Effects of Exercise Training on Cardiovascular Function and Plasma Lipid, Lipoprotein, and Apolipoprotein Concentrations in Premenopausal and Postmenopausal Women

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This study examined the effects of aerobic exercise on lipid levels in premenopausal and postmenopausal women. Fifty healthy middle-aged women (mean age, 50 years) were randomly assigned to 12 weeks of either aerobic exercise (walking and jogging) or nonaerobic strength exercise (circuit Nautilus training). Concentrations of total cholesterol, high density lipoprotein cholesterol, low density lipoprotein cholesterol, and very low density lipoprotein cholesterol were assessed, along with apolipoprotein (apo) A-I, apo A-II, apo B, and triglycerides. To document changes in aerobic capacity, maximum treadmill testing was performed with expired-gas analysis before and after the exercise program. Aerobic exercise was associated with an 18% improvement in peak \( V_o_2 \). Women in the aerobic group had an increased \( V_o_2 \), from 26.7 to 31.4 ml/kg/min (p<0.0001), while the \( V_o_2 \) of the women in the strength training group did not change (25.8 ml/kg/min before and after). There were no differential changes in lipid levels because all subjects experienced slight reductions in high density lipoprotein cholesterol and total cholesterol and increases in apo A-I and the apo A-I to apo B ratio. There was a tendency for the aerobic group to exhibit lower levels of apo A-II and a greater apo A-I to apo A-II ratio, however. We conclude that premenopausal and postmenopausal women experience similar changes in aerobic capacity and lipid levels with exercise and that the short-term effects of aerobic and nonaerobic exercise on lipid profiles are generally comparable. (Arteriosclerosis and Thrombosis 1991;11:912-917)

Coronary heart disease is a leading cause of death among women and accounts for one third of all deaths.1 Traditional risk factors such as hypertension, hyperlipidemia, and cigarette smoking appear to be as important for women as they are for men.2 For example, in both men and women coronary heart disease risk is increased with high levels of total (TC) and low density lipoprotein (LDL-C) cholesterol and with low levels of high density lipoprotein cholesterol (HDL-C).3,4 Women have lower levels of LDL-C and higher levels of HDL-C than do their male counterparts,5 however, and it has been suggested that endogenous or exogenous hormones may be responsible for gender differences in lipid patterns.6-12

Menopause is associated with progressive reductions of estradiol, progesterone, and 17-hydroxyprogesterone in plasma, along with increased gonadotropin concentrations.12,13 Cross-sectional studies have shown that postmenopausal women have higher TC, triglyceride, very low density lipoprotein cholesterol (VLDL-C), and LDL-C levels than do their premenopausal counterparts14,15; this pattern has been confirmed in a recent longitudinal study.16 Exercise training may be a nonpharmacological method for favorably altering lipid profiles. Cross-
sectional studies have shown higher levels of HDL-C among runners, skiers, tennis players, Olympic athletes, and more active men. However, the methodological limitations of cross-sectional data, that is, confounding factors such as differences in dietary habits, self-selection bias, genetic differences, imprecision of measurement of exercise levels, and so forth preclude any definitive conclusions. Cross-sectional data in women are even more problematic because women who exercise regularly often experience alterations in their reproductive function such as oligomenorrhea, amenorrhea, and shortened luteal phases. Given the influence of reproductive hormones on lipids, it is very difficult to attribute differences in lipid levels to the effects of exercise independent of hormonal status. Furthermore, longitudinal studies of exercise in women have yielded conflicting results. Several studies have failed to demonstrate significant changes in lipids with exercise training. However, small sample sizes, nonrandom designs, and imprecise methods for exercise training and testing make it difficult to draw any firm conclusions based on previous longitudinal data. The purpose of the present study was to assess the effects of exercise training on lipid values among women with the use of a randomized longitudinal design with greater methodological rigor than has been previously employed. In addition, we attempted to consider also the potential influence of sex hormones by comparing the effects of exercise training in premenopausal and postmenopausal women.

