Predictors of age-associated decline in maximal aerobic capacity: a comparison of four statistical models

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1Division of Gerontology, Department of Medicine, University of Maryland, and Geriatric Research, Education, and Clinical Center, Geriatrics Service, Baltimore Veterans Affairs Medical Center, Baltimore 21201; 2Laboratory of Clinical Investigation, Metabolism Section, National Institute on Aging, Baltimore 21224; and 3Department of Kinesiology, University of Maryland, College Park, Maryland 20742

Rosen, Mitchell J., John D. Sorkin, Andrew P. Goldberg, James M. Hagberg, and Leslie I. Katznel. Predictors of age-associated decline in maximal aerobic capacity: a comparison of four statistical models. J. Appl. Physiol. 84(6): 2163–2170, 1998.—Studies assessing changes in maximal aerobic capacity (VO2max) associated with aging have traditionally employed the ratio of VO2max to body weight. Log-linear, ordinary least-squares, and weighted least-squares models may avoid some of the inherent weaknesses associated with the use of ratios. In this study we used four different methods to examine the age-associated decline in VO2max in a cross-sectional sample of 276 healthy men, aged 45–80 yr. Sixty-one of the men were aerobically trained athletes, and the remainder were sedentary. The model that accounted for 66% of the variance in VO2max and satisfied all the important general linear model assumptions. The other approaches failed to satisfy one or more of these assumptions. The results indicated that VO2max declines at the same rate in athletic and sedentary men (0.24 l/min or 9%/decade) and that 35% of this decline (0.08 l·min–1 decade–1) is due to the age-associated loss of fat-free mass; exercise; heteroscedasticity; weighted least squares; log-linear model; ratio

There is an age-associated decline in maximal aerobic capacity (VO2max) in trained and untrained men (6, 8, 10, 13, 22). This age-associated decline in VO2max is due to many factors, including decreases in maximum heart rate, stroke volume, arteriovenous O2 difference, and skeletal muscle mass and an increase in adiposity (10, 13, 22). Changes in physical activity habits, leading to a sedentary lifestyle, also contribute to the age-associ-
ated decline in VO2max (3, 12, 17, 22, 27). There is conflicting evidence on whether regular aerobic exercise training attenuates the age-associated decline in VO2max (13, 25, 28).

Different statistical models have been used to analyze the relationships among the physiological variables associated with the age-associated decline in VO2max. The statistical approach employed to adjust the VO2max for body size and composition must be considered carefully; the approach must be statistically valid. All other factors being equal, a larger individual would be expected to have a higher VO2max than a smaller individual. To account for differences in body habitus, the simple ratio of VO2max to a measure of body size [e.g., VO2max ml·kg body wt–1·min–1 or VO2max ml·kg fat-free mass (FFM)–1·min–1] is often used as the dependent variable in studies of the age-related decline in VO2max (3, 12, 27). We will refer to this model as the standard (RS) model. The use of ratios as dependent variables in regression models has been criticized for a variety of reasons (2, 9, 20, 28, 30, 31, 33), but the main drawback is that the ratio Y/X is correlated with X (21, 32, 33). In a classic paper, Pearson(23) showed that if X, Y, and Z are three random variables and X, Y, and Z are uncorrelated, X/Z and Y/Z are correlated under minimally restrictive assumptions (23). In the case of VO2max, the VO2max/body size ratio may not make VO2max totally independent of body size. Given the physiological and functional importance of the VO2max-age relationship, it is important that this relationship is assessed in valid statistical and mathematical terms to ensure appropriate interpretation of the results.

Two alternatives to the RS model have been used in the statistical analysis of the age-related change in VO2max: ordinary least-squares (OLS) regression of VO2max on a measure of body size, such as FFM or weight (31), and log-linear (LL) or allometric models (20, 21). OLS and LL models are not without problems. OLS residuals in VO2max models are often heteroscedastic; i.e., they increase in variability as the measure of body habitus increases (20, 33). Heteroscedasticity can affect the standard errors of the parameter estimates and thus adversely affect tests of significance (24). LL models have been criticized for their tendency to overfit biological data, modeling what is sometimes a linear phenomenon with a nonlinear model (1). Additionally, LL models assume a zero intercept, which usually involves extrapolation well beyond the range of observed data (1). A variant of LL is the Box-Cox transformation (4), in which the dependent variable is raised to
the power (i.e., $\dot{V}O_{2\text{max}}^2$) that maximizes the likelihood that the model residuals follow a normal distribution. This method has not been widely used in studies that have examined the age-associated decline in $V_{O2\text{max}}$.

