Available online at www.sciencedirect.com
ScienceDirect
Metabolism Clinical and Experimental 56 (2007) 444–450
Metabolism
Clinical and Experimental
www.elsevier.com/locate/metabol

Endurance exercise training raises high-density lipoprotein cholesterol and lowers small low-density lipoprotein and very low-density lipoprotein independent of body fat phenotypes in older men and women

Amy Halverstadt[a,*], Dana A. Phares[a], Kenneth R. Wilund[b], Andrew P. Goldberg[c,d], James M. Hagberg[a]

[a]*Department of Kinesiology, University of Maryland, College Park, MD 20742-2611, USA*
[b]*Department of Kinesiology, University of Illinois at Urbana at Urbana-Champaign, Urbana, IL 61801, USA*
[c]*Division of Gerontology, University of Maryland School of Medicine, Baltimore, MD 21201, USA*
[d]*Geriatric Research, Education, and Clinical Center, Baltimore VA Medical Center, Baltimore, MD 21201, USA*

Received 3 April 2006; accepted 16 October 2006

Abstract

Endurance exercise training improves plasma lipoprotein and lipid profiles and reduces cardiovascular disease risk. However, the effect of endurance exercise training, independent of diet and body fat phenotypes, on plasma lipoprotein subfraction particle concentration, size, and composition as measured by nuclear magnetic resonance (NMR) spectroscopy is not known. We hypothesized that 24 weeks of endurance exercise training would independently improve plasma lipoprotein and lipid profiles as assessed by both conventional and novel NMR measurement techniques. One hundred sedentary, healthy 50- to 75-year-olds following a standardized diet were studied before and after 24 weeks of aerobic exercise training. Lipoprotein and lipid analyses, using both conventional and NMR measures, were performed at baseline and after 24 weeks of exercise training. Relative and absolute maximum oxygen consumption increased 15% with exercise training. Most lipoprotein and lipid measures improved with 24 weeks of endurance exercise training, and these changes were consistently independent of baseline body fat and body fat changes with training. For example, with exercise training, total cholesterol, triglycerides, and low-density lipoprotein cholesterol (LDL-C) decreased significantly (2.1 ± 1.8 mg/dL, $P = .001$; −17 ± 3.5 mg/dL, $P < .0001$; and −0.7 ± 1.7 mg/dL, $P < .0001$, respectively), and high-density lipoprotein cholesterol subfractions (HDL_3-C and HDL_2-C) increased significantly (1.9 ± 0.5 mg/dL, $P = .01$, and 1.2 ± 0.3 mg/dL, $P = .02$, respectively). Particle concentrations decreased significantly for large and small very low-density lipoprotein particles (−0.7 ± 0.4 nmol/L, $P < .0001$, and −1.1 ± 1.7 nmol/L, $P < .0001$, respectively), total, medium, and very small LDL particles (−100 ± 26 nmol/L, $P = .01$; −26 ± 7.0 nmol/L, $P = .004$; and −103 ± 27 nmol/L, $P = .02$, respectively), and small HDL particles (−0.03 ± 0.4 μmol/L, $P = .007$). Mean very low-density lipoprotein particle size also decreased significantly (−1.7 ± 0.9 nm, $P < .0001$) and mean HDL particle size increased significantly with exercise training (0.1 ± 0.0 nm, $P = .04$). These results show that 24 weeks of endurance exercise training induced favorable changes in plasma lipoprotein and lipid profiles independent of diet and baseline or change in body fat.

1. Introduction

Cardiovascular disease (CVD) is a critical, worldwide public health threat [1]. Current evidence suggests that in addition to conventional plasma lipoprotein lipid measures, novel measures of plasma lipoprotein subfraction concentration, size, and composition should be considered when evaluating CVD risk, as they may provide a better risk assessment because of their distinct composition and functions [2-4]. For example, concentrations of total and small low-density lipoprotein (LDL) particles, large high-density lipoprotein (HDL) particles, and large very low-density lipoprotein (VLDL) particles better reflect CVD risk than absolute measures of cholesterol concentrations, thus improving the early detection of CVD risk [3-8]. In addition, the Adult Treatment Panel (ATP) III report lists small LDL particle concentration as an emerging risk factor and recommends small VLDL particle concentration as a potential target of cholesterol-lowering therapy [7,9-11].

