Exercise Intensity: Its Effect on the High-Density Lipoprotein Profile

Terri Spate-Douglas, MHS, RN, Randall E. Keyser, PhD


Objective: To determine the effect of aerobic exercise intensity on the active subfraction of serum high-density lipoprotein (HDL) concentration.

Design: A randomized control, before-and-after investigation that tested the hypothesis that high-intensity exercise training would result in improvements in serum concentrations of HDL subfraction 2 (HDL₂) greater than those accompanying moderate-intensity training.

Setting: Exercise tests were completed in a hospital stress testing laboratory, and cholesterol analyses were performed in a university research laboratory. Exercise training was performed in the community at a site determined by the subject.

Subjects: Subjects were 25 healthy female employees of a teaching hospital.

Intervention: Maximum treadmill tests and serum cholesterol profiles were assessed in 25 women before and after a 12-week aerobic walking regimen; 12 women in a high-intensity exercise group (HIG) walked at a target heart rate of 80% and 13 women in a moderate-intensity exercise group (MIG) walked at a heart rate of 60% of their heart rate reserve for a distance of 2 miles three times weekly.

Main Outcome Measures: The main dependent variable was HDL₂; other measures of the HDL profile were total HDL and HDL₃. Peak oxygen uptake (VO₂) was also evaluated as a dependent variable to ensure a general aerobic adaptation resulted from the exercise regimen. Measures were analyzed as pretraining to posttraining change scores and absolute values using independent and dependent t tests as appropriate. Statistical significance was assigned at p < .05.

Results: Total HDL was 32.3 ± 8.5mg/dL before and 40.3 ± 10.6mg/dL after training in the MIG and 31.6 ± 6.2mg/dL before and 38.2 ± 12.0mg/dL after training in the HIG. HDL₂ was 14.2 ± 5.7mg/dL before and 18.5 ± 6.9mg/dL after training in MIG. HDL₂ was 13.0 ± 6.2mg/dL before and 19.6 ± 8.9mg/dL after training in the HIG. Total HDL and HDL₂ increased significantly in both groups as a result of exercise training, and intragroup differences were not observed. HDL₃ was not affected by exercise training. Training resulted in significant increases in peak VO₂ in both MIG and HIG (29.0 ± 5.0 to 31.9 ± 5.4mL/kg/min in the MIG and 30.7 ± 5.2 to 33.5 ± 6.3mL/kg/min in the HIG). Intergroup differences in change scores for peak VO₂, HDL, and HDL₂ were not observed.

Conclusion: The results and analyses did not support the hypothesis that the HIG would acquire increases in HDL₂ profile beyond those observed for the MIG. Moderate-intensity training was sufficient to improve the HDL profile, and high-intensity training appeared to be of no further advantage as long as total training volume (total walking distance per week) was constant.

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EPIDEMIOLOGIC STUDIES have identified a strong inverse relationship between plasma high-density lipoprotein (HDL) and coronary atherosclerosis.¹ HDL has been underscored as the strongest predictor of both prevalence and severity of atherosclerosis²,³ and is thought to be the primary carrier mechanism in reverse cholesterol transport. Serum concentrations higher than 60mg/dL appear to exert a protective effect against atherosclerosis.⁴ Information obtained from the Helsinki Heart Study⁵ suggest that therapies that increase HDL are associated with a decrease in the incidence of coronary artery disease. Angiographic analyses of this relationship have varied.⁶ Serum HDL exists in two forms, HDL₂ and HDL₃; the former is thought by most to be the active and protective subfraction.⁷ Total serum HDL concentrations greater than 42mg/dL and HDL₂ levels higher than 25mg/dL have been associated with 3.2- and 4.0-fold decreases in the risk of acute myocardial infarction.⁸ Failure to differentiate among HDL and the HDL₂ and HDL₃ subfractions may explain some of the variation among angiographic findings leading to the inability to corroborate reports of reduced coronary artery disease associated with HDL-increasing therapies. Physical activity positively influences HDL₂ levels⁹,¹⁰ and is associated with decreases in morbidity and mortality.¹¹ Physical activity thresholds for cardiorespiratory fitness¹² have been identified. Specific training volume and intensity requirements for favorably changing HDL₂ levels are not known.