In this paper an alternative method to modeling $V_{O2\text{max}}$ is proposed: weighted least squares (WLS). WLS models retain the advantages of OLS models, producing “best linear unbiased estimates” (BLUE) and overcoming the problem of heteroscedasticity (16, 24). Because of the widespread use of the RS models in studies of $V_{O2\text{max}}$, the potential errors caused by the failure of the RS to remove the effect of body size on $V_{O2\text{max}}$, and the potential problems caused by the heteroscedasticity inherent in OLS models of $V_{O2\text{max}}$, we believe that further analysis of the age-related decline in $V_{O2\text{max}}$ is warranted. Therefore, we compare the results obtained from RS, OLS, LL, and WLS models of the age-associated decline in $V_{O2\text{max}}$. In each case we examine how well the model satisfies the general linear model (GLM) assumptions of normality and homoscedasticity.

**METHODS AND MATERIALS**

**Subjects**

This study was approved by the Institutional Review Boards of the University of Maryland School of Medicine and Johns Hopkins University Bayview Medical Center. All subjects provided informed consent before participation. Over an 8-yr period, healthy nonsmoking men, ages 45–80 yr, with no prior history of cardiovascular disease and a wide range of body mass index (BMI) and physical conditioning status, were recruited to participate in exercise training and weight loss studies (14, 35). Characteristics of the subjects are summarized in Table 1. All subjects underwent a history and physical examination and evaluation of fasting blood chemistries. Subjects were healthy and on no medications. Exclusion criteria included history of coronary artery disease (by clinical history and electrocardiogram), pulmonary disease, hyper-tension (blood pressure $\geq 160/90$ mmHg), hyperlipidemia, diabetes mellitus (fasting plasma glucose $\geq 140$ mg/dl), or any other significant medical problems that would interfere with their ability to undergo maximal exercise treadmill testing. The study sample included a cohort of 61 healthy athletes recruited from participants of the Maryland Senior Olympics and athletic clubs in the Baltimore-Washington metropolitan area and 215 sedentary subjects (35). The sedentary subjects exercised $\leq 20$ min twice per week. The athletes exercised vigorously at least four times per week and had $<25\%$ body fat by hydrodensitometry.

### Table 1. Subject characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Group</th>
<th>n = 61</th>
<th>n = 215</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yr</td>
<td>62.4 ± 6.1</td>
<td>60.0 ± 7.9*</td>
<td></td>
</tr>
<tr>
<td>Weight, kg</td>
<td>69.8 ± 6.9</td>
<td>91.2 ± 13.2*</td>
<td></td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>23.1 ± 2.2</td>
<td>29.5 ± 3.5*</td>
<td></td>
</tr>
<tr>
<td>Height, cm</td>
<td>174 ± 6</td>
<td>175 ± 7</td>
<td></td>
</tr>
<tr>
<td>%Body fat</td>
<td>15.1 ± 5.2</td>
<td>28.4 ± 5.9*</td>
<td></td>
</tr>
<tr>
<td>FFM, kg</td>
<td>59.2 ± 5.8</td>
<td>64.0 ± 7.5*</td>
<td></td>
</tr>
<tr>
<td>$V_{O2\text{max}}$, l/min</td>
<td>3.38 ± 0.48</td>
<td>2.68 ± 0.51*</td>
<td></td>
</tr>
</tbody>
</table>

Values are means ± SD. BMI, body mass index; FFM, fat-free mass; $V_{O2\text{max}}$, maximal aerobic capacity. *P < 0.01 compared with athletes.

**Measurement of Body Composition**

Height and weight were measured, and BMI was computed as the ratio of body weight in kilograms to height in meters squared. Body surface area in meters squared was calculated as $(\text{height in cm})^{0.718} \times (\text{weight in kg})^{0.427} \times 0.007449$ (7). Body density was determined by hydrostatic weighing, with percent body fat calculated after correction for residual lung volume with use of the Siri model (29). FFM was calculated as body weight minus fat mass.