* Corresponding author. Tel: +1 301 405 2571; fax: +1 301 405 5578.
E-mail address: halveraa@aol.com (A. Halverstadt).

0026-0495/$ – see front matter © 2007 Elsevier Inc. All rights reserved.
doi:10.1016/j.metabol.2006.10.019

Although lipoprotein subclass concentrations and particle size can be measured by nuclear magnetic resonance (NMR) spectroscopy, relatively few studies have used this methodology in a specific population to assess changes in lipid/lipoprotein profiles after endurance exercise training.

Endurance exercise training improves plasma lipoprotein and lipid profiles and thus reduces CVD risk [7,9-11]. In a meta-analysis of 52 exercise training studies, Leon and Sanchez found an average increase of 4.6% in HDL cholesterol (HDL-C), a reduction of 3.7% in triglycerides (TGs), and a reduction of 5.0% in LDL cholesterol (LDL-C) [9,10]. In another review, Durstine et al [11] concluded that 15 to 20 miles of brisk walking or jogging (expenditure of 5021-9205 kJ/wk) was associated with HDL-C increases of 2 to 8 mg/dL. Kraus et al [7] recently found that a relatively high amount of regular exercise improved overall lipoprotein profiles, including an increase in total HDL concentration, large HDL particle concentration, and HDL particle size, even without clinically significant weight loss. However, there is still debate relative to whether these training-induced changes in plasma lipoprotein and lipid profiles are independent of initial levels of body fat and their changes with training [7,12-17].

Thus, we sought to investigate the independent effects of 24 weeks of standardized endurance exercise training on conventional and novel NMR measures of plasma lipoprotein subfractions. We hypothesized that exercise training, independent of diet, baseline body fat, and change in body fat with training, would beneficially affect plasma lipoprotein and lipoprotein lipid levels assessed by both conventional and NMR subfraction measures.

2. Methods

One hundred sedentary men and women volunteered for this study. Subjects were screened by telephone to determine their initial eligibility. The University of Maryland College Park Institutional Review Board approved the study and written informed consent was obtained from all subjects. To be eligible, subjects had to meet the following criteria: healthy, sedentary (physical activity performed for less than 20 minutes on no more than 2 occasions per week), 50 to 75 years old, normotensive or with blood pressure controlled with medications not affecting plasma lipoprotein lipid levels, nondiabetic, nonsmoking, no history of CVD, body mass index (BMI) less than 37 kg/m^2, and have at least one National Cholesterol Education Program (NCEP) lipid abnormality (see "Screening" below). All women were more than 2 years past menopause and maintained their hormone replacement therapy (HRT) status, either on or not on, for the duration of the study.

2.1. Screening

Screening visit 1. Medical histories were reviewed to ensure eligibility, including confirmation of BMI less than 37 kg/m^2. A 12-hour overnight-fasting blood sample was drawn for plasma lipoprotein lipid profile analysis. Subjects had 1 or more NCEP lipid abnormalities (cholesterol >200 mg/dL, HDL-C <40 mg/dL, triglycerides [TGs] >200 mg/dL). For each subject, total plasma cholesterol and LDL-C levels were less than the 90th percentile and plasma HDL-C was greater than the 20th percentile for their age and gender to exclude familial hypercholesterolemia or hypoalphalipoproteinemia.

Screening visit 2. Fasting blood samples were drawn, and subjects underwent an oral glucose tolerance test. Subjects were excluded if fasting glucose was greater than 126 mg/dL or 2-hour glucose was greater than 200 mg/dL.

