Habitual physical activity, anabolic hormones, and potassium content of fat-free mass in postmenopausal women

Ross D Hansen and Barry J Allen

ABSTRACT

Background: Total body potassium (TBK) is known to decline throughout adulthood. The relations between physical activity, age, anabolic hormones, and TBK have rarely been considered.

Objective: We sought to describe the relation between habitual physical activity, age, serum estradiol, and insulin-like growth factor I (IGF-I) and TBK in postmenopausal women.

Design: TBK, fat-free mass (FFM), moderate-to-vigorous-intensity physical activity (MVPA; assessed with use of a semistructured interview), and serum concentrations of estradiol, IGF-I, and IGFBP-3 were quantified in 51 healthy white women aged 54–76 y.

Results: The potassium content of FFM declined curvilinearly with age, indicating an accelerated loss of skeletal muscle after 65 y of age. With the data split into high (n = 25) and low (n = 26) MVPA groups, the active women had 6.5% more potassium per FFM than did their less-active counterparts (P < 0.01). In multiple regression analysis, MVPA was the major determinant of the potassium content of FFM (β = 0.02), such that an active 70-y-old had the potassium content value of a 55-y-old sedentary woman. Serum estradiol, IGF-I, and IGFBP-3 were not significant determinants of the potassium content of FFM.

Conclusions: These data suggest that (1) habitual physical activity can significantly influence FFM potassium content; (2) physical activity must, therefore, be considered if the effect of aging per se on TBK is to be clarified; and (3) MVPA, such as that pursued by the active women in the present study (eg, walking, dancing, floor exercises, and swimming), can assist in preventing sarcopenia in older women.


KEY WORDS Total body potassium, fat-free mass, physical activity, aging, postmenopausal women, estradiol, insulin-like growth factor I, sarcopenia

INTRODUCTION

Total body potassium (TBK) is highly correlated with body cell mass and skeletal muscle mass because potassium is predominantly an intracellular electrolyte occurring in a relatively high concentration in muscle tissue. Adipose tissue contains negligible potassium (1).

Several reports of an age-related decline in TBK throughout adulthood have appeared in the literature since 1950, when TBK measurements became available (2–6). Few reports have focused on such declines in postmenopausal women, although Aloia et al (7) reported evidence for an accelerated decline of TBK in women at the time of menopause.

Two important issues need to be resolved if this aging trend is to be understood. First, is the decline in TBK completely independent of other age-related body-composition changes, such as increasing adiposity? Second, to what extent is habitual physical activity a confounding influence? Because activity is known to maintain or increase skeletal muscle mass (8), which is rich in potassium, then an observed age-related decline in TBK may simply reflect a decline in physical activity with advancing age. An additional consideration is age- and menopause-related declines in the secretion of anabolic hormones, such as estrogen and insulin-like growth factor I (IGF-I), which can affect body composition (7, 9–11).

None of the studies mentioned above thoroughly investigated the combined effects of age and physical activity on TBK in older women, and few considered the effect of additional factors, such as adiposity and hormonal concentrations. The objective of the present study was, therefore, to describe the relation between physical activity, age, anabolic hormone status, and TBK in a group of women 54–76 y old. TBK was expressed as a fraction of fat-free mass (FFM) to account for variability in body size and adiposity. It was hypothesized that both age and habitual physical activity would be significant, independent determinants of the potassium content of FFM, when considered together with the influence of hormonal status.
SUBJECTS AND METHODS

Subjects

Fifty-one white women aged 54–76 y were recruited from the North Shore and Inner West regions of Sydney to participate in the present cross-sectional study, which involved comprehensive assessment of body composition, physical activity, dietary patterns, and hormonal concentrations (12). Each subject gave informed consent for the study, which was approved by the Royal North Shore Hospital Medical Research Ethics Committee and Radiation Protection Committee. All subjects were, by self-report, weight stable, nonsmokers, apparently healthy, and postmenopausal (defined by cessation of menses ≥12 mo before recruitment). More than one-half of the subjects had been receiving estrogen replacement therapy for ≥12 mo in the form of subcutaneous implants (n = 14), transdermal patches (n = 6), oral estrogens (n = 6), and other forms (n = 2). Selected subject characteristics are summarized in Table 1.

