Eight weeks of moderate-intensity exercise training increases heart rate variability in sedentary postmenopausal women

Radim Jurca, PhD, Timothy S. Church, MD, PhD, Gina M. Morss, MA, Alexander N. Jordan, MS, and Conrad P. Earnest, PhD Dallas, Tex

Background  Regular exercise is associated with increased heart rate variability (HRV). However, results from studies examining the effect of exercise training on HRV in postmenopausal women are inconclusive. In addition, the effect of hormone replacement therapy (HRT) on HRV remains a subject of speculation.

Methods  We examined 88 sedentary postmenopausal women in a randomized controlled trial who were assigned to exercise (n=49) or control (n=39) groups. The exercising women performed 8 weeks of aerobic exercise training at a heart rate equivalent to 50% of VO2max, consisting on average of 44 minutes per session, 3 to 4 times per week. Resting HRV was measured in each participant at baseline and after 8 weeks of intervention. Ten minutes of resting R-R intervals were analyzed by time (standard deviation of mean R-R intervals, root of mean square successive differences) and frequency domain methods: low-frequency (LF) was defined as 0.04 to 0.15 Hz, high-frequency (HF) as 0.15 to 0.40 Hz, and total spectral power as 0.00 to 0.40 Hz. The LF and HF components in normalized units were also calculated.

Results  At baseline, there were no significant differences in HRV between control and exercise groups. Additionally, there were no differences in any HRV variables when women were grouped by HRT use (no HRT, estrogen-only HRT, and progestin-containing HRT). After 8 weeks, women randomly assigned to the exercise group increased all absolute time and frequency domain indexes (all \( P < .001 \)) and reduced resting heart rate (\( P = .002 \)) compared with women in the control group. The LF and HF components expressed as normalized units remained unchanged after exercise intervention. Additionally, HRT use did not modify the exercise-induced changes in HRV.

Conclusions  We conclude that moderate aerobic exercise increases HRV in sedentary postmenopausal women. This benefit is not influenced by the use of HRT. (Am Heart J 2004;147:e21.)
are limited by a small sample size (n < 10). Thus, data from a large sample size are needed in this area.

A further complication in studying the effect of exercise on HRV in postmenopausal women is the use of hormone replacement therapy (HRT) and the various combinations of HRT use, which have been suggested by some to modify HRV. However, the available literature is conflicting and inconclusive. Some groups have reported estrogen HRT to increase parasympathetic tone\(^{20,21}\) and decrease sympathetic nerve discharge,\(^{22,23}\) whereas others reported that estrogen has a minimal effect on autonomic tone.\(^{24,25}\) Short-term (up to 6 months) application of progestin-containing HRT is reported to increase parasympathetic tone.\(^{25}\) whereas others report no effect on HRV.\(^{26}\) Another report found that women taking HRT with progestin for at least 6 months had reduced HRV compared with women on HRT without progestin.\(^{27}\) Thus, the available data examining the effect of various types of HRT on HRV are equivocal, and more data are needed. The lack of a consensus in regard to the effect of HRT on HRV necessitates the careful consideration of HRT use in any study that examines HRV in postmenopausal women.

The primary goal of this study was to investigate the effect of an 8-week exercise training intervention on HRV in sedentary, postmenopausal women participating in a large, supervised, aerobic exercise study. Secondary goals are to examine the association between HRT use and HRV and whether HRT use modifies the exercise-induced changes in HRV.

### Methods

#### Participants

We recruited sedentary postmenopausal women from the Dallas metropolitan area through television, radio, and newspaper advertisements. Study inclusion criteria included women who were nonsmokers, sedentary over the previous 6 months,\(^{28,29}\) with body mass index 25 to 40 kg/m\(^2\), systolic blood pressure between 120 to 159 mm Hg (diastolic blood pressure <100 mm Hg), and HRT status stable for the past 6 months. The Institutional Review Board of The Cooper Institute approved all methods and procedures, and all participants provided written informed consent to participate. Women who met the inclusion criteria were randomly assigned to either the exercise group (n = 49) or the control group (n = 39). All participants were screened for medications known to alter HR and had no history of respiratory or cardiac diseases. Forty-nine of the participants were taking HRT. Before initiation into the study, all participants were assessed at baseline for height, body mass, resting blood pressure, cardiopulmonary fitness, and resting R-R intervals. The R-R interval assessment was repeated for all women after 8 weeks. This report only presents HRV data. Other outcomes are presented elsewhere as part of a larger clinical trial.