Screening visit 3. Qualified subjects then underwent a physical examination to detect cardiovascular, pulmonary, or other chronic diseases that would preclude exercise testing or training [18]. A Bruce maximal treadmill exercise test was administered to ensure they had no evidence of overt CVD [19]. Blood pressure, heart rate, and electrocardiogram were recorded before the test, at the end of every exercise stage, and during recovery. Maximum oxygen consumption ($\dot{V}O_2$max) was also measured. For study inclusion, subjects had less than 2 mV ST-segment depression and no cardiovascular signs or symptoms during this test [18].

2.2. Dietary stabilization and body weight control

All subjects underwent 6 weeks of dietary instruction with a registered dietician on the American Heart Association Dietary Guidelines for the General Population (AHA Diet) [20]. The instruction consisted of 2 classes per week, 1 hour per class, for a total of 12 hours. Subjects followed the dietary guidelines and were weight stable for more than 3 weeks before undergoing baseline testing. Throughout the study, subjects continued to follow the AHA Diet and remained weight stable to eliminate the potentially confounding effects of diet and substantial weight loss on outcome measures. To monitor body weight, subjects were weighed at every dietary session (12 appointments), at every baseline testing appointment (3-5 appointments), at every exercise session (72 sessions), and at every final testing appointment (3-5 appointments). Dietary monitoring to ensure compliance consisted of subjects completing 7-day diet records during weeks 1 and 24 of exercise training; completing food frequency questionnaires during the dietary sessions and at weeks 8, 16, and 24 of exercise training; and interacting with the study dietician once every 2 weeks throughout the 24 weeks of exercise training. To be included in the analyses, subjects could not lose more weight than could be explained by the energy expenditure attributable to their exercise training program.

2.3. Baseline testing

To analyze conventional plasma lipoprotein lipid levels, subjects had fasting samples drawn on 2 separate occasions and the values were averaged. If these measures differed by

more than 10%, a third separate measurement was included in the average. Conventional plasma TG, cholesterol, HDL-C, LDL-C, HDL_2-C, and HDL_3-C were measured as described previously [21]. NMR techniques (LipoScience, Raleigh, NC) also were used to determine plasma lipoprotein lipids, using techniques previously standardized and validated against conventional methods of separation and analysis [2,22,23]. In brief, NMR uses radiofrequency signals emitted by lipoprotein subclass particles when a magnetic field is applied to plasma to assess particle concentration. This method capitalizes on the fact that each lipoprotein subclass particle of a given size emits its own characteristic signal, and the amplitude of the signal provides a direct measure of the lipoprotein particle concentration. Particle size was calculated. The NMR measures were made on a single blood sample. Baseline and final test samples were analyzed at the same time. The NMR measures included particle concentrations (nanomoles per liter) for 10 subclasses of VLDL, LDL, and HDL, as well as mean VLDL, LDL, and HDL particle size diameter (in nanometers). Lipoprotein subclasses are grouped by size as large (>60 nm), medium (35-60 nm), and small (27-35 nm) VLDL; intermediate-density lipoprotein (IDL) (23-27 nm); large (21.2-23 nm), total small (18-21.2 nm), medium small (19.8-21.2), and very small (18-19.8 nm) LDL; and large (8.8-13 nm), medium (8.2-8.8), and small (7.3-8.2 nm) HDL.

Body composition was analyzed by dual-energy x-ray absorptiometry (DPX-L, Lunar, Madison, WI) [24]. All subjects underwent a second maximal treadmill exercise test to assess $\dot{V}O_2$max [25]. Standard criteria were used to determine if $\dot{V}O_2$max had been achieved: no further increase in oxygen uptake with increase in workload (<150 mL/min), exceeding age-predicted maximal heart rate, or achieving a respiratory exchange ratio of greater than 1.15 [25].

2.4. Exercise training

Endurance exercise training consisted of 24 weeks of supervised endurance exercise consisting of 3 sessions per week [21]. Subjects were allowed to use various types of aerobic exercise training equipment: bikes, treadmills, elliptical machines, skier machines, stepping machines, and rowers. Training began with 20 minutes at 50% $\dot{V}O_2$max and progressed to 70% $\dot{V}O_2$max for 40 minutes where it remained for the final 14 weeks. Subjects added a lower intensity 45- to 60-minute exercise session during weeks 12 to 24. Inclusion in the final analyses required subjects to have completed 75% or more of training sessions.

