Effect of Prolonged Exercise Training Without Weight Loss on High-Density Lipoprotein Metabolism in Overweight Men

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This study examined the effect of exercise training without weight loss on high-density lipoprotein (HDL) metabolism in overweight men. We evaluated HDL metabolism using ^{125}I-radiolabeled autologous HDL in 17 overweight men aged 40 ± 7 years (mean ± SD) before and after 1 year of exercise training. Subjects consumed defined diets in a metabolic kitchen during the metabolic studies. They performed endurance exercise under supervision for 1 hour four times weekly and maintained their pretraining body weight. Maximal oxygen uptake ($\dot{V}O_2$max) increased 27% ($P < .001$) with exercise training. HDL-cholesterol (HDL-C) and apolipoprotein (apo) A-I increased 10% and 9%, respectively ($P < .001$ for both), whereas triglycerides and apo B decreased 7% and 10%, respectively ($P < .05$). Postheparin lipoprotein lipase increased 11% (P = NS). Hepatic triglyceride lipase activity (HTGLA) decreased 12% ($P < .05$). The fractional catabolic rate (FCR) of HDL protein and of apo A-I decreased 5% and 7%, respectively ($P < .05$ for both). The synthetic rate of apo A-I increased 13% ($P < .01$). Increased HDL after exercise training is associated with both decreased HDL protein catabolism and increased HDL apo A-I synthesis. Weight loss is not required to increase HDL-C with exercise training in overweight men, but without weight loss, even prolonged exercise training produces only modest changes in HDL-C concentrations.

HIGH-DENSITY LIPOPROTEIN (HDL)-cholesterol (HDL-C) concentrations are markedly elevated in endurance athletes compared with sedentary controls,[1-3] and exercise training produces modest increases in HDL-C levels in previously sedentary subjects.[4,5] Serum triglycerides are also reduced in active subjects[2,3] and with exercise training,[5] but exercise has little effect on total and low-density lipoprotein (LDL) cholesterol concentrations. The metabolic mechanisms that increase HDL concentrations with exercise are not clear. HDL apoprotein survival is enhanced in endurance athletes compared with untrained controls,[1,2] but to our knowledge, only one prior study examined HDL metabolism before and after exercise training.[5] The physiologic changes required to increase HDL-C with exercise are also not well defined. Some investigators have suggested that weight loss associated with exercise training is primarily responsible for HDL-C changes.[4,6] However, others have documented increases in HDL-C after exercise training without changes in body weight or estimated body fat,[5] and at least one study suggests that the effects of exercise training and weight loss are independent and additive.[7] Consequently, the present study further examined HDL-C levels and HDL apoprotein survival before and after 1 year of exercise training without weight loss in overweight sedentary men.

SUBJECTS AND METHODS

Protocol

The study consisted of 12 months of exercise training at a stable body weight. Lipid levels were obtained and studies of HDL metabolism were performed before and after training during 18 days of a controlled diet. Subjects remained physically inactive during the first metabolic study. Subjects then exercise-trained under supervision for 1 year. All men were counseled to maintain their initial body weight during these 12 months.

Subjects

Subjects were recruited by advertisement in local newspapers. Subjects were required to be healthy and free of orthopedic problems likely to interfere with exercise, not to have smoked cigarettes for at least 1 year, to weigh more than the 75th National Health and Nutrition Examination Survey (NHANES)[8] percentile for their height, and to have exercised no more than once per week during the preceding 6 months. Respondents to the newspaper advertisement were interviewed by telephone, and potential subjects were invited to a screening visit. All subjects provided written informed consent before screening. Two lipid values were obtained approximately 1 week apart. To recruit subjects with reasonably stable HDL-C concentrations, a third blood sample was obtained if the initial two HDL-C values differed by greater than 10%. Subjects were excluded if no two of the three HDL-C levels were within 10% or if any total cholesterol or triglyceride determination was greater than 300 mg/dL.

Potential subjects underwent a complete physical examination, a screening maximal exercise test, and serological testing for human immunodeficiency virus and hepatitis B infection, and were disqualified if abnormalities were detected. One subject each was excluded for hypertension and a pes cavus foot deformity. A subject who developed left bundle branch block during exercise was included after a thallium exercise stress test was normal.

Subjects entered the research protocol in groups of five or six. Six subjects discontinued participation because of time limitation (n = 4), recurrence of a neck injury unrelated to exercise training (n = 1), and family illness (n = 1). Seventeen men completed the training protocol and form the basis for this report.

Controlled Diet Periods

Subjects were maintained on controlled diets for 18 days during each study of HDL metabolism. Alcohol was prohibited for 2 weeks before and throughout each diet period. Breakfast was served in a metabolic kitchen. Lunch and dinner were provided in the morning for consumption during the day. Adherence to the diets was complete as assessed by

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Submitted May 21, 1996; accepted August 6, 1996.

