Gender differences in the decline in aerobic capacity and its physiological
determinants during the later decades of life

Edward P. Weiss,1 Robert J. Spina,1 John O. Holloszy,1 and Ali A. Ehsani1,2
1Section of Applied Physiology, Division of Geriatrics and Nutritional Sciences, and 2Cardiovascular Division,
Department of Internal Medicine, Washington University School of Medicine, St. Louis, Missouri

Submitted 4 November 2005; accepted in final form 15 February 2006

Weiss, Edward P., Robert J. Spina, John O. Holloszy, and Ali A. Ehsani. Gender differences in the decline in aerobic capacity and its physiological determinants during the later decades of life. J Appl Physiol 101: 938–944, 2006. First published February 23, 2006; doi:10.1152/japplphysiol.01398.2005.—We investigated the hemodynamic determinants of the age-associated decline in maximal oxygen uptake (V\textsuperscript{\textcircled{\text{O}2}}\text{max}) and the influence of gender on the decline in V\textsuperscript{\textcircled{\text{O}2}}\text{max} and its determinants in old and very old men and women. Sedentary, 60- to 75-yr-old women (n = 71) and men (n = 29), with no evidence of cardiovascular disease, underwent maximal treadmill exercise tests during which V\textsuperscript{\textcircled{\text{O}2}}\text{max} and maximal cardiac output (Q\textsuperscript{\text{max}}) were determined. V\textsuperscript{\textcircled{\text{O}2}}\text{max} and age were inversely related in both women (−23 ± 2 ml·min\textsuperscript{−1}·yr\textsuperscript{−1}; P < 0.0001) and men (−57 ± 5 ml·min\textsuperscript{−1}·yr\textsuperscript{−1}; P < 0.0001). The absolute slope of the Q\textsuperscript{\text{max}} vs. age relationship was twofold steeper in men than in women (P < 0.0001). Q\textsuperscript{\text{max}} was also inversely related to age in a gender-specific manner (women = −87 ± 25 ml·min\textsuperscript{−1}·yr\textsuperscript{−1}; P = 0.0009; men = −215 ± 50 ml·min\textsuperscript{−1}·yr\textsuperscript{−1}; P = 0.0002; P = 0.01 women vs. men). Age-related changes in maximal exercise arteriovenous oxygen content difference (a-vDO\textsubscript{2}) were marginally different (P = 0.08) between women (−0.12 ± 0.03 ml·dl\textsuperscript{−1}·yr\textsuperscript{−1}; P = 0.0003) and men (−0.22 ± 0.04 ml·dl\textsuperscript{−1}·yr\textsuperscript{−1}; P < 0.0001). Age-associated decreases in Q\textsuperscript{\text{max}} and a-vDO\textsubscript{2} contributed equally to the declines in V\textsuperscript{\textcircled{\text{O}2}}\text{max} in both men and women. In the later stages of life, V\textsuperscript{\textcircled{\text{O}2}}\text{max}, Q\textsuperscript{\text{max}}, and a-vDO\textsubscript{2} decrease with age more rapidly in older men than they do in older women. As a result, the gender differences dissipate in the later decades of life. Declines in Q\textsuperscript{\text{max}} and a-vDO\textsubscript{2} contribute equally to the age-related decrease in V\textsuperscript{\textcircled{\text{O}2}}\text{max} in men and women.