**Measurement of $V_{O2\text{max}}$**

An exercise treadmill test to $\geq 85\%$ of the predicted age-adjusted heart rate (220 – age) was performed according to the protocol of Bruce and Horsten (5) to exclude subjects with previously undiagnosed heart disease. On a subsequent visit the $V_{O2\text{max}}$ was determined using a modified Balke protocol, as previously described (14). The grade of the treadmill was increased every 2 min until the subject was exhausted and could not continue (14). The $V_{O2\text{max}}$ tests fulfilled at least two of the three following criteria: 1) the heart rate at maximal exercise was $\geq 85\%$ of the age-adjusted maximal heart rate, 2) the respiratory exchange quotient was $\geq 1.10$, and 3) there was a plateau in $O_2$ consumption defined as a change in $O_2$ consumption of $<0.2$ l/min during the final two collection periods. Absolute $V_{O2\text{max}}$, measured in liters per minute, is used in the statistical modeling.

**Statistical Analysis**

All statistical analyses were performed using SAS version 6.11 run on the Windows 3.1 operating system.

Statistical models of $V_{O2\text{max}}$. Four statistical models were used to determine the age-associated decline in $V_{O2\text{max}}$.

1) The form of the RS model is

$$V_{O2\text{max}}/FFM = \beta_0 + \beta_1X_1 + \beta_2X_2 + \ldots + \epsilon$$

where $X_1$, $X_2$, etc., are independent variables, $\beta_0$, $\beta_1$, etc., are parameters, and $\epsilon$ is a normally and independently distributed error term having equal variance for all levels of the independent variable(s) in the target population.

2) The form of the OLS regression is

$$V_{O2\text{max}} = \beta_0 + \beta_1X_1 + \beta_2X_2 + \ldots + \epsilon$$

where $X_1$, $X_2$, etc., are independent variables, $\beta_0$, $\beta_1$, etc., are parameters, and $\epsilon$ is an error term with the same properties as in Eq. 1. OLS estimation ensures that the residuals of the model are uncorrelated with FFM, $X_2$, etc. (24).

3) The univariate form of the LL model is

$$V_{O2\text{max}} = \beta_0X_1^{\beta_1}$$

where $\beta_0$ and $\beta_1$ are parameters and $\delta$ is an error term. Equation 3 is referred to as an allometric model. The multivariable form is

$$\dot{V}_{O2\text{max}} = \beta_0X_1^{\beta_1}X_2^{\beta_2} \ldots X_p^{\beta_p}$$

$$\exp(\beta_{p+1}W_1 + \beta_{p+2}W_2 + \ldots + \beta_{p+k}W_k)$$

where $X_1$, $X_2$, etc., are variables related in an LL manner to $V_{O2\text{max}}$, $W_1$, $W_2$, etc., are variables related linearly to $V_{O2\text{max}}$, $\beta_0$, $\beta_1$, etc., are parameters, and $\delta$ is an error term.
For example, when age is used in the multivariable model, Eq. 4 becomes

$$Y = b_0 FFM_1 \exp(b_2 \text{AGE} \bar s)$$

One approach to estimating the parameters of the univariate or multivariate models is to use OLS on the logarithmic transformation of the model, e.g.,

$$\log(\hat{V}_O_{2\max}) = \log(b_0) + \beta_1 \log(FFM) + \log(h)$$

or

$$\log(\hat{V}_O_{2\max}) = \log(b_0) + \beta_1 \log(FFM) + \beta_2 \text{AGE} + \log(h)$$

An alternative approach is to estimate the coefficients in the original scale by use of nonlinear regression methods. In this study the former method was used.

When the univariate form of the LL model is used, it is usual practice to verify that the variable $\hat{V}_O_{2\max}/FFM_1$, which is proportional to the residuals of Eq. 3, has a correlation near zero with FFM (32, 33).

4) WLS regression is identical to OLS regression, except each subject $i$ receives a weight $w_i$. The goal of WLS is to minimize the sums of the squares

$$\sum_{i=1}^{n} w_i \left[ \hat{V}_O_{2\max(i) \text{ (obs)}} - \hat{V}_O_{2\max(i) \text{ (pred)}} \right]^2$$

where the first and second terms in parentheses are the observed and predicted $\hat{V}_O_{2\max}$ values, respectively. In OLS, $w_i = 1$ (for all i). For example, if the error variance increases along with the values of a regressor (e.g., FFM), observations that have higher values on the regressor receive lower weights than observations that have lower values. The model then reflects the greater uncertainty in the predicted values at higher values of the regressor.

