Cardiovascular hemodynamics with increasing exercise intensities in postmenopausal women

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McCole, Steve D., Michael D. Brown, Geoffrey E. Moore, Joseph M. Zmuda, Jeffrey D. Cwynar, and James M. Hagberg. Cardiovascular hemodynamics with increasing exercise intensities in postmenopausal women. J. Appl. Physiol. 87(6): 2334–2340, 1999.—We sought to determine the cardiovascular responses to increasing exercise intensities in postmenopausal women with different physical activity levels and hormone replacement therapy (HRT) status. Forty-four women (11 sedentary, 19 physically active, 14 master athletes; 24 not on HRT, 20 on HRT) completed treadmill exercise at 40, 60, 80, and 100% of maximal oxygen consumption. Oxygen consumption, heart rate, blood pressure, and cardiac output, determined via acetylene rebreathing, were measured at each exercise intensity. HRT did not affect cardiovascular hemodynamics. Stroke volume (SV) decreased significantly between 40 and 100% of maximal oxygen consumption in all groups, and the decrease did not differ among groups. The greater oxygen consumption of the athletes at each intensity was due to their significantly greater cardiac output, which was the result of a significantly greater SV, compared with both of the less active groups. The athletes had significantly lower total peripheral resistance at each exercise intensity than did the two less active groups. There were no consistent significant hemodynamic differences between the physically active and sedentary women. These results indicate that SV decreases in postmenopausal women as exercise intensity increases to maximum, regardless of their habitual physical activity levels or HRT status.

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Methods

Subjects

Forty-four healthy postmenopausal women were recruited on the basis of their habitual level of physical activity (sedentary, physically active, or competitive master athletes) and hormone replacement status (on HRT or not on HRT). Postmenopausal status was determined by self-reported lack of menses for >2 yr and elevated levels of follicle-stimulating hormone and luteinizing hormone. Sedentary women had not participated in regular aerobic exercise for >2 yr. Women who participated in aerobic exercise for >90 min/wk, >3 days/wk, but who were not training for endurance-based competitive events were classified as physically active (20). The female athletes were competitive distance runners who were training vigorously and regularly placed in regional, national, and international competitions. The HRT group consisted of a majority of women on oral combined estrogen and progestin (16 of the 20 women on HRT); 10 of these women were taking progestin continuously, while the remaining 6 were on a cyclic regimen (Table 1). The ranges of estrogen and progestin dosages were similar in all groups. The physical activity level

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Table 1. Hormone replacement therapy regimens

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>Regimen Summary</th>
<th>Dose Range, mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sedentary women</td>
<td>3</td>
<td>100% on combined estrogen/progestin</td>
<td>0.625</td>
</tr>
<tr>
<td></td>
<td></td>
<td>67% daily progestin</td>
<td>2.5-10</td>
</tr>
<tr>
<td></td>
<td></td>
<td>33% cyclic progestin</td>
<td></td>
</tr>
<tr>
<td>Physically active</td>
<td>9</td>
<td>67% on combined estrogen/progestin</td>
<td>0.625-1.0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>45% on daily progestin</td>
<td>2.5-10</td>
</tr>
<tr>
<td></td>
<td></td>
<td>22% on cyclic progestin</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>33% on estrogen only</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>87% on estrogen/progestin</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>50% daily progestin</td>
<td>0.3-1.0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>37% cyclic progestin</td>
<td>2.5-10</td>
</tr>
<tr>
<td></td>
<td></td>
<td>13% on estrogen only</td>
<td></td>
</tr>
<tr>
<td>Athletic women</td>
<td>8</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

and HRT status of all subjects had been constant for at least the 2 yr before the study. Whereas the sedentary and physically active women were recruited from the Pittsburgh metropolitan area, it was necessary to recruit the female athletes from across the United States to achieve sufficient numbers for study. All subjects were free of known heart disease and were not taking medications that could affect their response to exercise. The Institutional Review Board of the University of Pittsburgh approved this study, and all subjects provided their informed voluntary consent before testing.

To ensure that they were free of CV disease, sedentary and physically active subjects underwent a screening graded maximal exercise test according to a modified Naughton protocol (6). V\(_{O_2}\)max was measured in a subsequent exercise test in those women completing the screening test without evidence of CV disease. The female athletes completed a single maximal treadmill exercise test for both screening and to measure V\(_{O_2}\)max. Blood pressure (via auscultation of the brachial artery), heart rate (HR), and electrocardiogram (ECG) were monitored before, during, and after and oxygen consumption (V\(_{O_2}\)) was measured during all exercise tests. Exercise continued until the subject reached exhaustion or signs or symptoms of CV decompensation occurred (1). Body composition was determined with dual-energy X-ray absorptiometry (DPX-L, Lunar, Madison, WI).