The purpose of this study was to determine the effect of high-versus moderate-intensity cardiorespiratory exercise training on serum HDL₂ concentrations. We arbitrarily selected a 12-week exercise training duration to coincide with other ongoing health promotion programs sponsored by the institution.

SUBJECTS AND METHODS

Subjects

The subjects of the study were 25 female employees of a 529-bed teaching hospital and their acquaintances who answered in-house advertisements and volunteered to participate in the study. Inclusion criteria included absence of pertinent medical or health history indicative of cardiovascular, pulmonary, neurologic, metabolic, or musculoskeletal diseases that would limit exercise or training at the time of the study. In

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addition to those recommended by the American College of Sports Medicine, exclusion criteria included lipid-altering medications, antihypertensive medications, medications known to limit the heart rate or blood pressure response to exercise, abnormal electrocardiogram or blood pressure, cigarette smoking or recent history of smoking cessation, and participation in a routine exercise program during the 6 months before the study. The subjects were randomly assigned to two groups: a moderate-intensity exercise group (MIG) of 13 subjects and a high-intensity exercise group (HIG) of 12 subjects. The descriptive characteristics of the subjects are summarized in table 1. Age and height were similar for both groups. Body weight was significantly higher in the MIG than in the HIG. The rationale for the study, procedures, risk of participation, confidentiality, and rights as a human subject were explained, and written consent to participate was obtained from each subject in accordance with the respective institutional human rights committees.

Apparatus

Heart rate and electrocardiogram were measured using a 12-lead electrocardiograph with electrodes placed in the Mason-Likar configuration. Tests were conducted on a motorized treadmill with speed and percent grade controlled by a microprocessor. The exercise intensity was automatically increased every 3 minutes according to the standard Bruce protocol. Oxygen uptake and other cardiorespiratory variables were measured using a metabolic cart. Blood pressure was auscultated at the brachial artery using a mercury sphygmomanometer and stethoscope. A 21-gauge needle and a 10mL heparinized plastic test tube were used for each blood sample. Training information from the thrice-weekly home exercise sessions was recorded by each subject in a personal exercise log with space for date; pulse rate before, during, and after exercise; distance walked; duration of session; and general comments.

Procedure

Subject evaluation. General information regarding a walking health program was distributed throughout the hospital. Women who were interested in the program were informed of the study and chose to participate either in the study or in the walking program only. Women who self-selected to be part of the study underwent an initial interview, had blood drawn for cholesterol measurement, and underwent a maximal exercise test no longer than 24 hours after the blood was drawn. During the initial interview, the informed consent procedure was completed and the health history was obtained. Participants were instructed to abstain from food, beverages (with the exception of water), and exercise for at least 12 hours before blood was drawn.

After the 12-hour fast and while observing universal precautions, a 21-gauge needle was inserted into the median cubital vein and 10mL of blood was extracted and frozen immediately. Within 2/ hours of the blood draw, subjects completed a maximal treadmill exercise test. Resting heart rate, electrocardiogram, and blood pressure were measured after a 5-minute rest in the supine position. After resting information was recorded, subjects walked on the treadmill as the Bruce protocol was initiated and advanced. Heart rate was measured continuously. Blood pressures and 12-lead electrocardiograms were recorded every 3 minutes and at peak exercise. The test endpoint was volitional exhaustion. After the test, subjects completed an active cool-down and sitting rest while remaining on the electrocardiographic monitoring equipment for at least 6 minutes and until heart rate and blood pressure approximated baseline.

Exercise training. Using data obtained from the maximal exercise tests, target heart rates were calculated by the heart rate reserve method with training intensity set at 60% heart rate reserve for the MIG and 80% heart rate reserve for the HIG. The procedure for these calculations was as follows:

Target for MIG = 0.6 (Peak Heart Rate - Resting Heart Rate) + Resting Heart Rate

or

Target for HIG = 0.8 (Peak Heart Rate - Resting Heart Rate) + Resting Heart Rate.