Body-composition techniques

Height and weight were measured as described previously (13). TBK (in g) was measured by a supine geometry, sodium iodide detector-based method, which incorporates corrections for variability in subject mass, height, and torso dimensions, as described by Hansen and Allen (14), with precision and accuracy (expressed as CVs) of 1.5% and 4.5%, respectively.

FFM (in kg) was estimated as the mean of 2 methods to minimize the errors associated with using only one method to determine FFM (15). The first method involved measuring the biceps, triceps, subscapular, and suprailliac skinfold thicknesses with constant pressure calipers (Holtain, Crymych, United Kingdom) and predicting body density through skinfold thickness by using the age- and sex-specific equation of Durnin and Womersley (16). As reported previously, the precision of this FFM measure is 1.1% (13). The second method involved bioelectrical impedance analysis with the use of a swept-frequency instrument (SEAC model SB2.3; UniQuest, Queensland, Australia) and application of the equation of Lukaski et al (17). As reported previously, the precision of this FFM measure is 1.6% (13). This mean FFM estimate agreed to within 1.2 kg with a 4-compartment-derived FFM measure, as described previously (13).

TBK was then expressed as a fraction of FFM, ie, K/FFM (g/kg). TBK was also expressed as a fraction of height (K/ht, in g/cm) to facilitate a comparison with previous studies.

Habitual physical activity pattern

Each subject participated in a semi-structured interview, which permitted quantification of the type, frequency, duration, and intensity of physical activity routinely pursued during the previous 6 mo. This interview was a modified version of a method (18) that was validated for use with Australian women of this age range. The modification facilitated the assessment of all activity (household, occupational, and recreational) rather than recreational activity alone, such that the variable energy expenditure per fortnight in moderate-to-vigorous-intensity physical activity (EEMVPA) could be estimated. Subjects reported the intensity of each routine activity as very vigorous, fairly vigorous, not very vigorous, or not at all vigorous. The metabolic equivalent (MET) of each activity at the reported intensity was then determined from standardized tables (18, 19). An activity with a MET value ≥4 was classified as moderate-to-vigorous-intensity physical activity, and the associated energy expenditure per fortnight was calculated as follows:

\[ \text{Energy expenditure} = \text{MET value} \times \text{duration (h/fortnight)} \times \text{weight (kg)} \]

where 1 MET = 4.18 kJ·kg\(^{-1}\)·h\(^{-1}\) (1 kcal·kg\(^{-1}\)·h\(^{-1}\)).

The EEMVPA value was then obtained by adding the calculated energy expenditures for all activities with a MET value ≥4. On the basis of previous applications of this type of energy expenditure variable (20), the women were categorized as low (EEMVPA ≤5 MJ/fortnight or high (EEMVPA >5 MJ/fortnight) in activity status. An EEMVPA of 5 MJ/fortnight approximates