Cardiac output was measured at 40, 60, 80, and 100% of V\(_{O_2}\)max during treadmill exercise by using an acetylene rebreathing technique on the basis of the procedures of Triebwasser et al. (33). During submaximal exercise, cardiac output was measured after ~6 min at the desired V\(_{O_2}\). During maximal exercise the cardiac output determination began when the subject's V\(_{O_2}\) was within 5% of her V\(_{O_2}\)max or she indicated that she was unable to complete another 60 s of exercise. V\(_{O_2}\) and ECG were monitored throughout exercise, and blood pressure was measured immediately preceding each cardiac output determination. SV, total peripheral resistance (TPR), and arteriovenous O\(_2\) difference were calculated by using standard equations.

**Statistics**

All data are reported as means ± SD. Differences among groups at each intensity were determined by ANOVA with Bonferroni adjustments made on all significant F-values. To evaluate differences in the response to increases in exercise intensity among the different groups, a two-factor ANOVA with repeated measures on one factor (exercise intensity) was performed. Contrast statements were used to determine differences in the response to exercise between exercise intensities. P < 0.05 was considered statistically significant.

**RESULTS**

**Subject Characteristics (Table 2)**

The 44 women in the study averaged 63 ± 5 yr of age (range 53–75 yr). There were no significant differences among groups in the length of time the women had been postmenopausal or their duration of HRT. The physically active and athlete groups exercised for a similar number of hours per week and had been exercising for a similar number of years. The athletes averaged 29.0 ± 9.6 miles/wk of running at the time of the study.

There were no differences in age, height, or weight among any of the different physical activity or HRT groups (Table 2). The female athletes had significantly lower body fat and fat mass than did the other two groups of women and significantly greater lean mass than did the sedentary, but not the physically active, women. There were no significant body composition differences between the physically active and sedentary women.

The athletic women had a significantly greater V\(_{O_2}\)max than did the less active groups. The V\(_{O_2}\)max of the physically active women was greater than that of the sedentary group, but the difference was only significant when V\(_{O_2}\)max was expressed in liters per minute (Fig. 1).

Table 2. Subject characteristics of the three subject groups

<table>
<thead>
<tr>
<th></th>
<th>Sedentary Women (n = 11)</th>
<th>Physically Active Women (n = 19)</th>
<th>Athletic Women (n = 14)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yr</td>
<td>63 ± 5</td>
<td>63 ± 6</td>
<td>65 ± 4</td>
</tr>
<tr>
<td>Ht, cm</td>
<td>157 ± 6</td>
<td>159 ± 6</td>
<td>161 ± 7</td>
</tr>
<tr>
<td>Wt, kg</td>
<td>58.6 ± 5.5</td>
<td>64.4 ± 9.1</td>
<td>58.5 ± 7.9</td>
</tr>
<tr>
<td>%Fat</td>
<td>36.5 ± 4.3</td>
<td>37.3 ± 4.5</td>
<td>26.2 ± 6.5†</td>
</tr>
<tr>
<td>Fat mass, kg</td>
<td>21.5 ± 4.0</td>
<td>24.2 ± 5.9</td>
<td>15.4 ± 5.3†‡</td>
</tr>
<tr>
<td>Lean mass, kg</td>
<td>37.1 ± 2.7</td>
<td>40.1 ± 4.1</td>
<td>43.1 ± 6.3†</td>
</tr>
<tr>
<td>Length of time PM, yr</td>
<td>13 ± 8</td>
<td>13 ± 8</td>
<td>19 ± 11</td>
</tr>
<tr>
<td>Duration of HRT, yr</td>
<td>5.0 ± 4.4</td>
<td>10.3 ± 6.8</td>
<td>12.9 ± 12.3</td>
</tr>
<tr>
<td>Physical activity, h/wk</td>
<td>5.3 ± 2.5</td>
<td>5.2 ± 1.5</td>
<td></td>
</tr>
<tr>
<td>Length of time training, yr</td>
<td>12 ± 7</td>
<td>15 ± 5</td>
<td></td>
</tr>
</tbody>
</table>

Values are means ± SD; n, no. of women. PM, postmenopausal; HRT, hormone replacement therapy. § Data include only those women undergoing HRT. †Significantly different from sedentary, P < 0.05. ‡Significantly different from physically active, P < 0.05.
There were no differences in maximal HR among the different habitual physical activity groups.