Methods

Subjects

All participants were screened by a telephone questionnaire to make sure that they were healthy, between the ages of 45 and 55 years, not taking medication, nonobese (<20% above normal weight as determined by the 1985 Metropolitan Life Tables44), normotensive, and sedentary. No subject was engaged in any form of regular exercise before enrollment in the study. Menopausal status was confirmed by laboratory studies and clinical history. Women were considered premenopausal if they had follicle stimulating hormone levels less than or equal to 40 mIU/ml, if they reported regular menstrual cycle lengths, if they had not been pregnant within the past 2 years, and if they had not taken hormones orally in the past year. Women were considered postmenopausal if they had follicle stimulating hormone levels greater than 40 mIU/ml, if they had not taken oral contraceptives or estrogen replacement therapy in the past year, and if they had not experienced any menses in the 12 months preceding their participation in the study. Informed consent was obtained from each subject, and subjects who successfully completed the study were given a free membership at Duke University’s Preventive Approach to Cardiology exercise facility.

A total of 65 subjects were initially recruited from newspaper, radio, and television advertisements to serve as subjects for this study. Four “premenopausal” women were excluded because their follicle stimulating hormone levels exceeded 40 mIU/ml, and four “postmenopausal” women were excluded because their follicle stimulating hormone levels were less than 40 mIU/ml. An additional seven subjects dropped out of the study after they had their initial laboratory tests but before they completed any other assessment procedure, leaving a total of 25 premenopausal and 25 postmenopausal women.

Procedures

Assessments. Comprehensive evaluations of cardiovascular risk factors were obtained at baseline and again after 3 months. All premenopausal women kept a menstrual diary and were assessed at the same time of their menstrual cycle (luteal phase) at each testing session.

Lipids. Triglycerides were measured enzymatically35 on the Ektachem 400 Analyzer (Eastman Kodak, Rochester, N.Y.). TC was measured enzymatically36 with reagents from Boehringer-Mannheim Diagnostics, Indianapolis, Ind. HDL-C fractions were isolated by the precipitation technique with dextran sulfate (50,000±5,000 d), obtained from the Washington Research Foundation, Seattle, Wash., and MgCl2 (0.5 mol/l MgCl2).37 The cholesterol fraction was determined enzymatically. LDL-C concentrations were estimated by Friedewald’s equation38

\[ \text{LDL} = \text{TC} - (\text{HDL-C} + \text{triglycerides} / 5) \]

Apolipoprotein (apo) A-I, apo A-II, and apo B concentrations were measured immunoturbidimetrically39 with antisera from Boehringer-Mannheim Diagnostics and calibrators from the Washington Research Foundation. Cholesterol and apolipoprotein measurements were performed on the Cobas-BIO centrifugal analyzer (Roche Analytical Instruments, Nutley, N.J.). All samples were stored at -70°C until completion of the study, and paired samples were subsequently assayed concurrently. All analyses were performed on aliquots from the same plasma sample.

Aerobic fitness. Blood pressure was determined by standard cuff sphygmomanometry in the sitting position, and body weight was determined by a standard balance scale. Graded treadmill exercise testing was conducted before exercise training with a modification of the Balke protocol in which metabolic equivalent levels were increased at 1-minute intervals.40 Fasting subjects exercised to exhaustion under continuous electrocardiographic monitoring. Heart rate (HR) measurement was obtained with a Hewlett-Packard 4685-A digital cardiograph. Expired air was collected by facemask for quantification of minute ventilation, O2 consumption, and CO2 production with an MMC Horizon System 2 Beckman metabolic cart. Samples were obtained at 15-second intervals, and peak values were determined from an...
average of the samples obtained during the last 60 seconds. Borg ratings41 were obtained at each stage of the treadmill test and at the completion of the test.