If the weights are chosen to be proportional to the reciprocal of the error variance and the other GLM assumptions are met, the WLS model has the desirable property of producing parameter estimates that are BLUE. Moreover, the estimated variances of the parameters will be unbiased and so will the t-tests on which these variances are based. If heteroscedasticity exists, the estimates of the variance of the parameters produced by OLS are not minimum variance estimates, so OLS estimates will not, in general, be BLUE (24).

In this study, WLS weights took the form $w_i = 1/FFM_i^2$. When this form is used, the following assumption, known as multiplicative heteroscedasticity, is implied

$$\alpha_i^2 = \sigma_i^2 FFM_i^\alpha$$

In Eq. 9, $\alpha_i^2$ is the error variance at the level of FFM that equals FFM, $\sigma_i^2$ is the error variance from the OLS model, and $\alpha$ is the parameter related to the degree of heteroscedasticity (homoscedasticity implies $\alpha = 0$). Equation 9 suggests that the variation of the residuals of model shown in Eq. 2 increases as FFM increases. This assumption is usually examined by plotting the fitted residuals $\hat{e}$ against FFM. Harvey (11) provided a method for obtaining the maximum likelihood (ML) estimator of $\alpha$. Other ways of obtaining the ML estimates of $\alpha$ and $\alpha$ have been proposed (16).

It is possible to demonstrate that using the weights $1/FFM_i^2$ is equivalent to transforming the linear model by dividing each term by $FFM_i^{1/2}$ (24). For example, if FFM is the only regressor, the transformed model is

$$\hat{V}_O_{2\max}/FFM_1^2 = (\beta_0/FFM_1^2) + \beta_1 FFM_1^{-1/2} + (1/FFM_1^2)$$

The model can be estimated by fitting the regression on the transformed variables.

Equation 10 shows that the variance of the transformed residuals is constant as long as the weights $w_i$ are proportional to the reciprocal of the error variance. Given the usual assumption that the independent variables are fixed, we can write the variance of the error term as

$$\text{var}(\hat{e}/FFM_1^2) = (1/FFM_1^2) \text{var}(e_i)$$

Now, apply Eq. 9, setting $\alpha_i^2 = \text{var}(e_i)$

$$(1/FFM_1^2) \text{var}(e_i) = (1/FFM_1^2) \text{var}(\hat{e}) = \sigma_i^2$$

There is another interesting consequence of Eq. 10. If $\alpha_i = 2$, Eq. 10 becomes

$$\hat{V}_O_{2\max}/FFM = \beta_0 FFM + \beta_1 + e/FFM$$

Then, if $\beta_0 = 0$ (zero intercept), Eq. 13 is structurally identical to the RS model (Eq. 1) with only an intercept term. This suggests that if $\alpha = 2$ and $\beta_0 = 0$, the RS model (Eq. 13) will be homoscedastic. Moreover, if the transformation does not greatly perturb the correlation matrix, multivariable RS models should also have this property, given the previous assumptions.

It is possible to extend Eq. 9 to include multiple regressors, e.g.,

$$\sigma_i^2 = \sigma_i^2 FFM_i^\alpha_i \text{HEIGHT}_i^2$$

The weights for WLS derived from Eq. 10 are $1/(FFM_1^2) \text{HEIGHT}_i^2$. Note that the regressors in Eq. 9 or 14 need not necessarily be regressors in the OLS model (Eq. 2).

Factors related to the age-associated decline in $\hat{V}_O_{2\max}$.

We initially examined models that included age, FFM, body weight, fat mass, height, BMI, body surface area, and a dichotomous exercise training variable (ET) that denoted whether the individual was an athlete (0 = sedentary, 1 = athlete). Body weight, fat mass, BMI, height, and body surface area were not significant predictors in any of the models at the 0.05 level when FFM was included and were not included in the analyses.