MAXIMAL AEROBIC CAPACITY (V\textsuperscript{\textcircled{\text{O}2}}\text{max}) decreases progressively with age (3), with men showing a greater decline than women (3, 7, 12, 13, 26, 29). V\textsuperscript{\textcircled{\text{O}2}}\text{max} is determined by the capacity of the cardiovascular system to provide oxygenated blood to the working muscles, as reflected in maximal cardiac output (Q\textsuperscript{\text{max}}), and the capacity of the working muscle to extract oxygen from the blood, as manifested by arteriovenous oxygen content difference (a-vDO\textsubscript{2}). Therefore, the age-related decline in V\textsuperscript{\textcircled{\text{O}2}}\text{max} can be a consequence of a reduction in Q\textsuperscript{\text{max}}, a-vDO\textsubscript{2}, or both. Several studies have suggested that age-related reduction in Q\textsuperscript{\text{max}} is at least partly responsible for the age-related decrease in V\textsuperscript{\textcircled{\text{O}2}}\text{max} (1, 10, 11, 14, 19). However, others challenged this notion and concluded that Q\textsuperscript{\text{max}} may not change with age (18, 20). Furthermore, it is unclear whether the mechanisms underlying diminished aerobic capacity in older individuals are affected by gender. Therefore, we sought to study these issues in a large cohort of sedentary, older men and women. In an earlier study (19), our laboratory found that both determinants of V\textsuperscript{\textcircled{\text{O}2}}\text{max} (i.e., Q\textsuperscript{\text{max}} and a-vDO\textsubscript{2}) were considerably lower in 60- to 70-yr-old men and women than in younger subjects. As an extension of these earlier findings, and because the number of people living to very old age is increasing rapidly, we focused on older, 60- to 92-yr-old men and women in the present study. We hypothesized that V\textsuperscript{\textcircled{\text{O}2}}\text{max} declines in older men and women as a result of age-related reductions in both Q\textsuperscript{\text{max}} and a-vDO\textsubscript{2}. Furthermore, because there is a paucity of data comparing age-associated changes in maximal exercise capacity and cardiovascular function during maximal aerobic exercise in older men and women, we hypothesized that the age-related decline in V\textsuperscript{\textcircled{\text{O}2}}\text{max} is greater in men than in women and that reductions in Q\textsuperscript{\text{max}} and a-vDO\textsubscript{2} contribute to these declines in both men and women.

METHODS

Subjects. Data for the present study were obtained from baseline tests performed on sedentary, nonsmoker subjects who were recruited for two exercise-training trials: one on 60- to 75-yr-old subjects (n = 56), and the other on 77- to 92-yr-old subjects (n = 44). For both studies, sedentary was defined as having not performed regular vigorous exercise of 20 min/day, 2 times/wk, over the 6 mo before screening. The physiological adaptations to training in both studies have been published (2, 4, 5, 15, 24). The Human Studies Committee at Washington University School of Medicine approved the studies, and subjects in both studies gave informed, written consent. None of the 60- to 75-yr-old participants had clinical evidence of heart disease, particularly coronary artery disease, as determined by clinical assessment and diagnostic exercise stress testing. Subjects were excluded if they had the following: 1) a history of coronary artery disease, 2) congestive heart failure, 3) aortic aneurysm, 4) insulin-dependent diabetes mellitus, 5) atrial fibrillation, 6) history of stroke, 7) self-reported history of hypertension, 8) if they were taking cardiac medications (i.e., beta-blockers, calcium channel blockers, angiotensin-converting enzyme inhibitors, and angiotensin II receptor blockers), or 9) if electrocardiographic evidence of myocardial ischemia (defined as >0.1 mV ST segment depression that is either horizontal or downsloping) occurred during the stress test. The second group, i.e., 77- to 92-yr-old subjects, consisted of subjects who had mild or moderate frailty (2, 4), as well as those who were not frail (5). All of the subjects had to be independent living and community dwelling, and the mildly to moderately frail participants all had some degree of difficulty performing activities of daily living, as has been described in detail previously (2). The rationale for including frail subjects is that frailty is an inherent characteristic of old age. The original enrollment criteria for the second group were different from those for the 60- to 75-yr-old subjects in that the presence of clinical evidence...
of cardiovascular disease and the use of cardiac medications were not exclusion criteria for the very old subjects. Therefore, to minimize the possibility of these confounding limitations for the present study, we applied the more rigorous exclusion criteria used previously for the 60- to 75-yr-old subjects and excluded the 77- to 92-yr-old subjects with clinical coronary artery disease and those who were taking cardiac medications. Because a higher proportion of the mild and moderately frail than the nonfrail subjects did not meet these criteria, and because severely frail individuals were screened out, the proportion of frail subjects in the 77- to 92-yr age range in this study may be lower than that in the general population. Among the 77- to 92-yr-old subjects, only 44 (32%) met the rigorous criteria listed above and were included in the present study. Therefore, data presented in this report are from 100 sedentary, asymptomatic, nonsmoker subjects.