CV Hemodynamics

Effects of HRT. HRT status was not associated with any differences in Vo2, cardiac output, HR, SV, arteriovenous O2 difference, blood pressure, or TPR across the 40–100% of Vo2max range of exercise intensities. HRT status also did not affect the change in these variables as exercise intensity increased. Figure 2 demonstrates the similarity of the SV response in the women on and not on HRT. Furthermore, subgroup analyses indicated that there were no significant differences between those women on and not on HRT within any physical activity group. Therefore, women on and not on HRT were combined for the remainder of the analyses.

Fig. 1. Oxygen consumption (Vo2), cardiac output, arteriovenous (a-v) O2 difference, heart rate, and stroke volume at exercise intensities of 40–100% of maximal Vo2 (Vo2max) in sedentary (○), physically active (●), and master athlete (▼) postmenopausal women. bpm, Beats/min. For an explanation of the significant changes as exercise intensity increased, see text. *Significantly different from sedentary group at same exercise intensity, P < 0.05. #Significantly different from physically active group at same exercise intensity, P < 0.05.
Effects of habitual physical activity levels. As a result of their higher \( V_{O2\max} \), the female athletes had a greater \( V_O2 \) than did either of the less active groups at each of the four exercise intensities (40, 60, 80, and 100% of \( V_{O2\max} \); Fig. 1). The physically active women had a greater \( V_O2 \) than did the sedentary women only at 80 and 100% of \( V_{O2\max} \) and only when expressed as liters per minute.

In each habitual physical activity group, cardiac output increased significantly as exercise intensity increased from 40 to 60 to 80% of \( V_{O2\max} \). The increase in cardiac output from 80 to 100% of \( V_{O2\max} \) was significant in the sedentary and physically active groups but not in the athletes. The athletes had a significantly greater cardiac output than did the two less active groups of women at each exercise intensity. There were no differences in cardiac output between the physically active and sedentary women at any exercise intensity. Arteriovenous oxygen difference increased significantly for each group over the range of exercise intensities, but there were no significant differences between groups at any of the exercise intensities. Thus, at each intensity, the greater \( V_O2 \) of the athletes was due solely to their significantly larger cardiac output.

The greater exercise cardiac output in the athletes was due to their significantly larger SV at each intensity because there was no differences in HR among any of the groups at any of the four exercise intensities (Fig. 1). Although there were no differences in HR among the groups, HR increased significantly in all groups with each increase in intensity. \( SV \) was not significantly different between the physically active and sedentary women at any exercise intensity. There were no significant differences between \( SV \) at 40 and 60% of \( V_{O2\max} \) in any of the physical activity groups. However, \( SV \) decreased significantly in each group of women as exercise intensity increased from 60 to 100% of \( V_{O2\max} \). This decrease in \( SV \) was similar in all three physical activity groups. Cardiac output was increased, or at least maintained, because the increase in HR compensated for the reduction in \( SV \).

In general, the groups had similar systolic blood pressure (SBP), diastolic blood pressure (DBP), and mean arterial pressure (MAP) at all of the exercise intensities (Fig. 3). As exercise intensity increased both SBP and MAP increased significantly for each group. DBP did not change as exercise intensity increased. Although each group significantly reduced their TPR with the increase in exercise intensity from 40 to 100% of \( V_{O2\max} \) the TPR of the athletes was, with one exception, significantly lower than either of the other two groups of women at each exercise intensity (Fig. 3). There were no differences in TPR between the physically active and sedentary women.

**DISCUSSION**

The major finding of this study is that the SVs of postmenopausal women decrease significantly as exercise intensity increases to maximal, regardless of the level of habitual physical activity. In the present study, SV was maximal at 40–60% of \( V_{O2\max} \) and then decreased significantly in all three physical activity groups as exercise intensity approached maximum. Although such a decline in SV has been reported in sedentary individuals (31), such a finding is not typically seen in trained individuals. Previous studies in young, trained men and women have reported that SV either plateaus or increases as exercise intensity approaches maximum (5, 27, 28). Similarly, in studies of male athletes of the same age as the women in the present study, SV has been reported to either plateau (27) or to continue to increase as exercise intensity increases (4). Only Proctor et al. (25) have reported a decline in SV in trained subjects as exercise intensity increased. Like the present study, the subjects studied by Proctor and colleagues were endurance-trained postmenopausal women. Thus it appears that postmenopausal female athletes, unlike young men and women and older men, are unable to maintain SV as exercise intensity increases to maximum. Furthermore, the decline in SV was similar for all three physical activity groups. This similarity between the physical activity groups is not typically seen in older men or young men or women (4, 5, 27, 28, 31).