<table>
<thead>
<tr>
<th>TABLE 1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subject characteristics and comparisons of low- and high-activity subgroups†</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>All subjects</th>
<th>Low activity (n = 26)</th>
<th>High activity (n = 25)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>63 ± 7 (54–76)§</td>
<td>64 ± 7</td>
<td>62 ± 6</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>161.7 ± 5.3 (152.7–174.6)</td>
<td>161.7 ± 6.0</td>
<td>161.6 ± 4.5</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>67.4 ± 11.9 (47.2–93.7)</td>
<td>68.0 ± 13.9</td>
<td>66.8 ± 9.7</td>
</tr>
<tr>
<td>EEMVPA (MJ/fortnight)*</td>
<td>9.81 ± 11.9 (0–50.29)</td>
<td>1.74 ± 1.89</td>
<td>18.27 ± 12.13§</td>
</tr>
<tr>
<td>FFM (kg)</td>
<td>41.4 ± 4.8 (30.8–53.1)</td>
<td>41.1 ± 5.4</td>
<td>41.8 ± 4.3</td>
</tr>
<tr>
<td>Percentage of fat (%)#</td>
<td>37.8 ± 5.6 (26.4–49.5)</td>
<td>38.6 ± 6.0</td>
<td>37.0 ± 5.1</td>
</tr>
<tr>
<td>Total body potassium (g)</td>
<td>92.6 ± 14.7 (55.6–142.4)</td>
<td>89.0 ± 13.4</td>
<td>96.4 ± 15.37</td>
</tr>
<tr>
<td>K/ht (g/cm)</td>
<td>0.57 ± 0.08 (0.36–0.88)</td>
<td>0.55 ± 0.07</td>
<td>0.60 ± 0.097</td>
</tr>
<tr>
<td>K/FFM (g/kg)</td>
<td>2.23 ± 0.204 (1.81–2.68)</td>
<td>2.17 ± 0.18</td>
<td>2.30 ± 0.21#</td>
</tr>
<tr>
<td>Serum estradiol (pmol/L)</td>
<td>235 ± 325 (16–1476)</td>
<td>153 ± 229</td>
<td>320 ± 389</td>
</tr>
<tr>
<td>Serum IGF-I (µg/L)</td>
<td>181 ± 79 (26–482)</td>
<td>186 ± 72</td>
<td>175 ± 87</td>
</tr>
<tr>
<td>Serum IGFBP-3 (mg/L)</td>
<td>2.5 ± 0.5 (1.6–3.9)</td>
<td>2.6 ± 0.5</td>
<td>2.4 ± 0.5</td>
</tr>
</tbody>
</table>

†± SD. EEMVPA, energy expenditure (per fortnight) in moderate-to-vigorous-intensity physical activity; FFM, fat-free mass; K, potassium; ht, height; IGF-I, insulin-like growth factor I; IGFBP-3, IGF binding protein 3.

‡Range in parentheses.

*EEMVPA data were obtained from semi-structured interview data. The 25th, 50th, and 75th percentile values for EEMVPA were 0, 4.56, and 14.33 MJ/fortnight, respectively.

*Significantly different from low-activity group (Student’s t test for unpaired data): #P < 0.0001, 7P < 0.05, 8P < 0.01.

*FFM was determined by the mean of skinfold- and bioelectrical-impedance-analysis–determined FFM.

#Percentage of fat = 100 (weight − FFM)/weight.
walking at a fairly vigorous intensity (MET = 4) 6 times per fortnight for 45 min per session, for a 65-kg subject.

Dietary pattern

The subjects’ dietary patterns were assessed via a 12-item food frequency questionnaire, which was used in a large-scale randomized survey of Australian women (21). Subjects reported how often they ate whole-grain and cereal foods, fresh fruit and vegetables, poultry, fish and seafood, eggs, red meats, dairy products, frozen meals, fast foods, pastries, and salty snacks and how often they added table salt to cooked food. Possible frequency responses ranged from “never or a few times a year” to “a few times a day” on a 7-point scale. This instrument was included to permit comparison of the group as a whole with the previously mentioned population-based results and to reveal potential dietary differences between the high- and low-activity subgroups.

Hormonal assays

A fasting venous blood sample was drawn for hormonal analysis. Serum β-estradiol was determined with standard radioimmunoassay kits (Sorin Biomedica Diagnostics, Milan, Italy). The intraassay CV for the concentration range of 100–2000 pmol/L was <8%, the interassay CV was <10%, and the sensitivity was <18 pmol/L at 95% CI (22). Serum IGF-I was also determined by radioimmunoassay (Bioclone Australia Pty Ltd, Sydney, Australia), with all samples measured in a single assay. Intraassay precision is typically 3–5.4% CV, and sensitivity is <1 pmol/L for this assay. Serum IGF binding protein 3 (IGFBP-3) was determined in a single assay as described by Baxter and Martin (23); intraassay precision is typically 4.5–6% CV and sensitivity is <0.01 mg/L for this assay.