2.5. Final testing

After completing exercise training, all subjects underwent the same tests as at baseline. All blood samples were drawn 24 to 36 hours after a usual exercise training session.

2.6. Statistics

Subject characteristics, baseline plasma lipoprotein lipid measures, and plasma lipoprotein lipid changes with exercise training are presented as mean ± SEM. Paired *t* tests were used to analyze changes in subject characteristics with exercise training. Correlation analyses were run for baseline body fat, training-induced changes in body fat, and training-induced changes in lipoproteins and lipoprotein lipids. Analysis of covariance was used to analyze lipoprotein and lipid changes with exercise training. Sex, HRT status, and baseline value of the plasma lipoprotein being analyzed were included simultaneously as covariates. In addition, no body fat measure, baseline body fat, or change in body fat was also included as a covariate depending on which model was being analyzed. The first analyses were run without any body fat measure as a covariate to determine if training affected plasma lipoprotein lipids (model 1). Then, the analyses were run with baseline percent body fat as an additional covariate to determine if lipoprotein and lipoprotein lipid responses to exercise training were independent of baseline body fat levels (model 2). Finally, the analyses were run with change in percent body fat with training as the additional covariate to determine if exercise training had an effect on lipoprotein and lipoprotein lipid changes independent of training-induced changes in percent body fat (model 3). Statistical significance was set at $P \leq .05$. Statistical procedures were performed using SPSS 10.0 software (SPSS, Chicago, IL).

3. Results

The study population consisted of 58 women and 42 men with a mean age of 58 ± 0.6 years. Of the women, 24 were on HRT. Seventy-five subjects were Caucasian, 19 were African American, and 6 were of other races. Using ethnicity as a covariate did not affect any statistical results; therefore, all subjects were included in the analyses, and ethnicity was not used as a covariate. With exercise training, body weight and body fat decreased significantly, and $\dot{V}O_2$max increased significantly (Table 1).

Significant correlations were found only between baseline body fat and change in HDL size ($r = -0.24$, $P = .02$) and for the training-induced change in body fat and change in HDL-C ($r = -0.25$, $P = .01$), HDL_2-C ($r = -0.28$, $P = .005$), and IDL ($r = 0.27$, $P = .007$).

Without accounting for baseline body fat or change in body fat, all conventionally measured plasma lipoprotein

Table 1
Subject characteristics: baseline and change with exercise training

Characteristic	Baseline	Change with training	*P*
Weight (kg)	80 ± 1.6	−1.3 ± 0.2	<.0001
Body fat (%)	36 ± 1.0	−1.4 ± 0.2	<.0001
Lean body weight (kg)	47 ± 1.1	0.5 ± 0.2	<.001
$\dot{V}O_2$max (mL/kg per minute)	25 ± 0.5	3.8 ± 0.3	<.0001
$\dot{V}O_2$max (L/min)	2.0 ± 0.1	0.3 ± 0.0	<.0001

Values are expressed as means ± SEM. n = 97 to 100 for the different measures. *P* indicates statistical probability for significance of the change with exercise training.

Table 2
Conventionally measured plasma lipoprotein lipids (in milligrams per deciliter): baseline and change with exercise training

Characteristic	Baseline	Change with exercise training (model 3)	P
TC	207.0 ± 3.1	−2.1 ± 1.8	.001
TG	148.0 ± 7.0	−17.0 ± 3.5	<.0001
HDL-C	48.0 ± 1.4	3.3 ± 0.5	.09
HDL_2-C	5.0 ± 0.7	1.2 ± 0.3	.02
HDL_3-C	43.0 ± 0.9	1.9 ± 0.5	.01
LDL-C	129.0 ± 2.7	−0.7 ± 1.7	<.0001