Exercise Training

Subjects were randomly assigned to one of two exercise programs. One group participated in aerobic endurance exercise three times per week for 12 consecutive weeks. These sessions consisted of 15 minutes of warm-up exercises including stretching and light biking on a stationary bicycle (<1 kp/min) followed by 35 minutes of continuous walking and jogging on a 400-m outdoor track at an intensity of at least 70% of the subjects’ HR reserve, which was determined at the time of their initial treadmill test by the standard formula

$$[(HR_{\text{maximum}} - HR_{\text{rest}}) \times 0.70 + HR_{\text{rest}}]^{42}$$

The other group participated in strength and flexibility training twice a week. Strength and flexibility training exercises consisted of 20 minutes of stretching and flexibility exercises followed by 35 minutes of circuit Nautilus training. The Nautilus training used seven exercise stations and nine exercises, including leg extension, leg curl, overhead pulldown, pullover, two chest press exercises, overhead press, side lateral raise, and arm curl. Subjects performed 12–15 repetitions at a given work load. Resistance was increased when the subject was able to complete 15 repetitions.

Subjects in the strength and flexibility exercise group did not engage in any aerobic exercise throughout the duration of the study. Although there was a difference in the amount of exercise in the aerobic and strength training groups, data generally suggest that strength training is not associated with significant cardiovascular training effects.43 All subjects were requested to maintain their usual dietary habits throughout the study. Dietary habits were assessed by self-report, including a 4-day food diary and a 2-week retrospective food recall questionnaire.

Results

Initial Differences Between Premenopausal and Postmenopausal Women

The final sample consisted of 50 healthy women aged 45 to 57 years. All had at least a high school education, and 83% were college graduates. All but one subject were Caucasian. There were no differences in any demographic characteristics of the premenopausal and postmenopausal women except that the premenopausal women were slightly younger than the postmenopausal women (47±2 versus 42±3 years, mean±SD, p<0.001). Analysis of variance (ANOVA) revealed that premenopausal women had lower TC levels than did postmenopausal women (209±47 versus 236±30 mg/dl, p<0.03) and lower LDL-C levels (124±35 versus 151±31 mg/dl, p<0.01). There were no differences in HDL-C, triglycerides, VLDL-C, apo A-I, apo A-II, apo B, or the apo A-I to apo B ratio. However, when age was included as a covariate in an analysis of covariance (ANCOVA), there were no lipid differences between the women. There were also no differences between premenopausal and postmenopausal women with respect to their peak VO₂ (27.0±4.8 versus 25.7±3.8 ml/kg/min, p=0.81).

Effects of Exercise Training on Cardiorespiratory Function

Forty-six women (23 premenopausal and 23 postmenopausal) completed the exercise programs. Twenty-two subjects (11 premenopausal and 11 postmenopausal) completed the strength training program (mean of 24.7 sessions), and 24 subjects (12 premenopausal and 12 postmenopausal) completed aerobic training (mean of 35.4 sessions). Four subjects (two aerobic and two strength training) dropped out for the following reasons: death in immediate family (one), initiation of estrogen therapy (one), and noncompliance with exercise protocol (two). Subjects in the aerobic group were at or above their prescribed training range 77% of the time (range, 58–100%), and subjects reported moderate levels of physical exertion (mean of 13 ratings of perceived exertion) during their training sessions. There were no baseline differences between the aerobic and strength training groups with respect to either their initial fitness levels or their lipid levels.

To assess cardiovascular training effects, a two-way (status×group) ANCOVA was performed with age and initial values at time 1 serving as covariates. The mean values are presented in Table 1. Compared with the strength training group, the aerobic group had significantly lower HRs at rest (68±9 versus 76±9 beats/min, p<0.006), exercised for longer on the treadmill (11.1±1.7 versus 8.9±1.3 minutes, p<0.0002), and had higher peak VO₂ (31.4±5.9 versus 25.8±4.7 ml/kg/min, p<0.0002). There were no menopausal status interactions, which indicates that premenopausal and postmenopausal women achieved comparable improvements in aerobic fitness with exercise training. Participants in the aerobic group increased their aerobic fitness by 18% (p<0.0002) while participants in the strength training group increased their peak VO₂ by less than 1% (p=0.91).