#### Heart rate variability measurement

Participants were asked to fast for at least 3 hours, not to consume caffeine-containing products for 12 hours, and to abstain from alcohol use and heavy exercise for 48 hours before testing. Participants rested quietly in the supine position for 25 minutes in a semidark room with a temperature between 22 to 23°C. Participants controlled their respiration rate by breathing with a metronome at a fixed rate of 12 breaths per minute (0.2 Hz). Beat-to-beat measurements of R-R intervals were made during the entire period. The R-R interval measurements were conducted at the same time of day for each participant.

We used an IBM-compatible PC equipped with a program for signal processing and heart rate variability analysis (Polar Precision Performance SW 3.02, Polar Electro OY, Kempele, Finland). The 2-channel electrocardiographic signal was detected by a Polar Heart Rate Monitor and transmitted online to a PC through a Polar Advantage Interface receiver. The QRS timing accuracy of Polar Advantage Interface is fixed to 1 ms. The computer program labeled each QRS complex, and the resulting signal was passed through a filter that eliminates ectopic beats and artifacts. Additionally, an R-R interval tachogram was displayed for manual editing, and areas of ectopy or artifacts were identified and removed by manual deletion. Each edited R-R interval was replaced with an average value. Segments containing >15% of edited R-R intervals were interpreted as premature beats and were excluded from data analysis. These segments accounted for <2% of edited 10-minute intervals in every subject. The filtering techniques are described in earlier reports.\(^{30,31}\) HRV was quantified from the last 10 minutes of the R-R interval recording.

We used an autoregressive model to estimate the power spectrum densities for the frequency domain. The power spectra were quantified by measuring the area in 3 frequency bands: high-frequency power (HF, 0.15 to 0.40 Hz), low-frequency power (LF, 0.04 to 0.15 Hz), and total-frequency power (PT, 0.00 to 0.40 Hz). Although it is generally accepted that HF is mediated by variations in parasympathetic activity, the LF power reflects both parasympathetic and sympathetic modulations.\(^{32}\) In addition, the LF and HF oscillatory components are presented in normalized units (nu). The normalized unit expresses the power centered in the frequency of interest divided by total power less very-low-frequency power.

In addition to frequency domain indexes of HRV, we analyzed time-domain measures of HRV, which are derived from direct measurements of R-R intervals. We calculated the standard deviation of all R-R intervals (SDNN) over the given measurement period and the square root of the mean of the sum of the squares of differences between adjacent R-R intervals (rMSSD). SDNN reflects all the cyclic components responsible for variability in the period of recording, whereas rMSSD is considered to be an index of parasympathetic modulations in HR.\(^{32}\)

#### Blood pressure measurement

Baseline blood pressure measurements were obtained after 25 minutes of R-R interval collection. We discarded the first value from each sequence, subsequently averaging the last 3 values (± 5 mm Hg) to determine resting blood pressure. All blood pressure measurements were obtained through the use
of a Colin STBP-780 automated BP monitor (San Antonio, Tex).

Determination of VO$_{2\text{max}}$

Participants performed an exercise test on a bicycle ergometer (Lode Excalibur Sport Cycle Ergometer, Lode BV, Groningen, Netherlands). Each test started with an initial tension load of 30 W for 2 minutes. After this first stage, tension was increased to 50 W for 4 minutes, followed by 20 W increases every 2 minutes until exhaustion. Open-circuit spirometry measurements were obtained with the use of a Parvomedics True Max 2400 Metabolic Measurement Cart (Salt Lake City, Utah). VO$_{2\text{max}}$ was determined as the greatest quantity of oxygen consumed for the last 30-second period of a completed stage and corresponding to a respiratory exchange ratio > 1.1 and a HR > 85% of age-predicted maximum. All participants met the inclusion criteria.

Exercise training program

Participants in the control group did not participate in any supervised exercise and were asked not to change their physical activity habits during the study. All participants in the exercise group completed 8 weeks of supervised aerobic exercise, alternating exercise sessions on a treadmill and a recumbent leg ergometer (Life Fitness, Franklin Park, Ill) each session. Exercise intensity was kept within ±5 beats to HR equivalent to 50% of VO$_{2\text{max}}$. HR was monitored during the entire exercise session by an HR transmitter (Polar Vantage NV). Participants in the exercise group were asked not to exercise outside of the study.

All women randomly assigned to an exercise group began exercising for 60 minutes per week, equivalent to 4 kCal/kg per week. Participants extended their caloric expenditure by adding 15 extra minutes each week, equivalent to 1 kCal/kg per week, until they accumulated 120 to 165 minutes of exercise during each week. Participants exercised 3 to 4 times per week. Rationale for the gradual increase of caloric expenditure was to prevent soreness, fatigue, injuries, and to enhance participant compliance. Participants were weighed each week, and their weight was multiplied by the exercise dosage to determine the number of calories to be expended for the week. Power output was calculated at 3-minute increments by speed and grade combinations for the treadmill and Watts for the recumbent leg ergometer. When HR fell outside the prescribed training zone, power output was increased or decreased to keep HR within the desired exercise intensity.