To determine whether the slopes of the age-related decline in $\hat{V}_O_{2\max}$ differed between athletes and sedentary subjects, analyses were also performed with RS, OLS, and WLS models that included interactions between age and ET. For each model type we obtained estimates of the age-associated decline and effect of ET on $\hat{V}_O_{2\max}$. Because the LL model is log linear, it does not permit a test of the hypothesis of parallel linear declines in $\hat{V}_O_{2\max}$.

Contribution of skeletal muscle loss to the age-associated decline in $\hat{V}_O_{2\max}$.

We estimated the contribution of the loss of skeletal muscle to the decline in $\hat{V}_O_{2\max}$ as

$$\text{%contribution} = 100 \cdot \frac{\beta_{\text{AGE (adjusted)}} - \beta_{\text{AGE (unadjusted)}}}{\beta_{\text{AGE (unadjusted)}}}$$

where $\beta_{\text{AGE (adjusted)}}$ and $\beta_{\text{AGE (unadjusted)}}$ are the regression coefficients for age in the models adjusted and unadjusted for FFM.
Effect of Age Unadjusted for Body Habitus

All the parameter estimates of the OLS model

\[ \dot{V}_{O2max} = \beta_0 + \beta_1 \text{AGE} + \beta_2 \text{ET} + \epsilon \]  

were significant at \( P < 0.01 \) (Table 3). This model accounted for 48\% of the variance in \( \dot{V}_{O2max} \). There was no evidence of lack of normality (Wilks-Shapiro test, \( P > 0.10 \)) or heteroscedasticity due to lack of fit (White's test, \( P > 0.7 \)). However, it is of interest that multiplicative heteroscedasticity with FFM was present [Harvey's test, \( \chi^2 (1) = 4.22, P < 0.05 \)]. There was no significant interaction between age and ET. Therefore, the absolute age-associated rate of decline in \( \dot{V}_{O2max} \) was 0.36 l/min, was the same in athletes and sedentary men. The OLS estimate of the effect of exercise training (the coefficient of ET) was 0.78 l/min (Table 3).

All the parameters of the LL model

\[ \dot{V}_{O2max} = \beta_0 \exp(\beta_2 \text{AGE} + \beta_3 \text{ET})\delta \]  

were significant at \( P < 0.01 \) (Table 3). This model accounted for 46\% of the variance in \( \dot{V}_{O2max} \). The residuals were normally distributed, but there was evidence of heteroscedasticity due to lack of fit (White's test, \( P < 0.05 \)). Unlike the OLS and WLS models, in the LL model the percent decline of \( \dot{V}_{O2max} \) per decade is independent of the baseline value. The age-associated decline was proportional to \( \exp(-0.014 \text{AGE}) = 0.986 \exp(\text{AGE}) \).

To obtain the WLS model, the OLS model

\[ \dot{V}_{O2max} = \beta_0 + \beta_1 \text{AGE} + \beta_2 \text{ET} + \epsilon \]  

was adjusted for multiplicative heteroscedasticity by using weights \( 1/\text{FFM}^{0.87} \). All the parameter estimates were significant at \( P < 0.01 \) (Table 3). This model accounted for 49\% of the variance in \( \dot{V}_{O2max} \). The WLS model met all the GLM assumptions and yielded estimates of the training effect and of the age-associated decline that were nearly identical to the OLS model.

Effect of Age Adjusted for Body Habitus

The RS model was

\[ \dot{V}_{O2max}/\text{FFM} = \beta_0 + \beta_1 \text{AGE} + \beta_2 \text{ET} + \epsilon \]  

The ratio \( \dot{V}_{O2max}/\text{FFM} \) did not completely remove the effects of FFM; the correlation between the ratio and FFM was \(-0.17 \) (\( P < 0.01 \)). All parameter estimates for the model (Eq. 23) were significant at \( P < 0.01 \) (Table 3). The model accounted for 60\% of the variance in \( \dot{V}_{O2max} \). There was no evidence of heteroscedasticity due to lack of fit and no correlation between the absolute residuals and FFM (\( r = 0.01 \)). However, the residuals were not normally distributed (\( P < 0.02 \)). There was no significant interaction between age and ET. Thus the age-associated rate of decline relative to FFM was the same in athletes and sedentary men, \( \sim 0.0034 \text{ l·kg FFM}^{-1} \cdot \text{min}^{-1} \cdot \text{decade}^{-1} \). The estimate of the ET effect

### RESULTS

The correlations among selected measures of body size, age, and \( \dot{V}_{O2max} \) are shown in Table 2. All the body size variables correlated with \( \dot{V}_{O2max} \) (\( P < 0.01 \)). Regression results for the unadjusted and adjusted RS, OLS, LL, and WLS models are shown in Table 3. Only variables significant at \( P < 0.05 \) in the regression are listed.