Values are expressed as adjusted means ± SEM. Model 3 covariates are gender, HRT, baseline value of the plasma lipoprotein lipid, and change in body fat. n = 96 to 100 for the different measures. *P* indicates statistical probability for significance of the change with exercise training.

lipids except HDL-C and HDL_2-C changed significantly with exercise training. Total cholesterol (TC), TG, and LDL-C levels all decreased with exercise training (−2.0 ± 1.7 mg/dL, $P < .0001$; −16 ± 3.4 mg/dL, $P < .0001$; and −0.6 ± 1.7 mg/dL, $P < .0001$, respectively). HDL_3-C increased significantly with exercise training (1.9 ± 0.5 mg/dL, $P = .005$). After controlling for baseline body fat levels, the changes in TC (−2.2 ± 1.8 mg/dL, $P = .001$), TG (−16.4 ± 3.5 mg/dL, $P < .0001$), LDL-C (−0.8 ± 1.7 mg/dL, $P < .0001$), and HDL_3-C (1.8 ± 0.5 mg/dL, $P = .01$) with exercise training all remained significant. After controlling for change in body fat with exercise training, the changes with training for most conventionally measured lipids were still statistically significant and similar to those observed without any covariates and with baseline body fat levels as a covariate (TC = −2.1 ± 1.8 mg/dL, $P = .001$; TG = −17 ± 3.5 mg/dL, $P < .0001$; LDL-C = −0.7 ± 1.7 mg/dL, $P < .0001$; and HDL_3-C = 1.9 ± 0.5 mg/dL, $P = .01$) except that HDL_2-C increased significantly with exercise training (HDL_2-C = 1.2 ± 0.3 mg/dL, $P = .02$) and HDL-C showed a tendency to increase with training (HDL-C = 3.3 ± 0.5 mg/dL, $P = .09$) (Table 2).

Without accounting for baseline or change in body fat (model 1), most of the NMR-measured plasma lipoprotein particle concentrations and sizes also changed significantly with exercise training. Concentrations of large and small VLDL particles decreased significantly with exercise training (−0.7 ± 0.4 nmol/L, $P < .0001$, and −1.0 ± 1.6 nmol/L, $P < .0001$, respectively). Total LDL particle concentration also decreased significantly with exercise training (−102 ± 25 nmol/L, $P = .02$). This included significant decreases in the medium and very small LDL particle concentrations (−27 ± 7.0 nmol/L, $P = .002$, and −106 ± 26 nmol/L, $P = .01$, respectively), resulting in a significant decrease in total small LDL particle concentration (−133 ± 32 nmol/L, $P = .008$). Large LDL particle concentration increased significantly (31 ± 16 nmol/L, $P = .002$), as did IDL particle concentration (0.3 ± 2.6 nmol/L, $P < .0001$). The concentration of medium HDL particles decreased significantly with exercise training (−0.3 ± 0.4 μmol/L, $P < .0001$). Mean VLDL particle size also decreased significantly with exercise training (−1.7 ± 0.9 nm, $P < .0001$), and mean HDL particle size increased significantly with exercise training (0.1 ± 0.0 nm, $P = .02$). Change in LDL particle size approached significance (0.2 ± 0.1 nm, $P = .09$).

After controlling for baseline body fat levels (model 2), all NMR-measured outcomes except medium VLDL particle concentration were still statistically significant and similar to those observed without any covariates (model 1). Concentrations of large and small VLDL particles decreased significantly with training (−0.7 ± 0.4 nmol/L, $P < .0001$, and −1.0 ± 1.6 nmol/L, $P < .0001$, respectively). Total LDL particle concentration also decreased significantly with training (−102 ± 26 nmol/L, $P = .04$). This included significant decreases in the medium and very small LDL particle concentrations (−27 ± 7.0 nmol/L, $P = .004$, and −106 ± 26 nmol/L, $P = .02$, respectively), resulting in a significant decrease in total small LDL particle concentration (−132 ± 32 nmol/L, $P = .02$). Large LDL particle concentration increased significantly (30 ± 16 nmol/L, $P = .006$), as did IDL particle concentration (0.2 ± 2.6 nmol/L, $P < .0001$). The concentration of medium HDL particles decreased significantly with training (−0.3 ± 0.4 μmol/L, $P < .0001$). Mean VLDL particle size also decreased significantly (−1.7 ± 0.9 nm, $P < .0001$), and mean HDL particle size increased significantly with exercise training (0.1 ± 0.0 nm, $P = .03$). Although not statistically significant, mean LDL particle size increased (0.2 ± 0.1 nm, $P = .16$). For medium VLDL