Effects of Exercise Training on Lipids

First, changes in lipid values over the 12 weeks were assessed by a repeated-measures ANOVA. Comparison of time 1 and time 2 values showed that subjects in both exercise groups exhibited a slight decrease in HDL-C (from 62.9±13.2 to 60.4±11.1 mg/dl, p<0.02), an increase in apo A-I (from 154.2±19.2 to 163.0±18.9 mg/dl, p<0.01), and a trend for lower TC (from 223±40 to 217±42 mg/dl, p=0.08). Subjects in both groups also lost a slight amount of weight (from 146±19 to 145±19 lb, p<0.01).

To assess exercise effects on lipid values, data were analyzed by a series of two-way (status×group) ANCOVAs. Mean values by group and time are pre-
presented in Table 2. Because there was an age difference between the premenopausal and postmenopausal women, age as well as the initial lipid values served as covariates. There were no menopausal status interactions. The only significant exercise group effects were trends for apo A-I and the apo A-I to apo A-II ratio. The ANCOVA revealed that the aerobic group compared with the strength training group tended to have lower apo A-II values (41.9±9.7 versus 46.7±4.2 mg/dl, p<0.08) and consequently a higher apo A-I to apo A-II ratio (3.5±0.4 versus 3.8±0.5, p<0.08).

**Discussion**

Results of the study showed that the women who participated in 12 weeks of aerobic endurance exercise training increased their peak V̇O₂ by 18%. This level of improvement is comparable to those in men; moreover, female hormones do not appear to affect the training response because premenopausal and postmenopausal women of comparable ages showed similar improvements in aerobic power.

In general, aerobic endurance exercise for 3 months was generally not associated with improved lipid profiles. The only advantage for the aerobic group was a tendency for a greater apo A-I to apo A-II ratio. This increase without a change in total HDL-C suggests a shift in the relative amounts of HDL subpopulations. HDL₂ has a higher apo A-I to apo A-II ratio than does HDL₃. Therefore, the changes seen in this study may indicate an increase in the ratio of HDL₂ to HDL₃, which is regarded as a favorable index in lowering coronary heart disease risk. Such an increase in the ratio of HDL₂ to HDL₃ with strenuous exercise has also been previously reported.

The failure to find significant increases in HDL-C among women in the aerobic group is consistent with other prospective studies that failed to demonstrate improved lipid profiles among women exercisers. For example, Boyden et al assigned 32 menopausal women to an exercise group or to a control group. After 8 months of exercise training the women in the

**Table 2. Effects of Exercise on Lipids by Menopausal Status**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Menopausal Status</th>
<th>Strength Training</th>
<th>Aerobic Training</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Time 1</td>
<td>Time 2</td>
<td>Time 1</td>
</tr>
<tr>
<td>TC</td>
<td>222±58</td>
<td>216±56</td>
<td>246±31</td>
</tr>
<tr>
<td>LDL-C</td>
<td>132±35</td>
<td>131±36</td>
<td>159±28</td>
</tr>
<tr>
<td>HDL-C</td>
<td>62±12</td>
<td>58±12</td>
<td>63±15</td>
</tr>
<tr>
<td>VLDL-C</td>
<td>27±43</td>
<td>27±42</td>
<td>23±9</td>
</tr>
<tr>
<td>TGs</td>
<td>137±216</td>
<td>137±206</td>
<td>116±46</td>
</tr>
<tr>
<td>Apo A-I</td>
<td>148±18</td>
<td>159±12</td>
<td>161±21</td>
</tr>
<tr>
<td>Apo A-II</td>
<td>43±5</td>
<td>45±5</td>
<td>48±6</td>
</tr>
<tr>
<td>Apo B</td>
<td>120±44</td>
<td>122±48</td>
<td>129±30</td>
</tr>
<tr>
<td>Apo A-I:apo B</td>
<td>1.4±0.5</td>
<td>1.5±0.5</td>
<td>1.3±0.4</td>
</tr>
<tr>
<td>Apo A-I:apo A-II</td>
<td>3.6±0.6</td>
<td>3.5±0.5</td>
<td>3.4±0.5</td>
</tr>
</tbody>
</table>

