution</td>
<td>−44.8</td>
<td>18.8</td>
<td>.02</td>
</tr>
<tr>
<td>Underwater weighing</td>
<td>−34.3</td>
<td>19.2</td>
<td>.08</td>
</tr>
<tr>
<td>Total body potassium</td>
<td>+13.8</td>
<td>23.0</td>
<td>.55</td>
</tr>
</tbody>
</table>

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found a significant decline in REE with age after adjustment for FFM based on Moore’s prediction equation from TBW data (28). In addition, another study by Poehlman and colleagues (29) and the work by Vaughn and colleagues (30), both using UWW, and the study by Fukugawa and colleagues (31) using H$_{18}$O dilution showed a persistent decline in REE after adjustment for FFM, and in the case of the Vaughn paper, after adjustment for FFM, FM, and gender. To our knowledge, no previous attempt has been made to systematically study the effect of the various body composition measurements on the age-REE relationship.

On the whole, these data support the concept that interventions to maintain cell mass, and especially muscle mass, with age, such as exercise and maintenance of a healthy weight, should be encouraged in order to maintain REE as people age, thus maintaining a youthful level of energy expenditure and potentially preventing positive energy balance and subsequent obesity. These data do not support the idea that there are metabolic or hormonal effects of age that drive down REE beyond what can be explained by body composition changes. Rather, they emphasize the need to measure cell mass in elderly persons, rather than relying on water-based methods of measuring FFM.

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References


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