Graded exercise test and \( \dot{V}O_2 \text{max} \). \( \dot{V}O_2 \text{max} \) was determined by indirect calorimetry during a graded treadmill exercise test and as described previously (4, 15). Metabolic data were measured with a computer-interfaced system, including a dry gas meter (CD-4, Parkinson-Cowan), oxygen analyzer (S3-A, Applied Electrochemistry), \( CO_2 \) analyzer (LB-2, Beckman), and 5-liter mixing chamber. Oxygen uptake (\( \dot{V}O_2 \)) data were generated by the computer every 30 s. The highest average for two consecutive 30-s data points was considered \( \dot{V}O_2 \text{max} \). Blood pressure, measured via auscultation, and the subject was switched from the open-circuit \( \dot{V}O_2 \) measurement system to a closed-circuit system. Oxygen uptake was monitored continuously (as described above), and, when the \( \dot{V}O_2 \) was at or near the previously measured \( \dot{V}O_2 \text{max} \) value, the treadmill speed and grade were progressively increased to the expected, men were heavier, taller, and had a greater average \( \dot{V}O_2 \text{max} \) than women.

Age-associated decline in cardiovascular capacity: effects of gender. Inverse relationships between age and \( \dot{V}O_2 \text{max} \) were evident in both men (\( -57 \pm 5 \text{ ml min}^{-1} \text{ yr}^{-1}; P < 0.0001 \)) and women (\( -23 \pm 2 \text{ ml min}^{-1} \text{ yr}^{-1}; P < 0.0001 \)), but the slope of this relationship was twofold steeper (\( P < 0.0001 \)) in men than in women (Fig. 1). The gender difference in the relationship between age and aerobic capacity was also evident when \( \dot{V}O_2 \text{max} \) was expressed relative to body weight (men: \( -0.51 \pm 0.08 \text{ ml kg}^{-1} \text{ min}^{-1} \text{ yr}^{-1}; P < 0.0001 \); women: \( -0.22 \pm 0.04 \text{ ml kg}^{-1} \text{ min}^{-1} \text{ yr}^{-1}; P < 0.0001 \)). We also analyzed \( \dot{V}O_2 \text{max} \) data as percentages of the estimated values for 60-yr-old men and women (where the estimated values for 60-yr-old men were calculated from the regression equations depicted in Fig. 1A). Despite this adjustment to account for the higher starting values seen in men, the results were similar in that the slope of

### Table 1. Subject characteristics

<table>
<thead>
<tr>
<th>n</th>
<th>Women</th>
<th>Men</th>
<th>All Subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yr</td>
<td>83</td>
<td>33</td>
<td>116</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>65.3 ± 11.9</td>
<td>76 ± 9*</td>
<td>73 ± 9</td>
</tr>
<tr>
<td>Height, cm</td>
<td>160.6 ± 5.9</td>
<td>174.4 ± 5.3</td>
<td>164.6 ± 5</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>25.2 ± 4.5</td>
<td>27.2 ± 3.7</td>
<td>25.8 ± 4.3</td>
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<tr>
<td>Resting HR, beats/min</td>
<td>74 ± 10</td>
<td>73 ± 11</td>
<td>74 ± 10</td>
</tr>
<tr>
<td>Resting BP, mmHg</td>
<td>130 ± 21</td>
<td>134 ± 17</td>
<td>131 ± 20</td>
</tr>
<tr>
<td>Resting DBP, mmHg</td>
<td>78 ± 10</td>
<td>79 ± 11</td>
<td>78 ± 10</td>
</tr>
<tr>
<td>Cholesterol, mg/dl</td>
<td>207 ± 47</td>
<td>225 ± 106</td>
<td>212 ± 68</td>
</tr>
<tr>
<td>LDL-C, mg/dl</td>
<td>122 ± 28</td>
<td>113 ± 27</td>
<td>121 ± 28</td>
</tr>
<tr>
<td>HDL-C, mg/dl</td>
<td>57 ± 13</td>
<td>45 ± 9*</td>
<td>53 ± 13</td>
</tr>
<tr>
<td>Triglycerides, mg/dl</td>
<td>143 ± 82</td>
<td>152 ± 80</td>
<td>146 ± 82</td>
</tr>
<tr>
<td>( \dot{V}O_2 \text{max}, \text{ ml/min} )</td>
<td>1,232 ± 259</td>
<td>1,758 ± 542*</td>
<td>1,385 ± 433</td>
</tr>
<tr>
<td>( \dot{V}O_2 \text{max}, \text{ ml kg}^{-1} \text{ min}^{-1} )</td>
<td>19.1 ± 3.6</td>
<td>21.4 ± 6.3</td>
<td>19.7 ± 4.6</td>
</tr>
</tbody>
</table>