Values are mean±SD in mg/dl.
TC, total cholesterol; LDL-C, low density lipoprotein cholesterol; HDL-C, high density lipoprotein cholesterol; VLDL-C, very low density lipoprotein cholesterol; TGs, triglycerides; Apo, apolipoprotein.

*Time 1 > time 2 at p<0.10; time 1 < time 2 at p<0.05; time 1 > time 2 at p<0.01; aerobic training > strength training at p<0.10; aerobic training > strength training at p<0.01.
exercise group achieved a modest increase in aerobic capacity (as did the control group); however, there were no significant changes in TC, HDL-C, or apo A-I. McNaughton and Davies reported that women did not show any significant changes in lipid or lipoprotein levels after a 16-week aerobic dance program; however, they only studied five women and did not demonstrate that the subjects achieved a significant training effect. Williford et al also failed to observe any lipid changes in 10 young women who participated in a 10-week aerobic dance program despite a 12% improvement in aerobic capacity, and Perry et al did not find significant changes in lipoprotein fractions, although only six women were studied. In a larger longitudinal study, Brownell et al studied 61 sedentary men and women who participated in 10 weeks of aerobic exercise for 15–20 minutes three times per week. Men experienced a decrease in TC and LDL-C and an increase in HDL-C; however, women did not experience any lipid changes, and consistent with our data, HDL-C actually decreased slightly. It also should be noted that Wood et al observed that men who engaged in aerobic exercise were leaner and more fit than controls, but the former failed to exhibit changes in lipids, lipoproteins, or apolipoproteins after 1 year.

The present randomized trial of women included a healthy sample of both premenopausal and postmenopausal women that is larger than has been studied previously. We observed that both exercise groups experienced small but statistically significant decreases in HDL-C and tended to experience lower TC and increased apo A-I. The reason for the reductions in TC and HDL-C is not clear. It is unlikely that the changes were due to a systematic error in assay techniques because samples obtained at both time 1 and time 2 were stored together at −70°C and each pair was assayed concurrently. In addition, subjects reported that they maintained their usual diets throughout the 3-month exercise program, and they experienced minimal changes in body weight. It is possible that both aerobic exercise and strength training altered the lipid profiles, as there is evidence that strength training as well as aerobic exercise may reduce TC and LDL-C. In the absence of anonexercise control group, however, it is impossible to attribute the reduced TC levels to either form of exercise.

We observed relatively small changes in body weight, with participants in both aerobic and strength training groups losing an average of only 1 lb. There are data to suggest that lipid changes are associated with weight loss. In addition, we did not assess changes in body fat distribution. The distribution of body fat has been shown to be related to metabolic alterations; in particular, the amount of subcutaneous truncal or abdominal fat or visceral fat located within the intra-abdominal cavity may be important. Consequently, it is possible that altered body composition may have been related to changes in lipids. This possibility is unlikely because changes in physical activity are associated with minimal changes in waist to hip circumferences, and a reduction in body weight of 1 kg is associated with only a 0.001–0.003 change in this ratio. However, different proportions of subcutaneous versus visceral fat may be affected, and subjects with high visceral or truncal fat may have experienced greater improvements in lipid metabolism. Future research should examine changes in regional fat distribution with exercise and lipid patterns in premenopausal and postmenopausal women.

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