Statistical analysis

The Kolmogorov-Smirnov goodness-of-fit test (K-S) was used to check variables for normality of distribution. Simple linear regression analysis was used to describe age-related declines in potassium per FFM. Student’s t tests for unpaired data and Mann-Whitney U tests were used to determine differences between high and low activity subgroups. Multiple linear regression modeling (24) was used to determine the combined influence of independent variables (physical activity, age, serum estradiol, and IGF-I) on potassium per FFM. When appropriate, independent variables were entered in categorical form for this modeling. All analyses were conducted with SPSS for WINDOWS (release 6.1.4; SPSS Inc, Chicago), with the level of significance set at \( P < 0.05 \).

RESULTS

Basic subject characteristics

The 51 women exhibited a wide range of body sizes, adiposity, and hormonal concentrations (Table 1). A comparison of mean values and variances with published data (via Student’s t tests) indicated that the group as a whole was not significantly different in terms of height, weight, EEMVPA, and food-frequency responses from a randomly selected group of 191 Australian women aged 60–69 y surveyed previously (21). Such comparisons also indicated that the group was not significantly different in height, weight, and TBK from a sample of 25 healthy white women from Boston aged 50–69 y (25), and in weight and percentage of fat from a sample of 373 healthy Danish women aged 49–60 y (26).

Serum hormone concentrations

Serum estradiol showed a bimodal frequency distribution (Figure 1) attributable to elevated concentrations in the women receiving replacement estrogen (the mean concentration for these 28 subjects was \( 405 \pm 360 \) pmol/L). The mean value for those women not receiving replacement estrogen was \( 29 \pm 7 \) pmol/L. Because of the lack of a normal distribution for this parameter (K-S z score = 1.82; \( P = 0.003 \)), it was expressed in the categorical form of low (\( \leq 100 \) pmol/L) and high (\( >100 \) pmol/L). Serum IGF-I and IGFBP-3 concentrations (Table 1) were normally distributed and were similar to those reported by others for women of a comparable age range (27).

Distribution of TBK variables: age effect

TBK, K/ht, and K/FFM were normally distributed. The variable K/FFM displayed a significant, curvilinear relation with age (Figure 2), indicating an accelerated decline in this variable after 65 y of age.

Characteristics of high- compared with low-activity subjects

As noted above, the semistructured interview data permitted the calculation of EEMVPA. This variable was not normally distributed (Figure 3; K-S z score = 1.57; \( P = 0.015 \)) and applying the 5-MJ/fortnight criterion resulted in the stratification of subjects into low- (\( n = 26 \)) and high-activity (\( n = 25 \)) subgroups. Characteristics of these subgroups are summarized in Table 1, which shows that although the 2 groups were not significantly

![FIGURE 1. Frequency distribution of serum estradiol (log values).](https://academic.oup.com/ajcn/article-abstract/75/2/314/4689310)

![FIGURE 2. Decline in potassium per fat-free mass (K/FFM) with age.](https://academic.oup.com/ajcn/article-abstract/75/2/314/4689310)
different in terms of age, height, weight, or hormonal status, the active group had 6.5% more K/FFM than did their less active counterparts ($P < 0.01$). The active women also had significantly higher TBK ($P = 0.04$) and K/ht values ($P = 0.02$).

The mean EEMVPA for the high-activity subgroup was >10 times that of the low-activity subjects. The most common activities pursued at moderate-to-vigorous-intensity by the high-activity subjects were walking, dancing (including modern dancing and line dancing), aerobics (mainly floor exercises), gardening, swimming, and tennis. With rare exceptions, subjects reported performing these activities at a moderate intensity. For the low-activity group, walking, tennis, and gardening were the most common pursuits.

Mann-Whitney $U$ tests were used to compare the responses of the 2 subgroups to the 12 food-frequency questions because these responses were not normally distributed. There were no significant differences between the 2 subgroups for any of the food-frequency items surveyed.