Values are means ± SD; n, no. of subjects. Lipid data are missing on 3 men and 4 women. BMI, body mass index; HR, heart rate; SBP, systolic blood pressure; DBP, diastolic blood pressure; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; \( \dot{V}O_2 \text{max} \), maximal oxygen uptake. *P ≤ 0.05 vs. women.
AERobic capacity and its determinants in aging.

The independent contribution of each hemodynamic determinant of the age-associated decline in VO₂ max was quantified by calculating VO₂ max values that should Have resulted from differences in one hemodynamic factor while holding the value(s) for the other factor(s) constant (VO₂ max = Q max × a-vDO₂). For example, to determine how much of the observed -57 ml·min⁻¹·yr⁻¹ slope in VO₂ max in the men was due to

the relationship between age and VO₂ max was still steeper (P = 0.03) in men (-2.1 ± 0.2%/yr; P < 0.0001) than in women (-1.5 ± 0.2%/yr; P < 0.0001) (Fig. 1).

There was a gender-specific, inverse relationship between age and Q max in these older subjects, with men showing a steeper (P = 0.01) slope than women (men: -215 ± 50 ml·min⁻¹·yr⁻¹, P = 0.0002; women: -87 ± 25 ml·min⁻¹·yr⁻¹, P = 0.0009) (Fig. 2). The gender differences in the age vs. Q max slopes was still evident (P = 0.03) after normalizing Q max for body surface area (men: -95 ± 26 ml·min⁻¹·m⁻²·yr⁻¹, P = 0.001; women: -35 ± 14 ml·min⁻¹·m⁻²·yr⁻¹, P = 0.02). When Q max was expressed in relative terms as a percentage of the estimated Q max for 60 yr olds (using the same approach as described above for VO₂ max), men: -1.25 ± 0.29%/yr, P = 0.0002; women: -0.77 ± 0.22%/yr, P = 0.0009), the gender difference in the slopes for the relationships between age and Q max was no longer significant (P = 0.23, Fig. 2).

a-vDO₂ and age were inversely related (men: -0.22 ± 0.04 ml·dl⁻¹·yr⁻¹, P < 0.0001; women: -0.12 ± 0.03 ml·dl⁻¹·yr⁻¹, P = 0.0003). The aging effect in men tended to be greater than that in women (P = 0.08; Fig. 3). When a-vDO₂ was reported in relative terms as a percentage of the estimated a-vDO₂ for 60 yr olds, the slopes of the age vs. a-vDO₂ relationships were not statistically different between men and women (men: -1.32 ± 0.23%/yr, P < 0.0001; women -0.87 ± 0.23%/yr, P = 0.0003; P = 0.24 for comparison between men and women). Although SV during maximal exercise was greater in men than in women (94.0 ± 2.9 vs. 66.7 ± 1.8 ml, respectively; P < 0.0001), it was not related to age in men, men, or in the combined group (all P values ≥ 0.33) (Fig. 3). Normalization of SV max for differences in body surface area decreased the magnitude of difference between men and women. However, the difference was still significant (47.3 ± 1.6 vs. 39.9 ± 0.9 ml/m² in men and women, respectively; P < 0.0001). An inverse relationship between age and HR max was present for the group as a whole (-1.3 ± 0.2 beats·min⁻¹·yr⁻¹); however, this relationship was not significantly influenced by gender (P = 0.40) (Fig. 3).