Supported by National Institutes of Health Grant No. HL-28467 and by the Miriam Foundation, the Haire Family, William Jakober, and the McNulty Family.

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0026-0495/97/4602-0019$03.00/0

direct questioning and anonymous questionnaires administered at the end of the protocols.

Body weight was measured daily during the controlled diets, and energy intake was adjusted to maintain each subject's body weight. A basic diet composed of conventional foods and containing 2,400 or 2,800 kcal was provided to study subjects. This diet contained 17% protein, 43% carbohydrate, and 40% fat. Saturated, monounsaturated, and polyunsaturated fats accounted for 18%, 16%, and 6% of total calories, respectively. Cholesterol content was 550 mg/d during both diets. Caloric requirements were initially estimated using the Nutripractor computer program (Practocare, San Diego, CA) and were confirmed to be ±3.65% of total calories by chemical analysis (Tech S; National Food Laboratory, Washington, DC). Supplements to the basic diet were used to maintain individual body weights. The supplements were specially formulated muffins for which the composition of protein, fat, and carbohydrate was identical to that of the basic diet. We have previously tested this diet in sedentary subjects and have shown that stable lipid and lipoprotein concentrations are achieved after 14 days.[2] Potassium iodide (100 mg/d) was administered for 3 days before and during the metabolic studies to block thyroidal uptake of radioiodine.

The energy content of the diet during the second diet period was increased individually to cover the energy cost of exercise. The overall dietary composition was kept constant. Individual increases were designed to approximate the estimated energy expended during training, and were calculated as training intensity (75% measured maximal oxygen uptake [$\dot{V}o_2max$], L/min) × 50 (minutes trained per day) × 4.825 (calories burned per liter of oxygen) × 4 (days trained per week)/7 (days per week) to yield the additional calories per day.

Exercise Training

Subjects were required to participate in four supervised sessions weekly. Each session consisted of 5 minutes of warm-up and stretching exercises followed by 50 minutes of walking, jogging, and stationary cycling and 5 minutes of cool-down activity. Subjects self-selected their training mode, although some subjects were temporarily restricted to stationary cycling when minor orthopedic problems threatened to limit walking or jogging activity. Exercise intensity was designed to elicit 60% to 80% of the subject's measured absolute maximal heart rate. Training heart rate was monitored by palpation throughout each training session by a research technician. Subjects were required to attend all exercise sessions or to attend make-up sessions. During vacations or business trips, subjects recorded their exercise sessions in an exercise diary. Compliance with the program was high, and no subject missed more than 5 days of training over the 12 months. Breakfast and snacks were provided to the subjects after the training sessions to help maintain body weight.

Lipoprotein Measurements

Venous blood samples were obtained on days 1 and 9 to 19 of the diet periods. Subjects were seated during phlebotomy and had not eaten or exercised during the preceding 12 hours. Serum was separated from blood within 2 hours of phlebotomy and stored at −70°C. Cholesterol[9] and triglycerides[10] were assayed by enzymatic methods. LDL cholesterol level was calculated.[11] HDL-C and HDL_2 and HDL_3 subfractions were estimated by the double-precipitation method of Gidez et al.[12] Apolipoprotein (apo) A-I,[13] apo A-II,[14] and apo B[15] were determined with double-antibody radioimmunoassay. Purified apoproteins were used as standards for apo A-I and apo A-II. Ultracentrifugally isolated LDL was used as the standard for apo B. Interassay coefficients of variation for apo A-I, apo A-II, and apo B were 4.3%, 4.7%, and 5.4%, respectively. All lipid and lipoprotein samples from an individual subject were analyzed in a single autoanalyzer assay at the end of each diet period.

HDL Metabolic Studies

HDL apoprotein kinetics were studied during diet days 9 to 19. Plasma anticoagulated with heparin was obtained from fasting subjects 8 days before tracer administration. HDLs were isolated by sequential preparative ultracentrifugation (d = 1.080 to 1.21 g/mL) and were centrifuged through a protein-free salt solution at the higher density. Following dialysis against 0.15-mol/L sodium chloride, HDLs were radioiodinated using the iodine monochloride technique,[16] diluted in autologous lipoprotein-free serum, and sterilized by passage through a 0.2-mm filter. Fasting subjects were administered 45 to 50 μCi ^{125}I-HDL. Subsequent blood samples were drawn after 10 minutes at 1 hour, and daily for the next 10 days. Plasma volume was calculated from the isotopic dilution in the 1-hour (time 0) sample. Radioactivity attributable to apo A-I and apo A-II was quantified by immunoprecipitation. For the immunoprecipitation procedure, equal volumes of serum and 0.2-mol/L sodium cholate were incubated for 1 hour at 37°C. Lipoprotein-free goat anti–A-I or anti–A-II in sufficient quantity to fully precipitate the apoprotein was then added and incubated at 37°C for 1 hour. Polyethylene glycol (molecular weight, 8,000) was added to produce a final concentration of 2%, and the mixture was incubated overnight at 4°C. The sample was then centrifuged at 3,000 rpm for 30 minutes, radioactivity was determined in the supernatant and the precipitate, and radioactivity attributable to the specific apoprotein concentration was calculated. The plasma radioactivity die-away curve in each case was biexponential. The slopes and intercepts were calculated by computer methods with a curve-peeling program that uses modified least-squares analysis and a biexponential decay model. The distribution of HDL between intravascular and extravascular compartments was computed from the slopes and intercepts of the two exponentials.[17] The fractional catabolic rate (FCR) was determined from the area under the decay curve. Synthetic rates were calculated as the product of the FCR, plasma apoprotein concentration, and plasma volume.