Decline in potassium per fat-free mass with age as stratified by activity

The age-related declines in K/FFM in the high- and low-activity groups are shown in Figure 4. With the data stratified this way, linear reductions of K/FFM were evident in both groups, and the slopes of the regression lines were not significantly different. However, the regression line for the active subjects displayed an almost constant upward offset from that of the less active women, indicating a positive influence of moderate-to-vigorous-intensity physical activity across the age range studied.

Determinants of potassium per fat-free mass

Results of the multiple regression analysis are given in Table 2. Because serum IGFBP-3 was highly correlated with the serum IGF-I concentration ($r = 0.5, P < 0.001$) and because it is considered to be a key regulator of IGF-I availability to target tissues (23, 27), it was included in the model as an index of IGF-I bioactivity. In this model, when EEMVPA category, age, estradiol category, and IGFBP-3 concentration were entered simultaneously as determinants of K/FFM, the EEMVPA category was significant ($P = 0.024$); together with age it accounted for 21% of the variance in K/FFM. Neither serum estradiol nor IGFBP-3 was a significant determinant of K/FFM. The regression equation for this model was as follows:

$$K/FFM = 2.49 + 0.13 \times \text{EEMVPA category} - 0.008 \times \text{age} + 0.027 \times \text{estradiol category} + 0.06 \times \text{IGFBP-3}$$

in which $R = 0.47$ and $P = 0.018$. Examination of this equation shows that an active 70-yr-old had, on average, the K/FFM value of a 55-yr-old sedentary woman, assuming constant anabolic hormone values.

This relation between habitual physical activity, age, and K/FFM was not altered appreciably when serum IGF-I concentration was added to the model, when physical activity was entered as a continuous EEMVPA variable (with zero values excluded), or when only those women with a low estradiol concentration were included in the analysis.

Determinants of potassium per height and total body potassium

The simultaneous-entry model for predicting K/ht was qualitatively similar to that of K/FFM, with only the EEMVPA category ($P = 0.053$) approaching significance (Table 2).

When TBK was entered as the dependent variable and FFM was included with the other explanatory variables (EEMVPA category, age, estradiol category, and IGFBP-3), both FFM and EEMVPA category were significant determinants of TBK (Table 2). In this model, an active 70-yr-old had the TBK value of a 55-yr-old sedentary woman, assuming constant FFM and anabolic hormone values.

DISCUSSION

The primary objective of this study was to describe the relation between age, physical activity, hormonal status, and TBK in postmenopausal women. Intersubject variability in size and adiposity was controlled for by expressing TBK as a fraction of FFM. Comparisons with previous reports indicated that the women in the present study were generally representative of healthy white women aged 50–70 y in regard to anthropometric and TBK characteristics.

Normalization of total body potassium for body size

In many early studies investigating the potential influence of age on body composition, TBK was expressed as a fraction of body weight (K/wt). Although this approach holds merit in controlling
for body size, it is severely confounded by a known age-associated increase in adiposity (4, 9). Because the potassium content of fat is negligible, a rise in fat must reduce the value of K/wt. Because height should be independent of adiposity, others have normalized TBK by height (ie, K/ht) and have described significant age-related declines of K/ht in adult women (5, 25, 28). However, height declines with age, and this could bias these findings.

Use of the variable K/FFM avoids the confounding aspects of age-related variation in adiposity and body size and expresses TBK as a function of the fat-free body compartment in which it resides. As a result, this variable reflects the quality of the FFM (25) and should, therefore, represent a superior approach to that of both K/wt and K/ht, provided TBK and FFM are assessed by independent methods.

An alternative size normalization technique is the inclusion of FFM as an explanatory variable for TBK. The data summarized in Table 2 show that this analysis was consistent with the K/FFM approach.