After computation of the target heart rate, subjects were instructed in palpation of the radial pulse. Radial pulse rate was used to monitor the exercise intensity, and subjects adjusted walking pace to maintain the target heart rate. Subjects were then instructed to participate in a home-based exercise program by walking 2 miles three times per week at their individually prescribed target heart rate. A slow walking warm-up period of 5 minutes before training and a cool-down period of 5 minutes after training were also recommended to the participants. These periods were not included in the 2-mile training distance. Training logs were completed after each exercise session. Pulse rate was recorded in the training log before, during, and after each exercise session. Logs were used to ensure compliance with the training recommendations. Minimum compliance was accepted as participation according to the exercise prescription in at least 80% of 29 of the 36 sessions prescribed for the study. The importance of accurate monitoring of intensity, recording of information, and program adherence was emphasized biweekly at meetings of program participants and study personnel to review the exercise logs and subject progress. Subjects falling below the 80% adherence requirement were dismissed from the study.

Subject reevaluation. After completion of the exercise training phase, subjects again fasted and refrained from exercise in a manner similar to the initial evaluation. Blood was drawn for the posttraining cholesterol analysis. A posttraining maximal treadmill test was completed using the Bruce protocol. All data collection procedures were similar for the pretrained and posttraining exercise sessions to facilitate text-retest comparisons.

Subfractionation of HDL. Blood samples were immediately frozen at the time of acquisition in a 10mL heparinized test tube. Samples remained frozen until all samples had been obtained. All samples were then analyzed using the same laboratory equipment on the same day. A modification of the procedures of Warnick and colleagues was used to subfractionate HDL. The validity of this method as well as other dual-precipitation procedures is generally accepted. The method required two precipitations with dextran sulfate solution containing different amounts of magnesium chloride. Total HDL was measured after serum low-density lipoprotein and very low-density lipoprotein were selectively precipitated by magnesium-dextran sulfate and removed by centrifugation. The supernatant contained the cholesterol associated with the soluble

<table>
<thead>
<tr>
<th>Table 1: Subject Demographics</th>
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<tr>
<td>Age (yrs)</td>
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<tr>
<td>Height (cm)</td>
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<tr>
<td>Pretraining weight (kg)</td>
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<tr>
<td>Posttraining weight (kg)</td>
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</table>

Data are reported as mean ± SD.
concentration of magnesium chloride-dextran solution to precipitate HDL_3. The final supernatant was analyzed for HDL_3, and the difference in the total HDL and HDL_3 was recorded as a close approximation of HDL_2.

**Statistics and Research Design**

This study used longitudinal, prospective, and postselection randomization methods and a two-group, repeated-effects design to study the effect of training intensity on changes in the plasma HDL profile. It was hypothesized that exercising at an intensity of 80% heart rate reserve would increase serum HDL more than exercising at an intensity of 60% heart rate reserve. Independent t tests were used to test this hypothesis; the independent variable classes were the MIG and HIG. Dependent variables included total HDL and HDL_3, as well as HDL_2. Other dependent variables assessed by independent t tests were peak VO_2, heart rate, and test duration. These variables were used to determine the absence of a cardiorespiratory training adaptation. Variables were assessed as the actual values corresponding to the variables before and after training as well as the associated change scores. Dependent t tests were used to assess the intragroup pretraining versus posttraining differences. One-tailed probability of type I error ≤ 5% was required for significance (p ≤ .05). All data are reported as means ± SD.

**RESULTS**

Resting heart rate was similar for the MIG (pretraining, 80 ± 9; posttraining, 75 ± 10) and the HIG (pretraining, 78 ± 11; posttraining, 77 ± 8) before and after training. Heart rate (table 2) increased during exercise (p < .01), and a significant difference in the heart rate response was not observed between the MIG and HIG. Training heart rate was approximately 140 beats/min for the MIG and 160 beats/min for the HIG. As a result of training (table 3), exercise test duration and peak VO_2 were increased (p < .005) for both the MIG and the HIG. Improvement in exercise capacity was similar for both groups.

Total cholesterol decreased significantly (p ≤ .025) in the HIG but not in the MIG as a result of training (table 3). Total HDL before training was within ranges associated with increased risk for atherosclerosis in both the MIG and the HIG. Pretraining and posttraining total HDL, HDL_2, and HDL_3 concentrations were similar for the MIG and the HIG (table 3). Similar increases in total HDL (p < .02) and HDL_2 (p < .03) were observed for both groups (table 4). When expressed as a percentage of the pretraining concentrations, total HDL increased by 25% for the MIG and 21% for the HIG. Percent increase in HDL_2 was 50% for the HIG and 31% for the MIG. HDL_3 was not significantly altered by exercise training. When analyzed as a percentage of total HDL, the proportion of HDL_2 relative to total HDL increased with training from 41.1% ± 2.7% to 45.9% ± 4.2% in the MIG and 51.3% ± 4.7% in the HIG (p < .005 but not in the MIG (44.0% ± 3.6% before training and 45.9% ± 4.2% after training). Before training, %HDL_2/HDL was similar for the HIG and the MIG. After training, %HDL_2/HDL was significantly higher for the HIG (p < .01).