Table 3
NMR-measured plasma lipoprotein subfractions: baseline and change with exercise training

Characteristic	Baseline	Change with exercise training (model 3)	P
VLDL particle concentrations (nmol/L)			
Total	73 ± 3.1	−5.1 ± 2.5	.25
Large VLDL/chylomicrons	4.5 ± 0.5	−0.7 ± 0.4	<.0001
Medium VLDL	28 ± 1.7	−3.2 ± 1.5	.13
Small VLDL	40 ± 2.0	−1.1 ± 1.7	<.0001
LDL particle concentrations (nmol/L)			
Total	1436 ± 42	−100 ± 26	.01
IDL	40 ± 2.9	0.7 ± 2.5	<.0001
Large LDL	430 ± 25	29 ± 16	.008
Small LDL (total)	966 ± 55	−129 ± 33	.017
Medium small LDL	221 ± 12	−26 ± 7	.004
Very small LDL	745 ± 43	−103 ± 27	.02
HDL particle concentrations (μmol/L)			
Total	34 ± 0.5	0.7 ± 0.3	.70
Large HDL	5.4 ± 0.4	1.0 ± 0.2	.66
Medium HDL	5.5 ± 0.4	−0.2 ± 0.4	<.0001
Small HDL	23 ± 0.6	−0.03 ± 0.4	.007
Mean particle size diameter (nm)			
VLDL	50 ± 1.3	−1.7 ± 0.9	<.0001
LDL	21 ± 0.1	0.2 ± 0.1	.19
HDL	9 ± 0.0	0.1 ± 0.0	.04

Values are expressed as adjusted means ± SEM. Model 3 covariates are gender, HRT, baseline value of the plasma lipoprotein, and change in body fat. n = 97 to 100 for the different measures. *P* indicates statistical probability for significance of the change with exercise training.

particle concentration, a significant change was seen only when no body fat measure was used as a covariate.

Controlling for change in body fat (model 3) again produced results similar to those of models 1 and 2 in terms of amount of change and statistical significance of results for all NMR-measured outcomes (Table 3). Concentrations of large and small VLDL particles decreased significantly with training (-0.7 ± 0.4 nmol/L, $P < .0001$, and -1.1 ± 1.7 nmol/L, $P < .0001$, respectively). Total LDL particle concentration also decreased significantly with exercise training (-100 ± 26 nmol/L, $P = .01$), including significant decreases in the medium and very small LDL particle concentrations (-26 ± 7.0 nmol/L, $P = .004$, and -103 ± 27 nmol/L, $P = .02$, respectively). These changes resulted in a significant decrease in total small LDL particle concentration (-129 ± 33 nmol/L, $P = .02$). Large LDL particle concentration increased significantly (29 ± 16 nmol/L, $P = .008$), as did IDL particle concentration (0.7 ± 2.5 nmol/L, $P < .0001$). The concentration of medium HDL particles decreased significantly with exercise training (-0.2 ± 0.4 μmol/L, $P < .0001$). Mean VLDL particle size also decreased significantly with exercise training (-1.7 ± 0.9 nm, $P < .0001$), and mean HDL particle size increased significantly with exercise training (0.1 ± 0.0 nm, $P = .04$). Although not statistically significant, mean LDL particle size increased (0.2 ± 0.1 nm, $P = .19$) (Table 3).