Implication of the decline in potassium per fat-free mass with age

Limited K/FFM data have been published for middle-aged or postmenopausal women. Morgan and Burkinshaw (29) reported a mean (± SD) K/FFM value of 2.19 ± 0.16 g/kg for 29 women aged 44 ± 12 y. Khayyas et al (25) used total body carbon to quantify FFM and derived K/FFM values in a large group of healthy, free-living white Boston men and women, including 51 women aged 50–89 y. Their graphical data indicated a significant decline in K/FFM between the ages of 35 and 60 y, with a more rapid decline evident after 60 y of age. Mean K/FFM values were ≈2.15 and 1.85 g/kg in women aged 50–69 and >70 y, respectively. Mean values for comparable age groups in the present study (2.25 and 2.05 g/kg) are consistent with these Boston data, and the regression against age (Figure 2) also displayed an accelerated decline after the age of 65 y. The implication of this curvilinear relation with age is that older women inevitably experience substantial losses of skeletal muscle mass. Such losses are consistent with a drop in K/FFM because skeletal muscle is rich in potassium (1).

Potential for physical activity to minimize sarcopenia

The analyses that examined physical activity illustrate the potential for an active lifestyle to counteract, or even reverse, sarcopenia in older women. There was consistent, strong evidence that habitual, moderate-to-vigorous-intensity activity partly offset the age-related decline in K/FFM and, by implication, minimized sarcopenia. The analysis showed that the women who were more physically active had, on average, higher K/FFM values than did their less active counterparts throughout the age range studied (Figure 4). This effect, confirmed by multiple regression analysis, was such that an average active woman had the K/FFM value of a sedentary woman 15 y younger.

There is clearly a sound basis for this phenomenon. Physical training, especially when it involves resistance-type exercise, is known to minimize sarcopenia in older women and may even result in significant increases in skeletal muscle mass (8, 30). What is particularly interesting is that significant, positive effects on FFM were attributable to relatively moderate-intensity, predominantly aerobic activities such as walking, dancing, floor exercises, and swimming, which are both popular (21) and sustainable in the long term (31, 32) in this age group of women. Although some research groups vigorously advocate the use of high-intensity progressive resistance or strength training in the elderly, the potential contribution of moderate-intensity aerobic activity to minimize sarcopenia (8, 30, 33) has received little attention. Nevertheless, relevant data from one study indicated a protective effect of regular, aerobic forms of physical activity on skeletal muscle mass in older men and women. Sidney et al (34) observed a 4% increase in TBK (P < 0.05) when 14 subjects aged 60–70 y exercised for a year in a supervised program of walking that eventually progressed to

---

### TABLE 2
Multiple regression variables for prediction of potassium per fat-free mass (K/FFM), potassium per height (K/ht), and total body potassium (TBK)

<table>
<thead>
<tr>
<th></th>
<th>β²</th>
<th>P²</th>
<th>R² (%)</th>
<th>SEE²</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>K/FFM (g/kg)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EEMVPA category</td>
<td>0.130 ± 0.056</td>
<td>0.024</td>
<td>11.3</td>
<td>0.194</td>
</tr>
<tr>
<td>Age (y)</td>
<td>−0.008 ± 0.005</td>
<td>0.110</td>
<td>20.7</td>
<td>0.185</td>
</tr>
<tr>
<td>Estradiol category</td>
<td>0.027 ± 0.064</td>
<td>0.682</td>
<td>20.7</td>
<td>0.187</td>
</tr>
<tr>
<td>IGFBP-3 (mg/L)</td>
<td>0.060 ± 0.062</td>
<td>0.333</td>
<td>22.3</td>
<td>0.187</td>
</tr>
<tr>
<td><strong>K/ht (g/cm)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EEMVPA category</td>
<td>0.046 ± 0.023</td>
<td>0.053</td>
<td>7.7</td>
<td>0.081</td>
</tr>
<tr>
<td>Age (y)</td>
<td>−0.002 ± 0.002</td>
<td>0.292</td>
<td>15.2</td>
<td>0.079</td>
</tr>
<tr>
<td>Estradiol category</td>
<td>0.022 ± 0.027</td>
<td>0.410</td>
<td>15.4</td>
<td>0.079</td>
</tr>
<tr>
<td>IGFBP-3 (mg/L)</td>
<td>0.043 ± 0.026</td>
<td>0.099</td>
<td>20.3</td>
<td>0.078</td>
</tr>
<tr>
<td><strong>TBK (g)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FFM (kg)</td>
<td>2.326 ± 0.238</td>
<td>&lt;0.0001</td>
<td>66.7</td>
<td>8.568</td>
</tr>
<tr>
<td>EEMVPA category</td>
<td>5.460 ± 2.365</td>
<td>0.026</td>
<td>70.4</td>
<td>8.169</td>
</tr>
<tr>
<td>Age (y)</td>
<td>−0.359 ± 0.201</td>
<td>0.080</td>
<td>73.6</td>
<td>7.795</td>
</tr>
<tr>
<td>Estradiol category</td>
<td>0.537 ± 2.738</td>
<td>0.845</td>
<td>73.6</td>
<td>7.879</td>
</tr>
<tr>
<td>IGFBP-3 (mg/L)</td>
<td>2.098 ± 2.645</td>
<td>0.432</td>
<td>73.9</td>
<td>7.911</td>
</tr>
</tbody>
</table>