**DISCUSSION**

Both the high- and moderate-intensity exercise training regimens resulted in aerobic adaptations and elicited similar improvements in HDL profile. Improvements in both total HDL and HDL_2 were observed. Statistically significant and clinically relevant improvements in peak VO_2, HDL_2, and HDL_3 indicated that the statistical power of the sample was sufficient to identify important exercise training-mediated differences in pretraining and posttraining measures. The data did not support the hypothesis that high-intensity training would increase serum [HDL_2] more than moderate-intensity training. It was concluded that high-intensity training offered no generalizable benefit over moderate intensity training in improving plasma concentrations of HDL and HDL_2.

HDL is inversely related to atherosclerosis. Serum HDL concentrations lower than 35 mg/dL are thought to be associated with increased risk for atherosclerosis, 1-3. Serum HDL concentrations of 60 mg/dL or higher have been cited as a negative risk factor. 4 Each 10 mg/dL increase in HDL results in a 50% reduction in the risk of atherosclerosis. 23 Every 1 mL/dL increment in HDL appears to be associated with a 3.2% to 3.9% decrease in the incidence of coronary heart disease. 2,24 Even small increases in HDL levels may result in a large reduction in the risk of atherosclerosis. HDL levels were increased after training by approximately 8 mg/dL in the MIG and 7 mg/dL in the HIG, representing 35% and 40% reductions in the risk of atherosclerosis. 25 Thus, even moderate training resulted in dramatic improvement in the risk of diseases such as coronary heart disease, peripheral arterial disease, and stroke.

Total plasma HDL can be profiled by the proportions of its

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**Table 2: Exercise Responses Before and After Training**

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<thead>
<tr>
<th></th>
<th>MIG</th>
<th>HIG</th>
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<tbody>
<tr>
<td>Before</td>
<td>179 ± 14</td>
<td>178 ± 11</td>
</tr>
<tr>
<td>After</td>
<td>179 ± 14</td>
<td>182 ± 12</td>
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<tr>
<td>Test duration (min)</td>
<td></td>
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<tr>
<td>Before</td>
<td>7.98 ± 1.68</td>
<td>8.53 ± 2</td>
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<tr>
<td>After</td>
<td>9.22 ± 1.95*</td>
<td>9.75 ± 2.32*</td>
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<tr>
<td>Peak oxygen uptake (mL/kg/min)</td>
<td></td>
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<tr>
<td>Before</td>
<td>29.0 ± 5.0</td>
<td>30.7 ± 6.2</td>
</tr>
<tr>
<td>After</td>
<td>31.9 ± 5.4*</td>
<td>33.5 ± 6.3*</td>
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</table>

Data are reported as mean ± SD.

* Significantly higher than before training, p ≤ .05.

**Table 3: HDL Profile Before and After Training**

<table>
<thead>
<tr>
<th></th>
<th>MIG</th>
<th>HIG</th>
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<tbody>
<tr>
<td>Total HDL (mg/dL)</td>
<td>Before 188 ± 36</td>
<td>193 ± 34</td>
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<tr>
<td></td>
<td>After   187 ± 34</td>
<td>181 ± 40*</td>
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<tr>
<td>HDL_2 (mg/dL)</td>
<td>Before 32.3 ± 6.6</td>
<td>31.6 ± 6.2</td>
</tr>
<tr>
<td></td>
<td>After   40.3 ± 10.6*</td>
<td>38.2 ± 12.0*</td>
</tr>
<tr>
<td>HDL_3 (mg/dL)</td>
<td>Before 14.4 ± 6.7</td>
<td>13.0 ± 6.2</td>
</tr>
<tr>
<td></td>
<td>After   18.5 ± 6.9*</td>
<td>19.6 ± 8.9*</td>
</tr>
</tbody>
</table>

Data are reported as mean ± SD.

* Significantly different from before training concentration, p ≤ .05.