Table 2. Correlations between age, measures of body habitus, and \( \dot{V}_{O2max} \)

<table>
<thead>
<tr>
<th></th>
<th>Age</th>
<th>FFM</th>
<th>Fat Mass</th>
<th>Height</th>
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<tr>
<td>FFM</td>
<td>-0.40</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fat mass</td>
<td>-0.29</td>
<td>0.43</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Height</td>
<td>-0.24</td>
<td>0.65</td>
<td>0.25</td>
<td></td>
</tr>
<tr>
<td>( \dot{V}_{O2max} )</td>
<td>-0.38</td>
<td>0.39</td>
<td>-0.19</td>
<td>0.34</td>
</tr>
</tbody>
</table>

All correlations are significant at \( P < 0.01 \).
due to the difference in intercept was 0.016 l/min (Table 3).

For the OLS model
\[ \dot{V}_{O2\text{max}} = \beta_0 + \beta_1 \text{FFM} + \beta_2 \text{AGE} + \beta_3 \text{ET} + \epsilon \]  
all parameter estimates were significant at \( P < 0.01 \). The OLS model accounted for 64% of the variance in \( V_{O2\text{max}} \). There was no evidence of lack of normality or heteroscedasticity due to lack of fit. The absolute residuals correlated with FFM (\( r = 0.18, P < 0.01 \)). Harvey's test for multiplicative heteroscedasticity confirmed this finding: \( x^2 (1) = 7.52, P < 0.01 \). A plot of the residuals vs. FFM, in which the heteroscedasticity is depicted, is shown in Fig. 1. As in the RS model, the rates of decline were not significantly different in athletes and sedentary men. The calculated decline in \( V_{O2\text{max}} \) was 0.24 l·min\(^{-1}\)·decade\(^{-1}\), and the estimate of the exercise conditioning effect was 0.96 l/min.

For the LL model
\[ \dot{V}_{O2\text{max}} = \beta_0 \text{FFM}^{\beta_1} \exp(\beta_2 \text{AGE} + \beta_3 \text{ET}) \delta \] 
all parameter estimates were significant at \( P < 0.01 \). The model accounted for 63% of the variance in \( V_{O2\text{max}} \). However, there was evidence of lack of normality and of heteroscedasticity due to lack of fit (Wilks-Shapiro and White's tests, both \( P < 0.01 \)). There was no evidence of multiplicative heteroscedasticity; the absolute residuals were uncorrelated with FFM (\( r = 0.01 \)). For this model the age-associated decline was proportional to \( \exp(-0.009 \text{AGE}) = 0.99 \exp(\text{AGE}) \), suggesting an 8.4% decline in \( V_{O2\text{max}} \) per decade in athletes and sedentary men.

WLS results were based on the OLS model (Eq. 21) using weights \( 1/\text{FFM}^{1.30} \). The WLS and OLS estimates and standard errors were almost identical (Table 3). The WLS model explained 66% of the variance in \( V_{O2\text{max}} \) compared with 64% for OLS. The residuals met all the important GLM assumptions. As in the RS and OLS models, the rates of decline in \( V_{O2\text{max}} \) were the same in trained and untrained men (i.e., there was no significant interaction between age and ET). The WLS model yielded estimates of the training effect and of the age-related declines in \( V_{O2\text{max}} \) that were similar in athletes and sedentary men, as in the OLS model. A plot of the decline in \( V_{O2\text{max}} \) with age based on the coefficients from the WLS model is shown in Fig. 2.