---

1 EEMVPA, energy expenditure (per fortnight) in moderate-to-vigorous-intensity physical activity; IGFBP-3, insulin-like growth factor binding protein 3.
2 x ± SE. Partial regression coefficient with all listed independent variables included in the model.
3 Two-sided probability for the independent variable, with all variables included in the model.
4 Proportion of variance in the dependent variable explained by the model when this independent variable plus those above it were entered in the model.
5 SEE of the dependent variable, with this independent variable and those above it entered in the model.
6 0 = low, 1 = high.
7 0 = low, 1 = high.

---

Downloaded from https://academic.oup.com/ajcn/article-abstract/75/2/314/4689310 by guest on 22 April 2018
jogging. The largest gain in TBK (5%) was noted in a subgroup who exercised at a high intensity and frequency. This longitudinal finding is consistent with the current cross-sectional finding of a higher K/FFM (by 6.5%) in the high- than in the low-activity subgroup. Considered together, these findings indicate that predominantly aerobic activities such as walking, jogging, dancing, floor exercises, and swimming, pursued at moderate-to-vigorous intensity, can assist in preventing sarcopenia in older women. In contrast, other cross-sectional studies have failed to show a positive influence of aerobic activity on muscle mass in older men (35, 36), and aerobic training interventions have not consistently increased FFM in older individuals (37). More longitudinal studies are required to determine the extent to which aerobic activity can prevent sarcopenia in older individuals.

The present study shows, therefore, that physical activity can be a confounding factor in regard to the relation between TBK and age. A decline in TBK with age appears to be inevitable, even in active postmenopausal women, as evidenced in the almost identical regression slopes for the 2 subgroups in Figure 4. However, moderate-to-vigorous-intensity habitual physical activity, and not age, was the major determinant of K/FFM in the multivariate analysis. This strongly implies that physical activity must be considered as a covariate if the effect of aging on TBK is to be accurately shown. As a result, the findings of previous studies that failed to quantify physical activity should be interpreted with caution.

Influence of anabolic hormones

Serum estradiol concentrations did not significantly influence TBK variables in this study. Although estradiol replacement therapy is clearly anabolic for bone, significant effects of such therapy on muscle tissue have rarely been shown (22, 38, 39). It is interesting to note that one study reported an accelerated perimenopausal decline in TBK, implying that a drop in estrogen was at least partly responsible for this phenomenon (7). Another study showed that menopause was associated with a decline in FFM (26). Physical activity was not considered, however, in these analyses. Poehlman et al (40) noted a similar perimenopausal decline in FFM that was associated with reductions in resting metabolic rates and leisure-time physical activity in 18 women who had experienced natural menopause. Although it is possible that replacement estrogen may assist in preventing sarcopenia in postmenopausal women, randomized interventions, with control for physical activity, are necessary to clarify this issue.