Fat Tolerance Testing

Intravenous fat clearance (K_2) was assessed in the fasting state on day 19 of the controlled diet period as previously described[18] using a fat emulsion (1 mL/kg pretraining body weight, Intralipid 10%; Baxter-Travenol Laboratories, Deerfield, IL). The same amount of Intralipid was administered to an individual at each measurement period.

Lipase Determination

Heparin (75 IU/kg pretraining body weight) was injected intravenously immediately after the fat tolerance test, and plasma was obtained 10 minutes later to quantify lipoprotein lipase (LPLA) and hepatic triglyceride lipase (HTGLA) activities.[18] The same amount of heparin was administered after the second diet period.

Table 1. Exercise, Anthropometric, and Caloric-Intake Measurements (mean ± SD) at Baseline and After 12 Months of Exercise Training

Characteristic	Baseline	12 Months	Change
Age (yr)	40 ± 7		
Weight (kg)	93.0 ± 11.6	93.5 ± 11.6	0.6 ± 1.3
BMI (kg/m²)	28.1 ± 2.5	28.2 ± 2.6	0.2 ± 0.4
Body fat (%)	24.5 ± 4.5	23.7 ± 4.4	−0.8 ± 2.3
WHR	0.90 ± 0.04	0.89 ± 0.04	−0.01 ± 0.03
$\dot{V}o_2max$			
L/min	3.11 ± 0.39	3.95 ± 0.46	0.84 ± 0.34*
mL/kg/min	33.4 ± 2.9	42.5 ± 5.1	9.0 ± 4.0*
Calories (kcal/d)	3,065 ± 229	3,505 ± 256	440 ± 90*

Abbreviations: BMI, body mass index; WHR, waist to hip ratio.
*$P < .001$.

Table 2. Lipoprotein Concentrations, Lipolytic Activities, and Intravenous Fat Clearance Rate (mean ± SD) at Baseline and After 12 Months of Exercise Training

Parameter	Baseline	12 Months	Change
Cholesterol (mmol/L)			
HDL	1.01 ± 0.18	1.11 ± 0.23	0.10 ± 0.10‡
HDL_2	0.18 ± 0.12	0.24 ± 0.16	0.06 ± 0.07‡
HDL_3	0.82 ± 0.13	0.86 ± 0.11	0.04 ± 0.10
Total	5.40 ± 0.70	5.33 ± 0.54	−0.08 ± 0.47
LDL	3.75 ± 0.65	3.62 ± 0.52	−0.13 ± 0.39
Triglycerides (mmol/L)	1.45 ± 0.47	1.33 ± 0.44	−0.10 ± 0.19*
Apolipoproteins (mg/dL)			
A-I	119 ± 18	129 ± 14	11 ± 11‡
A-II	35 ± 5	35 ± 8	0 ± 6
B	126 ± 17	113 ± 16	−13 ± 18†
Lipase activity (μmol FFA/mL/h)			
LPLA	10.3 ± 3.0	11.4 ± 3.9	1.1 ± 3.0
HTGLA	17.6 ± 7.5	15.5 ± 6.3	−2.1 ± 3.3*
K_2 (%/min)	2.8 ± 0.6	3.0 ± 0.5	0.2 ± 0.6

Abbreviations: FFA, free fatty acids; K_2, intravenous fat clearance rate.

*$P < .05$.

†$P < .01$.

‡$P < .001$.

Exercise Measurements

Subjects were acclimated to the exercise test procedure by exercising with measurement equipment in place several days before the initial exercise test. Subjects subsequently performed a Bruce exercise test on a Quinton model 1860 treadmill (Quinton Instruments, Seattle, WA). Oxygen uptake was determined by standard open-circuit spirometric techniques[19] at rest and during each minute of the test until the subject could not continue. $\dot{V}O_2$max was defined as the highest $\dot{V}O_2$ achieved at exhaustion. Heart rate was recorded simultaneously with each $\dot{V}O_2$ determination by a Marquette Series 4000 electrocardiograph (Marquette Electronics, Milwaukee, WI).