Effect of Age Adjusted for FFM and Height

Nevill (19) suggested that height may be an important covariate in LL models of \( V_{O2\text{max}} \). In this study, height was not a significant predictor of \( V_{O2\text{max}} \) in any of the models, and its inclusion had little effect on the estimates of the age-associated decline. This may be due in part to the relatively small variation in height (coefficient of variation of 4%) in these subjects. Height also did not contribute when used in the model in Eq. 10 with FFM as a predictor of within-subject variance [Harvey's test \( x^2 (1) = 2.64, P > 0.05 \)].
Effect of Age Adjusted for FFM and Fat Mass

Toth et al. (30) suggested that the ratio of FFM to fat mass was an important factor contributing to the age-associated decline in \( \dot{V}O_{2\text{max}} \). In this study we found that neither fat mass nor the ratio of FFM to fat mass contributed significantly to any of the models (P > 0.05) when FFM was already included.

Contribution of Loss of FFM to the Age-Associated Decline in \( \dot{V}O_{2\text{max}} \)

The OLS, WLS, and LL models suggested that ~35% of the age-associated decline in \( \dot{V}O_{2\text{max}} \) was due to a loss of skeletal muscle. Given that \( \dot{V}O_{2\text{max}} \) declines 0.24 l·min\(^{-1}\)·decade\(^{-1}\), the loss of skeletal muscle accounts for 0.08 l·min\(^{-1}\)·decade\(^{-1}\) of this quantity. Because FFM was not in the RS model as a predictor, the RS model cannot provide an estimate of the contribution of FFM to the age-associated decline in \( \dot{V}O_{2\text{max}} \).

DISCUSSION

The WLS regression incorporating age, FFM, and a dichotomous indicator of physical conditioning status yielded a model of \( \dot{V}O_{2\text{max}} \) that accounted for the largest proportion of variance and met all the important GLM assumptions. Absolute \( R^2 \) for the WLS model was ~6% higher than for the RS model, 3% higher than the LL model, and 2% higher than for the OLS model (Table 3). These results support the use of WLS models to examine the physiological factors underlying the age-associated decline in \( \dot{V}O_{2\text{max}} \).

Despite their failure to satisfy the underlying GLM assumptions, the RS and OLS models incorporating age, FFM, and ET provided estimates similar to the WLS model of the age-associated decline in active and sedentary men. The RS model incorporating age, FFM, and ET produced estimates that were ~10% lower than those produced by the OLS and WLS models (the LL model suggested an exponential decay in \( \dot{V}O_{2\text{max}} \)). The OLS estimate was nearly identical to the WLS estimate, despite the failure of the OLS model to satisfy the assumption of homoscedasticity. This estimate (0.24 l·min\(^{-1}\)·decade\(^{-1}\)) suggests a 9% decline in \( \dot{V}O_{2\text{max}} \) between 60 and 70 yr of age, which is consistent with other studies that indicate that the average healthy sedentary man >25 yr of age is expected to lose 9–11% of his \( \dot{V}O_{2\text{max}} \) per decade (10, 13, 30).

Because the WLS models satisfied all the important GLM assumptions, the estimates produced by the WLS analysis were BLUE, and the t-tests of the regression coefficients were correct. All the other methods failed to satisfy one or more of the assumptions.

Some investigators recommend verifying the assumption of homoscedasticity when scaling for differences in body habitus (20, 33). In this study the findings were generally robust to violation of this assumption. Multiplicative heteroscedasticity did not significantly affect the OLS standard errors, and the OLS model \( R^2 \) increased slightly compared with the (homoscedastic) RS model. We also found that the estimates were virtually unchanged over the range \( r = 0–2 \) (data not shown). This insensitivity of the WLS estimates may have been due to the fact that the correlation between the absolute residuals and FFM was only \( r = 0.18 \). It is possible that WLS may have a greater impact on the estimates and standard errors when the correlation is higher, e.g., \( r > 0.30 \). Higher correlations have been reported elsewhere (33).

In the log-transformed LL models the residuals displayed lack of normality and heteroscedasticity due to lack of fit. A post hoc analysis (data not shown) determined that both problems were due to the presence of an indicator variable in the analysis. When separate analyses were carried out within the athlete and sedentary groups, the residuals were normally distributed and homoscedastic. Heteroscedasticity due to lack of fit is diagnostic of model misspecification and suggests that the logarithmic transformation was not the appropriate metric when the dichotomous training variable was included in LL models.