In the present study, serum IGF-I and IGFBP-3 were expected to be anabolic for skeletal muscle, and, therefore, to exert a positive influence on TBK variables; however, like estradiol, they failed to reach significance. In cell culture experiments, IGF-I appears to induce both the differentiation and the proliferation of myoblasts (41). Both IGF-I (11) and IGFBP-3 (42) were shown to be significant determinants of bone density in adults, but studies are inconclusive regarding their influence on muscle mass. Porch et al (43) reported a significant correlation between IGF-I and FFM in 112 women aged 20–87 years; however, when 59 elderly subjects (aged >60 years) were considered separately, a relation between IGF-I and FFM was not evident. Harris et al (44) found that low soft-tissue lean mass was associated with low IGF-I concentrations in 428 elderly women, but not in 242 elderly men. This relation in women failed to exist when lean mass was expressed per kilogram of body weight. Other investigators have failed to show a significant relation between IGF-I and FFM in elderly women (11) and men (45).

It is important to note that these findings do not negate the importance of circulating IGF-I in the maintenance of skeletal muscle tissue. Recent data indicate, however, that relatively small, localized modulations in the availability of IGF-I and IGFBP-3 at the tissue and cellular level, although not contributing to detectable changes in circulating concentrations, probably play a vital role in maintaining both bone and muscle tissue (46, 47).

Limitations of the study

The FFM measures used in the present study are not as accurate as other methods, such as underwater weighing, computed tomography, or magnetic resonance imaging, and are more likely to be influenced by age-related changes in fat patterning (15). However, the effect of any such age-related errors was minimized by 1) the use of equations validated in white women of the same age range as those participating in the present study and 2) the close matching of age of the 2 activity subgroups. There were almost equal numbers of high- and low-activity subjects for the age bands of 54–60, 61–70, and 71–76 years (Figure 4). Thus, any errors associated with applying these FFM methods should have had similar effects on both subgroups and should not bias the results.

The food-frequency questionnaire was limited to 12 items. As such, it is not a comprehensive representation of subjects’ dietary patterns. Nevertheless, an analysis of the responses indicates that there were no significant differences between subgroups regarding intake frequency of several major food groups and for some health-related dietary practices.

Given the cross-sectional design, the relation between moderate-to-vigorous-intensity physical activity and the potassium content of FFM cannot be interpreted as proof of a cause-and-effect relation. The consistent findings of the various analyses provide strong evidence, nevertheless, that engaging regularly in the types of physical activities reported by these women contributes significantly to the maintenance of muscle mass after menopause.

It is possible that the inclusion of a subset of women who were undergoing estrogen replacement therapy affected the findings; however, the multivariate analyses did not reveal any significant influences. It must be noted that because the radioimmunoassay used is specific for β-estradiol, the influence of other steroids, such as estriol, could not be assessed.

In summary, the present study considered the relation between habitual physical activity, ageing, anabolic hormones, and TBK in older women. The key finding was that moderate-to-vigorous-intensity physical activity was significantly associated with higher FFM potassium content throughout a 20-y postmenopausal section of the life span. Thus, the data provide reasonable evidence that such activity confers a significant benefit in terms of what has been coined ‘successful’ aging (31, 48, 49)—that is, maintaining a high degree of functionality and independence in the latter part of life.

We are grateful to Ali Aslani for technical assistance, to Rod Baber and Terry Moreton for assistance with subject recruitment, and to Robert Baxter, Brian Luttrel, Sri Meka, Mike Siniosich, and Gloria Watts for assistance with hormonal assays.

REFERENCES


27. Juul A, Main K, Blum WF, et al. The ratio between serum levels of insulin-like growth factor (IGF-I) and the IGF binding proteins (IGFBP-1, 2 and 3) decreases with age in healthy adults and is increased in acromegalic patients. Clin Endocrinol 1994;41:85–93.