Hemodynamic determinants of the decline in aerobic capacity. The independent contribution of each hemodynamic determinant of the age-associated decline in VO₂ max was quantified by calculating VO₂ max values that should have resulted from differences in one hemodynamic factor while holding the value(s) for the other factor(s) constant (VO₂ max = Q max × a-vDO₂). For example, to determine how much of the observed -57 ml·min⁻¹·yr⁻¹ slope in VO₂ max in the men was due to

Fig. 1. Associations between age and absolute maximal oxygen uptake (VO₂ max, A) and VO₂ max as a percentage of the regression-predicted VO₂ max for men and women at age 60 yr (B). The regression-based estimates for VO₂ max for men and women at age 60 yr were 2.695 and 1.503 ml/min, respectively. Solid circles and solid lines = men; open circles and dashed lines = women. *P ≤ 0.05 vs. zero for slope. †P ≤ 0.05 for slope in men vs. slope in women.

Fig. 2. Associations between age and maximal cardiac output (Q max, A), and Q max as a percentage of the regression-based estimates for Q max for men and women at age 60 yr (B). The regression-based estimates for Q max for men and women at age 60 yr were 17,284 and 11,164 ml/min, respectively. Solid circles and solid lines = men; open circles and dashed lines = women. *P ≤ 0.05 vs. zero for slope. †P ≤ 0.05 for slope in men vs. slope in women.
AEROCIC CAPACITY AND ITS DETERMINANTS IN AGING

941

Fig. 3. Associations between age and arteriovenous oxygen content difference (a-vDO2; A), maximum heart rate (HRmax; B), and maximum stroke volume (SVmax; C). Solid circles and solid lines = men; open circles and dashed lines = women. *P ≤ 0.05 for slope vs. zero. †P ≤ 0.05 for slope in men vs. slope in women.

age-related differences in Qmax, the relationship between age, and the product of the observed Qmax values and a fixed value for a-vDO2, was assessed (where the fixed value for a-vDO2 was the estimated value for subjects in the midpoint of the age range, i.e., 76 yr). In men, the portion of the age vs. VO2max slope that was estimated to be exclusively due to reductions in Qmax was \(-28 ± 7\ \text{ml} \cdot \text{min}^{-1} \cdot \text{yr}^{-1} (P = 0.0002)\), and the portion that was estimated to be due to reductions in a-vDO2 was \(-30 ± 5\ \text{ml} \cdot \text{min}^{-1} \cdot \text{yr}^{-1} (P < 0.0001)\). This suggests that decreases in Qmax and a-vDO2 contribute equally to the age-related decline in VO2max. Likewise, in women, the portions of the slope for the age vs. VO2max relationship that were estimated to be exclusively due to Qmax (\(-10 ± 3\ \text{ml} \cdot \text{min}^{-1} \cdot \text{yr}^{-1}, P = 0.0009\)) and to a-vDO2 (\(-12 ± 3\ \text{ml} \cdot \text{min}^{-1} \cdot \text{yr}^{-1}, P = 0.0003\)) were similar. None of the age vs. VO2max relationships was attributable to age-related variation in SVmax in either men (P = 0.33) or women (P = 0.93). Therefore, the portions of the slopes in the age vs. VO2max relationships for men and women that were due to decreases in Qmax were entirely due to age-associated decrements in HRmax (men: \(-19 ± 4\ \text{ml} \cdot \text{min}^{-1} \cdot \text{yr}^{-1}, P < 0.0001);\) women: \(-10 ± 1\ \text{ml} \cdot \text{min}^{-1} \cdot \text{yr}^{-1}, P < 0.0001)\).