4. Discussion

Our study demonstrates the positive effects of endurance exercise training on conventional and NMR measures of plasma lipoproteins and lipids, independent of diet, baseline body composition, and changes in body composition with training. As addressed in the ATP III guidelines and numerous recent studies, such findings are important, as the evaluation of CVD risk due to a poor plasma lipoprotein lipid profile could be enhanced through the analysis of lipoprotein subfractions in addition to the conventional lipoprotein lipid panel, as well as demonstrating CVD risk reduction independent of body fat levels or changes [2-4,26]. The value of measuring the lipoprotein subfractions is further highlighted by the fact that even small changes within specific size ranges for the lipoprotein particles are associated with important clinical differences in CVD risk [27]. For example, for a given level of LDL-C, individual CVD risk differs depending primarily on LDL particle number and secondarily on particle size [3,4,6]. Greater risk is conferred by having larger numbers of LDL particles and, when this particle number is elevated, having more smaller rather than larger LDL particles [3-5]. For VLDL, very large VLDLs are more strongly associated with CHD than smaller VLDLs, whereas for HDL particle subfractions, large HDLs are more protective than small HDLs [3,5,7]. Thus, although not statistically significant, beneficial changes were found with VLDL particle size decreasing and LDL size increasing with exercise training. HDL particle size did increase significantly with exercise training. Another benefit of measuring subfractions is that they can provide risk assessment information, such as detecting changes in subfraction concentrations with an intervention, even when the standard lipid panel remains unchanged [3,5,7]. In addition, with our training program consisting of 40 minutes of exercise, 3 days per week, at 70% of $\dot{V}O_2$max for a period of at least 14 weeks (subjects spent 10 weeks building up to the required intensity) and a weekend walk, the general population could be expected to participate in such an exercise program and benefit from it by reducing their CVD risk through plasma lipoprotein and lipid profile improvements, independent of initial body fat levels and change in body fat with training. Thus, these results have practical importance as health professionals search for tools that provide earlier detection of CVD risk and interventions that will reduce that risk in the general public.

Several studies show that endurance exercise training has a beneficial effect on conventional plasma lipoprotein lipids [7,28]. For example, although not statistically significant, we found HDL-C increased 3.3 mg/dL (7%) with exercise training, which is comparable with previous findings of increases of 2 to 8 mg/dL (4%-18% or a mean of 10%) [29]. However, the response of plasma lipoprotein lipids to even standardized exercise training is highly variable among individuals because we found that the increases in HDL-C ranged from an 8-mg/dL decrease to a 15-mg/dL increase, which is consistent with previous findings [7,9-11,30,31]. However, the influence of endurance exercise training on plasma lipoprotein subfraction concentrations, independent of diet, initial levels of body fat, or change in body fat, is not clear [7,26,28]. Kraus et al [7] studied the effects of different amounts and intensities of exercise on NMR-measured plasma lipoproteins and lipoprotein subfractions. Compared with a control group, subjects in all exercise groups improved lipoprotein lipid profiles. These improvements were achieved with minimal weight loss. However, the investigators did not assess whether even this minimal weight loss may have affected the changes in plasma lipoprotein and lipid profiles with exercise training. In addition, improvements were found in particle concentrations and size that would not have been detected with the conventional plasma lipoprotein lipid profile, highlighting the importance of lipoprotein subfraction assessment.

However, to date the question of whether baseline body composition or changes in body composition with training cause the change in lipoproteins and lipids that occur with training has not been definitively addressed [7,12-17]. Suggesting that changes in lipoprotein lipids with exercise training are dependent on initial body composition, Nicklas et al [12] found that plasma HDL-C and HDL_2-C increased significantly with exercise training in lean and moderately obese middle-aged and older men, but did not change significantly in obese men of the same age. Supporting changes in body weight/composition as the means by which training improves lipids, Wood et al [13] found that fat loss

produced comparable changes in lipoproteins whether achieved through diet or exercise. Several other studies also showed beneficial changes in lipoproteins with exercise training that were attributed to large amounts of weight loss that occurred with training [16,17]. However, supporting an independent effect of training on changes in lipoproteins, 2 studies [14,15] found an increase in HDL-C even with nonsignificant reductions in fat mass, and Kraus et al [7] found beneficial changes in lipoproteins and lipoprotein subfractions despite minimal weight change.