Statistical analysis

Baseline and follow-up characteristics of the study groups are presented as mean ± SD. Participants’ baseline characteristics were examined within randomized groups and categories of HRT use. An unpaired $t$ test was used for comparison between the 2 randomized groups. One-way analysis of variance was used for comparison among the 3 HRT groups at baseline. The Student paired $t$ test was used for comparison within groups. The mean change in each variable was compared between treatment groups by using analysis of covariance with adjustment for baseline value. All frequency components presented in absolute units (ms$^2$) were skewed; a natural logarithmic transformation was used to normalize the data. An $\alpha$-level of 0.05 was considered significant. All statistical analyses were performed by SAS Software, Version 8.2 (Cary, NC).

Results

Baseline characteristics

At baseline, participants in the exercise group had significantly higher diastolic blood pressure than did the participants in the control group. Other variables were similar in the 2 groups (Table I). Baseline demographic and physiologic variables were additionally categorized in the 3 groups on the basis of HRT use (Table II). The HRT users and nonusers groups were similar in age, ethnicity, body mass index, blood pressure, and HRV indexes. Baseline VO$_{2\text{max}}$ was significantly lower in women abstaining from HRT compared with women using HRT. Women using progestin-containing replacement therapy had higher baseline HR than women using estrogen only or women without HRT.

Compliance with the exercise training program

Mean total time spent exercising for individuals randomly assigned into the exercise training group was 1133 ± 149 minutes over the 8-week program. Participants averaged 3.2 ± 0.6 exercise sessions per week, with the average exercise session lasting 44 ± 11 minutes. Exercise compliance was excellent, with the average amount of energy expenditure prescribed (4902 ± 665 kcal/8wk) very closely matching the actual amount (4859 ± 607 kcal/8wk) of energy expenditure ($P$ for difference = .31).
Effect of aerobic exercise training on heart rate variability

At baseline, there were no significant differences between the exercise group and the control group for any HRV indexes. Individuals randomly assigned to the exercise training groups had significant increases in all HRV indexes presented in absolute units: rMSSD (+25%), SDNN (+18%), lnPHF (+11%), lnPT (+9%), and lnPLF (+6%), respectively. The normalized HF and LF powers remained unchanged after exercise intervention. Additionally, all HRV variables remained unchanged in the control group. To control for regression to the mean, we adjusted for baseline HRV values. The difference in changes adjusted for baseline value between groups was highly significant for all HRV variables (Table III).

Resting HR decreased in the exercise group and remained unchanged in the control group. To evaluate whether the decrease in resting HR was responsible for the improvement in HRV variables in the exercise group, we further adjusted for change in resting HR (Table III). All observed HRV changes in the exercise group remained statistically significant (all \( P \leq .05 \)). Because weight loss has been associated with HRV enhancement, we further adjusted for change in weight in the exercise group and found no effect on the direction or magnitude of change for all HRV variables in the exercise group (data not shown).

Discussion

The primary finding of the study is that 8 weeks of moderate-intensity aerobic exercise training can increase HRV in postmenopausal women. Furthermore, we did not find HRT use to be associated with any HRV indexes, nor did HRT use modify the exercise-induced improvements in HRV.
Population studies have found impaired HRV to be associated with increased risk for acute cardiovascular events and development of metabolic syndrome.6,7,33–36 Numerous studies have reported regular physical activity and increased fitness to be associated with reduced risk of CVD death.37 However, the mechanisms whereby regular exercise decreases the risk of death are only partially explained by traditional CVD risk factors. Previous studies, as supported by our observation, have reported significant improvement in both time-domain and frequency-domain markers of vagal modulation with exercise training, suggesting that positive benefits of regular exercise on the autonomic balance may be one additional mechanism whereby exercise provides CVD benefit.38–40

We have reported improvement in all absolute spectral frequency components. However, we found no effect of exercise on normalized frequency components. One way to interpret this is that the increase in absolute HF was accompanied by an increase in absolute LF and total power without redistribution of spectral frequency components. It is unclear whether either an increase in parasympathetic activity or both the increase in parasympathetic and a decrease in sympathetic activity are responsible for an increase in power of the LF component. We found greater LF power with exercise training in sedentary postmenopausal women, which is in agreement with other interventional studies and studies conducted on athletes.11,18,41 An enhancement of the parasympathetic tone might be one of the possible adaptations to aerobic exercise, as seen in greater HF power after the exercise intervention. The additional explanation of higher HRV after aerobic exercise might be an im-