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subfractions HDL₂ and HDL₃. HDL₂ concentration is a strong predictor of the presence and severity of coronary atherosclerosis. Exercise training–mediated antiatherogenic properties of the HDL profile appear to be specific to the HDL₂ subfraction. Although earlier group increased [HDL₂] to levels high enough to minimize atherosclerotic risk, the significant posttraining increase in [HDL₂] underscored the effectiveness of aerobic training in improving the risk for atherosclerosis. Prolonged training duration beyond 3 months and increased total caloric expenditure per session are likely to have resulted in further improvements in the HDL profile.

Well-accepted guidelines for the quantity of exercise, or training volume, necessary to develop and maintain cardiorespiratory fitness have been established. A variety of methods are available for monitoring intensity, many of which are based on the linear relationship of heart rate and VO₂. The heart rate reserve method closely corresponds to similar percentages of maximal VO₂. Previous studies have demonstrated that moderate training intensities are adequate to elicit improvements in HDL. Findings of the current study were in agreement, indicating that moderate intensity activity is sufficient to increase total plasma HDL and HDL₂ concentrations. Inaccuracy in intensity monitoring would affect this conclusion, particularly if subjects in the HIG reported exercising at higher intensities than they actually attained during the sessions. It is doubtful if those in the MIG exercised consistently at intensities higher than those of the study protocol. Twice-weekly reinforcement and keeping of training logs were methods implemented to control reporting inaccuracy as a source of error. Even if inaccuracy high training heart rates were recorded in the exercise logs, the results still indicated that moderate-intensity exercise is sufficient for improving the risk for atherosclerosis.

The short-term exercise response has been studied with respect to immediate and long-term recovery changes in total HDL. Stationary cycling for 30 minutes at 60% of the age-predicted maximal heart rate has been found to increase total HDL. Hughes and associates reported that at a constant intensity, exercise sessions of 45 minutes produced longer-lasting total HDL increases than sessions of 30 minutes, illustrating the effect of exercise duration and training volume on HDL profile changes. Crouse and coworkers observed increased total HDL 24 hours after single bouts of cycling but found no difference in this increase between high and moderate intensity trials as long as caloric expenditure was held constant. Haskell reviewed the literature and suggested that the threshold for effecting plasma lipoprotein changes may be a weekly training volume of approximately 1,000 kcal. Collectively, these studies underscore the necessity of holding the training volume constant when evaluating the effects of differing training regimens on the HDL profile. At a given weekly frequency, training volume can be controlled by increasing duration inversely with reduction of intensity to hold constant the number of calories expended throughout the activity. Training distance can also be held constant because the number of kilocalories required to cover a distance is constant within a range of velocities when walking on a treadmill or relatively flat terrain. The current study did not assess the short-term HDL profile response to exercise.

Factors other than exercise that positively affect HDL include cigarette smoking cessation and weight reduction to ideal body weight. It is possible that increased body weight contributed to the baseline levels of HDL that were lower than desired to improve risk of atherosclerosis in the MIG. Body weight did not change in either group, however, so weight reduction was not a determinant of improved improvement in the respective HDL profiles. This study maintained a constant training volume by having subjects in the HIG and the MIG walk similar distances. Both training regimens resulted in similar improvements in the HDL profile. The finding that intensities of 60% and 80% heart rate reserve had similar effects on the HDL profile was most likely caused by the similar training volumes over the 12-week training duration.

CONCLUSION

This study tested the hypothesis that plasma HDL₂ concentrations would be increased to a greater extent using high than moderate exercise intensity in women. The hypothesis was not supported by the data. It appeared that the proportion of the gain in total HDL afforded by HDL₂ increases may have been greater with high than with moderate intensity, but this suggestion must be interpreted with caution because gain scores in actual plasma HDL₂ concentrations were statistically similar. This study differed from previous training studies of exercise intensity and HDL profile in that the total volume of training was held constant. Women in both the HIG and the MIG had low baseline levels of total HDL and HDL₂ that placed them at increased risk for atherosclerosis. This risk was reduced by 35% to 40% as a result of training. The current study indicated that moderate intensity exercise is sufficient for reducing an individual’s risk of atherosclerosis. Furthermore, the results of this study suggest that when training volume is held constant, there is no advantage to high rather than moderate exercise intensities when the goal of the exercise program is to increase the antiatherogenic aspects of reverse cholesterol transport.

References