TPRmax was related to age in both men (8.4 ± 3.0 dyn·s⁻¹·cm⁻²·yr⁻¹, P = 0.01) and women (16.5 ± 3.1 dyn·s⁻¹·cm⁻²·yr⁻¹, P < 0.0001), and the slopes for the relationships in men and women were not statistically different (P = 0.12). In contrast, men and women were different (P = 0.003) with respect to the relationship between age and MBPmax. In women, we found a positive relationship between age and MBPmax (0.6 ± 0.2 mmHg/yr, P = 0.0006), while in men, MBPmax was not associated with age (P = 0.18).

DISCUSSION

The purpose of the present study was, first, to obtain information regarding the physiological basis for the reduction in VO2max after the age of 60 yr in sedentary men and women, and to assess the relative contribution of cardiac output and a-vDO2 to the deterioration of VO2max in advancing age. Second, we sought to determine whether gender influences the age-associated decline in VO2max after the age of 60 yr and to explore the physiological basis for gender-related differences. Results from the present study provide evidence that, in 60- to 92-yr-old subjects, the age-related decrease in VO2max is attributable to decrements in both Qmax and a-vDO2 and that HRmax is solely responsible for the decline in Qmax. Since the age-associated decline in Qmax was accompanied by an age-related increase in TPRmax in both men and women, MBPmax did not decline with age, and even increased with age in women. Another important finding of the present study is that, although the rate of age-associated decline in VO2max, Qmax, and maximal a-vDO2 is greater in men than in women, the relative contribution of Qmax and a-vDO2 to the decline in aerobic power appears to be similar for men and women.

Most previous studies have reported that the age-related decline in VO2max is attributable to reductions in both a-vDO2 and Qmax. a-vDO2 has been shown, unequivocally, to decrease with advancing age in 18- to 75-yr-old subjects (1, 14, 18, 19), and our findings in subjects as old as 92 yr are consistent with these observations. A number of studies have also shown that Qmax declines with age (1, 11, 13, 14, 19) and that the relative contribution of Qmax and a-vDO2 to the age-related decline in aerobic power appears to be similar for men and women.
to compensate for the decrease in \(HR_{\text{max}}\) and prevent a decrease in \(Q_{\text{max}}\).

The lack of an age-associated change in \(SV_{\text{max}}\) reported in the present study may appear contradictory to a previous report from our laboratory (19) in which we found that 60- to 72-yr-old sedentary men and women had a lower \(SV_{\text{max}}\) than 20 to 31 yr olds. One explanation is that the data from the earlier report reflect the changes in \(SV_{\text{max}}\) that occur during the early and middle decades of adulthood, while data from the present study reflect changes that occur in the later decades of life. It is plausible, therefore, that \(SV_{\text{max}}\) decreases with age until late adulthood, after which the decline in \(SV_{\text{max}}\) ceases.