### Table III. Heart rate variability at baseline and after training

<table>
<thead>
<tr>
<th></th>
<th>Control (n = 39)</th>
<th>Exercise (n = 49)</th>
<th>Change exercise vs control</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pre</td>
<td>Post</td>
<td>Pre</td>
</tr>
<tr>
<td>Heart rate (beats/min)</td>
<td>66.0 ± 6.4</td>
<td>65.8 ± 6.3</td>
<td>68.1 ± 8.5</td>
</tr>
<tr>
<td>Time domain measures</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>rMSSD (ms)</td>
<td>20.5 ± 8.0</td>
<td>19.5 ± 7.5</td>
<td>18.1 ± 8.0</td>
</tr>
<tr>
<td>SDNN (ms)</td>
<td>29.0 ± 8.1</td>
<td>30.1 ± 8.8</td>
<td>26.4 ± 7.6</td>
</tr>
<tr>
<td>Frequency domain measures</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>lnPHF (ms²)</td>
<td>5.19 ± 0.86</td>
<td>5.05 ± 0.79</td>
<td>4.73 ± 1.03</td>
</tr>
<tr>
<td>lnPT (ms²)</td>
<td>4.96 ± 0.65</td>
<td>5.04 ± 0.63</td>
<td>4.72 ± 0.78</td>
</tr>
<tr>
<td>lnPLF (ms²)</td>
<td>6.46 ± 0.52</td>
<td>6.67 ± 0.58</td>
<td>6.40 ± 0.72</td>
</tr>
<tr>
<td>HF (nu)</td>
<td>54.2 ± 14.9</td>
<td>49.5 ± 15.1</td>
<td>49.4 ± 19.6</td>
</tr>
<tr>
<td>LF (nu)</td>
<td>44.2 ± 14.6</td>
<td>48.4 ± 14.9</td>
<td>48.2 ± 18.8</td>
</tr>
</tbody>
</table>

Values are mean ± SD.
*P < .001 versus baseline.
†Adjusted for baseline value.
‡Adjusted for baseline value and heart rate change.

### Table IV. Heart rate variability at baseline and after training in exercise group categorized by hormone replacement therapy use

<table>
<thead>
<tr>
<th></th>
<th>No HRT (n = 22)</th>
<th>HRT (n = 27)</th>
<th>Change No HRT vs HRT</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pre</td>
<td>Post</td>
<td>Pre</td>
</tr>
<tr>
<td>Heart rate (beats/min)</td>
<td>68.4 ± 9.1</td>
<td>64.7 ± 7.1*</td>
<td>67.8 ± 8.1</td>
</tr>
<tr>
<td>Time domain measures</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>rMSSD (ms)</td>
<td>18.6 ± 10.0</td>
<td>22.8 ± 9.8*</td>
<td>17.8 ± 6.1</td>
</tr>
<tr>
<td>SDNN (ms)</td>
<td>26.9 ± 8.7</td>
<td>31.2 ± 9.9†</td>
<td>25.9 ± 6.7</td>
</tr>
<tr>
<td>Frequency domain measures</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>lnPHF (ms²)</td>
<td>4.69 ± 1.14</td>
<td>5.23 ± 1.07†</td>
<td>4.77 ± 0.96</td>
</tr>
<tr>
<td>lnPT (ms²)</td>
<td>4.46 ± 0.91</td>
<td>5.07 ± 1.05*</td>
<td>4.78 ± 0.68</td>
</tr>
<tr>
<td>lnPLF (ms²)</td>
<td>6.38 ± 0.93</td>
<td>6.74 ± 0.99†</td>
<td>6.42 ± 0.49</td>
</tr>
<tr>
<td>HF (nu)</td>
<td>49.7 ± 18.8</td>
<td>52.8 ± 15.4</td>
<td>49.3 ± 20.7</td>
</tr>
<tr>
<td>LF (nu)</td>
<td>47.8 ± 17.9</td>
<td>45.8 ± 14.9</td>
<td>48.4 ± 19.7</td>
</tr>
</tbody>
</table>