The mechanisms underlying the age-associated change in \( \dot{V}O_{2\text{max}} \) in healthy men are multifactorial. Factors implicated in the age-associated decline in \( \dot{V}O_{2\text{max}} \) include decreases in maximum heart rate, stroke volume, arteriovenous \( O_2 \) difference, and skeletal muscle mass, an increase in adiposity, and a decline in daily, regular physical activity (3, 10, 12, 13, 17, 22, 27, 30). In the present study the models adjusted for FFM accounted for more variance than the unadjusted models (Table 3). The unadjusted models yielded larger estimates of the percent decline in \( \dot{V}O_{2\text{max}} \) in the athletes and sedentary men than did models that included FFM. This difference between unadjusted and adjusted models, which has been noted in RS models that do not adjust for muscle mass (8), suggests that ~35% of the decline in \( \dot{V}O_{2\text{max}} \) is due to the age-associated decrease in skeletal muscle mass (OLS, WLS, and LL estimate). This finding is consistent with that of Toth et al. (30), who estimated the contribution...
to be 33%. Recent findings suggest that the decrease in VO₂max that is associated with the loss of skeletal muscle may be due, at least in trained subjects, to reduced aerobic capacity per kilogram of active muscle (26). Reduced aerobic capacity would result from age-associated changes in maximal O₂ delivery and be independent of any actual loss of muscle fibers.

In the present study the OLS and WLS models indicated that the athletes and sedentary men decreased their VO₂max at the same absolute rate, ~0.24 l·min⁻¹·decade⁻¹. However, the VO₂max was 0.96 l/min higher in the athletes than in the sedentary men at all ages. Although some cross-sectional studies report similar absolute declines in VO₂max over time in athletes and in sedentary individuals (25), other longitudinal studies suggest that VO₂max declines at a slower rate in athletes than in sedentary men (27). Hagberg (10) estimated that the 5.5% decline in VO₂max per decade in master athletes is ~50% of the rate of decline in age-matched sedentary men. It is noteworthy that there is a correlation between the change in training period of time and also preserve their FFM. The athletes in the present study were heterogeneous with respect to their VO₂max per kilogram of FFM and the intensity and duration of their training. This heterogeneity may have had an impact on the age-associated decline in VO₂max.

A strength of this study is that the athletes and untrained men underwent a vigorous medical evaluation, and only those men with no evidence of cardiovascular or other disease were enrolled. Also, the athletes enrolled in this study were selected only if they were still competitive in their age class. This reduced the potentially confounding effects of disease on the age-associated declines in cardiovascular fitness. Second, individuals with a wide range of obesity and fitness levels were included in the study population. Nevertheless, this study has several limitations. First, the subjects were not randomly selected from the at-large older population, limiting the generalizability of the study findings. The fact that several other studies found similar rates of loss of fitness with age suggests that any bias introduced by our subject-selection process is probably small. Another limitation was the use of hydrodensitometry as the method of assessing FFM. Hydrodensitometry does not yield a direct measurement of skeletal muscle mass; muscle mass must be calculated from the observed density. This calculation depends on several assumptions. In an aging population, changes in bone density and residual lung volume may confound the hydrodensitometric estimate of FFM and, hence, the contribution of FFM and fat mass to the age-associated decline in VO₂max (18). More direct measures of skeletal muscle mass, such as that provided by magnetic resonance imaging or dual X-ray absorptiometry, may provide a more accurate quantification of muscle mass and prediction of the age-associated decline in VO₂max. Third, younger men were not included in this study, which has affected the estimates of the intercept. Finally, training intensity was treated as a dichotomous variable. This may not adequately account for the heterogeneity in effects of exercise training and leisure time activities in the sedentary and athletic populations. Toth et al. (30) concluded that controlling for leisure time activity reduced the degree of decline in VO₂max in sedentary males.

In this study the OLS and WLS models possessed certain advantages over the corresponding RS and LL models. First, OLS and WLS were able to provide estimates of the contribution of the loss of FFM to the age-associated decline in VO₂max, which the RS model, without an explicit FFM term, could not. Another advantage of OLS and WLS was their suitability for testing the hypothesis of parallel linear declines in VO₂max in athletic and sedentary individuals; the nonlinear LL model was not appropriate for addressing this question. OLS or WLS should prove useful in studies where these issues (or similar ones) comprise part of the investigation, with WLS providing a slightly more efficient analysis.

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REFERENCES

2170 STATISTICAL MODELS OF AGE-ASSOCIATED DECLINE IN $V_O^{2max}$