A greater age-associated decline in \(V_{\text{O}_2}\text{max}\) in men, compared with women, has been reported by others (3, 7, 12, 13, 26, 29), and our findings confirm these previous reports. Furthermore, our data suggest that the decrease in \(V_{\text{O}_2}\text{max}\) is likely to be accelerated after the age of 60 yr. Although men have higher \(V_{\text{O}_2}\text{max}\) values than women through most of the adult lifespan, the greater age-associated decrements in \(V_{\text{O}_2}\text{max}\) in men should eventually result in the elimination of this gender-specific difference in advanced age. In fact, based on our data, the regression lines for men and women intersect at age 94 yr, only slightly beyond the age of the oldest individuals in the present study. Our data show that both the greater decline in \(Q_{\text{max}}\) and the greater decline in \(\text{a-vDO}_2\) in men than in women account for the gender-specific difference in the rate at which \(V_{\text{O}_2}\text{max}\) declines with advancing age. Most previous studies have reported the annual age-associated decline in \(V_{\text{O}_2}\text{max}\) to be 24 to 35 ml·min\(^{-1}\)·yr\(^{-1}\) in sedentary men (12, 21, 22) and 13 to 16 ml·min\(^{-1}\)·yr\(^{-1}\) in sedentary women (12, 23, 28). These age-related declines are much slower than the respective \(-57 \pm 5\) and \(-23 \pm 2\) ml·min\(^{-1}\)·yr\(^{-1}\) decrements seen in the present study. One explanation for this apparent discrepancy is that we did not study young individuals, and many of the subjects in our study were older than those in the previous studies. The upper age range for the previous studies was 75–84 yr, and, furthermore, there were only a few subjects in the upper end of the age spectrum (12, 21–23, 28). In contrast, 31 of our 100 subjects were 80–92 yr of age. It is plausible, therefore, that the greater decline in aerobic capacity may reflect a greater proportion of very old subjects who, by virtue of their old age, had mild frailty and physical inactivity. Thus very old men and women may exhibit more rapid deterioration in physiological function than their younger counterparts. The age-associated decline in \(V_{\text{O}_2}\text{max}\) is commonly described as a fixed percent per decade (11, 19, 22, 23, 28, 29). Mathematically, this suggests that the absolute reduction in \(V_{\text{O}_2}\text{max}\) per decade should progressively decrease as people age. Despite this premise that the absolute decline in \(V_{\text{O}_2}\text{max}\) should decrease with increasing age, the comparison of our data on very old subjects with that reported in the literature for 20- to 84-yr-old subjects (12, 21–23, 28) suggests otherwise, i.e., the rate of age-associated decline in \(V_{\text{O}_2}\text{max}\) increases with age rather than decreases. In support of this notion, a recent comparison of longitudinal changes in \(V_{\text{O}_2}\text{max}\) among subjects from a wide age range (8) indicated that the 8-yr decline in \(V_{\text{O}_2}\text{max}\) is much greater in men and women over 60 yr old (\(-50\) and \(24\) ml·min\(^{-1}\)·yr\(^{-1}\), respectively) than it is in 30–39 yr olds (\(-17\) and \(13\) ml·min\(^{-1}\)·yr\(^{-1}\), respectively).

The reason for the more rapid decline in \(V_{\text{O}_2}\text{max}\), \(Q_{\text{max}}\), and \(\text{a-vDO}_2\) among men compared with women is not clear. One possibility is that the men decline at a greater rate, simply because they have greater absolute cardiovascular functional capacity to begin with. To address this possibility, we calculated \(V_{\text{O}_2}\text{max}\), \(Q_{\text{max}}\), and \(\text{a-vDO}_2\) as percentages of the values that would be expected for the average 60-yr-old man and woman. Despite this normalization of men and women to a uniform starting value, the men still demonstrated a more rapid age-associated deterioration in \(V_{\text{O}_2}\text{max}\) than women. In contrast, the declines in \(Q_{\text{max}}\) and \(\text{a-vDO}_2\) when expressed relative to age 60-yr values, were no longer significantly different between men and women. Although the relative declines in \(Q_{\text{max}}\) and \(\text{a-vDO}_2\) are not statistically significantly different between men and women (\(P = 0.23\) and \(P = 0.24\), respectively), we may have lacked the statistical power to detect significance for these outcomes, since they are responsible for the age-related decline in \(V_{\text{O}_2}\text{max}\). It seems that at least some of the more rapid decline in maximal cardiovascular function in men is due to initially greater function, and some is due to other factors. One factor could be a greater age-associated decline in inotropic sensitivity to \(\beta\)-adrenergic agonist in men than in women, which is partly due to a greater \(\beta\)-adrenergic-stimulated increase in left ventricular systolic function in younger men than in younger women (31).

Another potential explanation for gender differences in the decline in cardiovascular function is that older men decrease their physical activity levels more than women as they age. Although we do not have leisure time physical activity data to assess this possibility in the present study, this explanation seems unlikely, since population-based data from the Minnesota Heart Survey suggest that women decrease their leisure time physical activity levels more than men (9). It is also important to recognize that the main type of physical activity that has a tangible effect on \(V_{\text{O}_2}\text{max}\) is structured vigorous endurance exercise. Because the men and women in the present study were specifically selected as individuals who did not participate in endurance training, it is unlikely that differential changes in other, nonendurance-training activities between men and women could explain the gender differences in the rate of \(V_{\text{O}_2}\text{max}\) decline. It has been reported that variations in habitual physical activity only account for \(\leq 5\%\) of the variation in \(V_{\text{O}_2}\text{max}\) among elderly men and women (27).