Values are mean ± SD.
*P < .05 versus baseline.
†P < .01 versus baseline.
‡P < .001 versus baseline.
§Adjusted for baseline value.
provement of cardiovagal baroreflex sensitivity reported in sedentary middle-aged and older men.42
It is significant that the positive changes in HRV occurred within a relatively short period of exercise (2 months) and from a relatively modest amount of exercise at moderate intensity. For example, during the last 2 weeks of the exercise program, the average participant was only exercising 169 minutes per week. The selected intensity of 50% VO2max is obtainable for nearly all individuals. Thus, both the weekly time commitment and exercise intensity were well within the consensus recommendation of 150 to 180 minutes per week of moderate intensity,13 yet resulted in substantial improvements in HRV. Whether greater exercise doses or longer trial periods result in greater change in HRV are areas for future work.
Our training program significantly reduced resting HR. Both resting HR and HRV depend on the autonomic nervous system, so they are not independent variables. To examine if the positive changes in HRV were the result of lower resting HR, we adjusted the changes in HRV for the changes in resting HR. This adjustment had minimal effect on change in HRV, suggesting that the exercise training–induced changes in HRV are not the result of lower resting HR. Furthermore, this suggests that HRV measures may be of greater sensitivity to detect changes in cardiac autonomic modulation on HR rather than evaluation of HR rhythm alone.
Preexisting training studies conducted on sedentary postmenopausal women have failed to show an increase in HRV with exercise training.14–16 However, Myslivecek et al15 showed an improvement in spontaneous baroreflex function, used as an index of parasympathetic modulation, and a decrease in sympathetic modulation after 12 weeks of a moderate-intensity walking program. Conversely, Davy et al14 demonstrated that 12 weeks of moderate-intensity aerobic exercise had no effect on HRV, spontaneous baroreflex sensitivity, VO2max, or body weight, despite producing a reduction in resting BP in postmenopausal women with elevated BP. Moreover, Perini et al16 found that 8 weeks of supervised aerobic training did not affect HRV in older postmenopausal women (70 to 80 years old). Importantly, none of these studies had more than 8 subjects in the training group, limiting their ability to draw conclusions. To our knowledge, our study is the first with adequate sample size to rigorously examine the effect of aerobic exercise training on HRV in postmenopausal women.

The effect of HRT on the autonomic nervous system remains inconclusive because of the variety of HRT therapies available and a limited number of studies examining this issue. At baseline, we did not find HRV to differ among groups of women using and not using HRT. Furthermore, HRT use did not modify the positive benefits of exercise training on HRV, and this was evident regardless of the type of HRT used. However, these findings must be taken cautiously because there was a small number of women in the progestin-containing category.

Our observation of the short-term adaptation to aerobic training associated with enhanced cardiac vagal activity in sedentary postmenopausal women may be caused by several metabolic, biochemical, hormonal, and neural changes in the body. An adequate short-term exercise training program may reduce daily stress, regulate body fat metabolism, slow resting HR, and improve cardiorespiratory capacity, all of which are associated with increases in cardiac vagal tone. Exercise has a beneficial effect on several risk factors for CVD, such as insulin resistance, lipid profiles, and arterial blood pressure, which may associate with the improvement in autonomic balance. Further studies are needed to define the mechanisms that underlie these interactions.

A limitation of the current study is the lack of ethnic diversity. The effect of race on HRV has been reported in the ARIC Study,44 in which black women have higher cardiac vagal tone than white women. Although our groups did not significantly differ by ethnicity, additional studies with a larger number of minority participants would be helpful in examining any potential interaction between ethnicity, exercise, and HRV. The current study does have important strengths such as a large sample size, a tightly controlled protocol, and a well-quantified, supervised exercise program.

In summary, the current study established that 8 weeks of a moderate-intensity aerobic exercise training program increases overall HRV in sedentary postmenopausal women. This benefit is not influenced by the use of HRT.

We thank Life Fitness for the donation of aerobic exercise training equipment to our exercise physiology laboratory.

References
10. Levy WC, Cerqueira MD, Harp GD, et al. Effect of endurance ex-
19. Boutcher SH, Stein P. Association between heart rate variability
17. Melanson EL, Freedson PS. The effect of endurance training on
15. Myslivecek PR, Brown CA, Wolfe LA. Effects of physical condition-
14. Davy KP, Willis WT, Seals DR. Influence of exercise training on
10. Levy WC, Cerqueira MD, Harp GD, et al. Effect of endurance ex-
7. Tsuji H, Venditti FJ Jr, Manders ES, et al. Reduced heart rate vari-
5. Kollai M, Kaizumi K. Reciprocal and non-reciprocal action of the
3. Tsuji H, Venditti FJ Jr, Manders ES, et al. Reduced heart rate vari-
2. Levy WC, Cerqueira MD, Harp GD, et al. Effect of endurance ex-
1. Tsuji H, Venditti FJ Jr, Manners ES, et al. Reduced heart rate vari-