In previous studies in untrained individuals, the decline in SV as exercise approaches maximal intensity has generally been attributed to a decrease in left ventricular filling that results from the higher HRs. It is typically assumed that endurance training compensates for this decrease, thus preventing the decline in SV. Gledhill et al. (5) reported that the greater SV in young trained men was the result of enhanced left ventricular filling rather than their enhanced emptying, which was also present. Fleg et al. (4) suggest that in older male athletes the greater SV was the result of a combination of an increase in end-diastolic volume and a decrease in end-systolic volume. Proctor et al. (25) suggest that the decline in SV that was seen in their postmenopausal women may have been related to the estrogen deficiency associated with menopause because the four postmenopausal women not receiving estrogen replacement appeared to demonstrate more of a decline...
in SV than did the four women that were receiving estrogen replacement (25). However, in the present study, with 20 of the 44 subjects receiving HRT, HRT use was not associated with different hemodynamic responses to the increase in exercise intensity (Fig. 2). Nor was HRT status associated with differing responses when examined separately within each of the three physical activity groups. Proctor and colleagues (25) also suggest that the decline in SV was more evident in their older subjects. It may be that the advanced age of our subjects (63 ± 5 yr) contributed to the decline in SV. Further study is necessary to address this potential gender-specific age effect seen in women but not men.

The increase in cardiac output that occurs as exercise intensity increases beyond 60% of VO$_{2\text{max}}$ was solely the result of the increase in HR that occurs as intensity increases. Even though there was a decrease in SV, the increase in HR was sufficiently large between each of the submaximal exercise intensities to result in a significantly greater cardiac output. However, when the intensity was increased from 80 to 100% of VO$_{2\text{max}}$, the increase in HR was not great enough to result in a significantly greater cardiac output in the athletic women.

The greater VO$_2$, at each exercise intensity, of the athletic women was due to their significantly larger cardiac output since arteriovenous oxygen difference was not significantly different among physical activity groups at any exercise intensity. The greater cardiac output, in turn, was the result of a significantly greater SV, because there was no difference in HR among the groups. In addition, there were no differences in SBP, DBP, or MAP among groups at any of the four exercise intensities. This suggests that the greater SV of the athletes is the result of enhanced central, rather than peripheral, CV factors, which may have resulted from their prolonged endurance training. An enhancement of either contractility or the Frank-Starling mechanism, or both, could potentially contribute to the enhanced central factors. Similar findings previously have been reported in training studies in young men and women and older men (14, 17, 30, 31). Such a finding might also be expected in women who have undergone vigorous endurance training for an average of 15 yr. Spina et al. (30) reported that previously
sediency postmenopausal women who undergo an endurance-training program of 9–12 mo do not improve central CV function (i.e., cardiac output and SV) (30). Clearly it is possible, because of the cross-sectional nature of the present study, that the athletes’ greater SV and cardiac output are the result of differences that were present before the initiation of training. A second possibility, however, is that the years of training performed by the athletes in the present study provided a sufficiently greater stimulus to induce beneficial adaptations to the CV system than might be achieved with the 6–12 mo of training typically used in longitudinal studies.

With few exceptions, the physically active women were not significantly different from the sedentary women in any of the CV variables measured in the present study. This is perhaps not unexpected as the Centers for Disease Control (CDC)/American College of Sports Medicine (ACSM) report indicates that meeting the minimum exercise guidelines may not be sufficient to improve CV fitness, but would likely reduce one’s risk for heart disease (20). And while none of the differences was significant in the present study, the data generally indicate trends toward greater SV, cardiac output, and VO2 and lower TPR in the physically active compared with the sedentary women throughout the range of exercise intensities in the current study.

HRT status was not associated with altered CV hemodynamics at any of the exercise intensities in the present study. This agrees with our previous findings that HRT was not associated with altered hemodynamics during maximal exercise (19). These results suggest that HRT use may not improve CV function during exercise. A randomized, longitudinal trial will be necessary to provide a definitive answer to this question. Our results also suggest that the gender differences in response to exercise in older men and women reported in previous studies may not necessarily have been due to the estrogen deficiency that is associated with menopause.

In conclusion, the results of the present study demonstrate that SV declines in postmenopausal women as exercise intensity approaches maximum, regardless of the level of habitual physical activity or HRT status. In addition, the greater VO2 attained by postmenopausal female athletes during submaximal and maximal exercise is the result of their greater SV and lower TPR. Furthermore, postmenopausal women who perform regular exercise in sufficient quantity to meet the guidelines of the CDC/ACSM do not have significantly different hemodynamics during exercise than do sedentary postmenopausal women who do not undergo regular exercise (20).

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REFERENCES