Although the absolute age-related declines in \(V_{\text{O}_2}\text{max}\), \(\text{a-vDO}_2\), \(Q_{\text{max}}\), and \(HR_{\text{max}}\) were greater in men than in women, we found that the age-associated reductions in \(Q_{\text{max}}\) and \(\text{a-vDO}_2\) contributed equally to the age-associated declines in \(V_{\text{O}_2}\text{max}\) for men and women. Furthermore, the entire age-associated decline in \(Q_{\text{max}}\) was attributable to decreases in \(HR_{\text{max}}\) for both men and women. These data suggest that aging of the skeletal muscle and of the central cardiovascular system contribute equally to the decline in aerobic capacity with advancing age during the later stages of life and that this is true for both men and women.

The \(V_{\text{O}_2}\text{max}\) values of individuals in the upper end of the age range studied were extremely low. In fact, the average \(V_{\text{O}_2}\text{max}\) for the oldest two men and the oldest two women was only 971 and 820 ml·min\(^{-1}\) (13.0 and 13.6 ml·kg\(^{-1}\)·min\(^{-1}\)), respectively. To put this into perspective, the energy expenditure required for these elderly subjects to stand statically (16) would require \(-50\%\) of \(V_{\text{O}_2}\text{max}\). This serious deficiency in cardiovascular function in very old men and women illustrates the importance of interventions known to increase \(V_{\text{O}_2}\text{max}\), such as exercise.
training, to delay the age at which cardiorespiratory fitness becomes so limiting that an individual can no longer function independently in activities of daily living.

Several limitations should be considered when interpreting the results of the present study. First, young subjects and those with clinical evidence of heart disease were not included in our study. The findings, therefore, are only applicable to individuals in the later decades of life who are free from clinical heart disease. Second, some of the older men and women had mild to moderate frailty, which may have affected the results. However, because the prevalence of physical frailty increases with age, the data on our oldest subjects more closely represent the elderly population than it would have if we had excluded all frail subjects. Third, although we specifically recruited individuals who did not perform habitual structured exercise, it is quite conceivable that the older subjects were less active in their daily living than the younger subjects, and this could have contributed to the decline in aerobic capacity, independent of the effects of aging per se. Another limitation is that undetected coronary disease may have been present in some participants, despite the relatively thorough screening process used in the present study. Because the frequency of occult heart disease increases with age and is more common in older men than in older women, coronary disease might have been partly responsible for the more rapid decline in VO2 max seen in our older subjects, compared with younger subjects, and it might have also been partly responsible for the greater rate of decline seen in men than in women. Lastly, we used a cross-sectional design, which has inherent limitations related to the inability to draw all of the subjects from the same population. While it cannot be known if this limitation affected our results, it is noteworthy that our cross-sectional estimates of the rate of decline in the present study are similar to those recently reported from a longitudinal study (8).

In summary, findings from the present study suggest that, after the age of 60 yr, VO2 max decreases with age due to reductions in both Q max and a-vDO2 and that these reductions occur more rapidly in men than in women. Furthermore, the age-associated declines in Q max and a-vDO2 contribute equally to the age-associated reductions in VO2 max in men and women. The age-associated decline in Q max is due to decreases in HR max with no significant effect of age on maximal exercise stroke volume. Because the rates of decline in VO2 max and its physiological determinants are considerably greater in older men than in older women, the gender-associated differences tend to dissipate in the later decades of life.

ACKNOWLEDGMENTS

Current affiliation for R. J. Spina: Department of Kinesiology, San Francisco State University, San Francisco, CA 94132.

GRANTS

This work was supported by National Institute on Aging (NIA) Grants AG-13629 and AG-05562, and General Clinical Research Center Grant RR-00036. E. P. Weiss was supported by NIA Grant AG-00078.

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