Our study extends the findings of Kraus et al [7] that endurance exercise training improves plasma lipoprotein and lipid profiles despite minimal weight change by standardizing diet and statistically controlling for body fat in addition to minimizing weight loss. For example, in our study, subjects had small but statistically significant reductions in weight and body fat. However, after statistically controlling for either baseline body fat or training-induced changes in body fat, significant beneficial plasma lipoprotein lipid changes were still evident, indicating an independent effect of training on plasma lipoprotein and lipoprotein lipids. More specifically, these analyses showed similar beneficial results overall except for HDL-C, HDL_2-C, and medium VLDL particle concentration. For all of these measures except medium VLDL concentration, the change with exercise training was significant only when accounting for changes in body fat, suggesting an independent effect of exercise training over and above the influence attributable to change in body fat. For medium VLDL particle concentration, the changes with training appeared attributable to changes in body fat and not to an independent effect of exercise training. Because of the known risk associated with small LDL particle size, it is important to note that although not statistically significant, LDL particle size did increase. This differs from the finding of Kraus et al, who did find a significant increase in LDL particle size in the exercise training groups compared with the control group. However, it does not appear that any covariates were used in this analysis. In our study, when all covariates except a body fat phenotype were used in the model, change in LDL particle size approached significance ($P = .09$), and when no covariates were used in the model, the change was highly significant ($P < .0001$).

In addition to controlling for body fat, our subjects followed a standardized diet and remained under dietary control before baseline testing and throughout exercise training, thus showing that the plasma lipoprotein lipid improvements could not have been the result of dietary alterations. Overall, these results further support the independent beneficial effect of exercise training on changes in plasma lipoprotein and lipoprotein lipid levels. This is important because it demonstrates that individuals can reap positive health benefits from moderate exercise training irrespective of their baseline body fat levels and without having any significant training-induced reductions in their body fat.

In addition, our subjects had at least one NCEP-defined lipid abnormality; thus, our results provide evidence for the benefits of a moderate endurance exercise training program on plasma lipoproteins and lipids in a population identified in the AHA Scientific Statement on Exercise and Physical Activity in the Prevention and Treatment of Atherosclerotic CVD as being understudied in terms of exercise training [28].

Major strengths of this study include dietary and initial physical activity control, a prolonged exercise training intervention, and NMR analysis of plasma lipoproteins. The control of diet and initial physical activity level, in conjunction with the prolonged exercise training and more precise lipoprotein measures, allowed for improved detection of associations between exercise training and changes in plasma lipoprotein and lipid levels without the confounding effects of disparate diets and exercise.

In conclusion, our data provide evidence for the beneficial effects of moderate intensity endurance exercise training, independent of diet, baseline body fat, and body fat change with training, on plasma lipoprotein and lipid profiles in middle- to older-aged women and men at risk for CVD. In addition, the findings provide further evidence that both conventionally measured plasma lipoprotein lipid levels and NMR-measured plasma lipoprotein subfractions (particle concentrations and size) are improved in an antiatherogenic direction by endurance exercise training. As the need to reduce CVD risk is critical, these findings help provide a foundation for formulating CVD risk reduction strategies, including feasible exercise training programs, for application to the general public.

Acknowledgment

This study was supported by National Institutes of Health grants AG00268 (A.H. and J.M.H.), AG023464 (A.H.), AG17474 (J.M.H.), and AG15389 (J.M.H.), the Geriatric Research, Education, and Clinical Center and Medical Research Service of the Department of Veterans Affairs (A.P.G.), and the University of Maryland Claude D. Pepper Older American Independence Center grant 2P60 AG12583 (A.P.G.).

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