Anthropometric Measurements

Percent body fat was estimated from the sum of skinfold thicknesses of the chest, abdomen, and thigh.[20] Circumference measurements of the natural waist and buttocks were used to determine the waist to hip ratio. Body weight was measured at each exercise session.

Statistical Analysis

Each subject's lipid values from the last 11 days of each diet period were averaged and used in data analysis. Changes from baseline were analyzed with a paired t test. Spearman correlation coefficients were used to examine relations between selected baseline variables and 1-year change and between 1-year change scores. Statistical significance was set at P less than .05. Results are expressed as the mean ± SD.

RESULTS

Exercise and Anthropometric Measurements

$\dot{V}O_2$max, expressed either as the absolute value or relative to body weight, increased 27% ($P < .001$) with exercise training (Table 1). Body weight, estimated percent body fat, and the waist to hip ratio did not change. Daily caloric intake was 3,065 ± 229 during the initial diet period and 3,505 ± 256 during the final diet period ($P < .001$).

HDL Concentrations

Average HDL-C concentrations increased 4 ± 4 mg/dL (0.10 ± 0.10 mmol/L), or 10% ($P < .001$), with exercise training. HDL-C failed to increase in only three of 17 subjects. Individual changes ranged from −3 to +11 mg/dL (−0.07 to +0.28 mmol/L) (Table 2 and Fig 1). A larger proportion of the increase in HDL-C with exercise training occurred in the HDL_2 subfraction. Apo A-I also increased 9% ($P < .001$), whereas apo A-II concentration did not change.

Other Serum Lipids, Lipase Activities, and Fat Tolerance

Triglyceride levels decreased 9 ± 17 mg/dL (0.10 ± 0.19 mmol/L), or 7% ($P < .001$), with exercise training, with individual changes ranging from −39 to +23 mg/dL (−0.44 to +0.25 mmol/L) (Fig 1). Triglycerides failed to decrease in only three of 17 men, one of whom also showed no increase in HDL-C. Total and LDL cholesterol concentrations did not change, but apo B levels decreased 10% ($P < .01$). LPLA

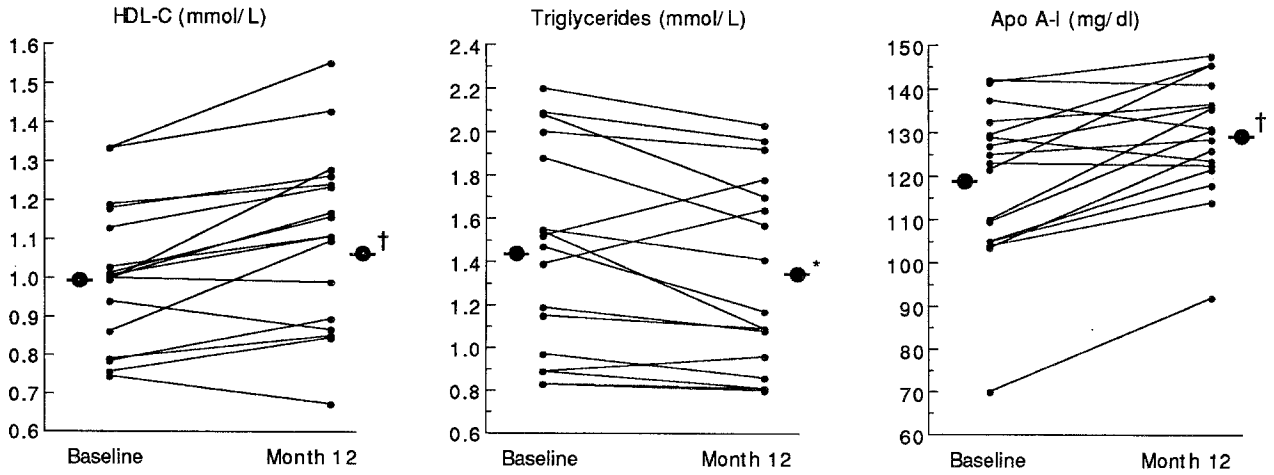

Fig 1. Individual and mean HDL-C, triglyceride, and apo A-I values at baseline and after 1 year of exercise training. *$P < .05$; †$P < .001$.

Table 3. Parameters of HDL Metabolism (mean ± SD) at Baseline and After 12 Months of Exercise Training

Parameter	Baseline	12 Months	Change
Plasma volume (mL)	3,092 ± 354	3,442 ± 273	350 ± 374‡
FCR (pools/d)			
HDL	0.220 ± 0.031	0.210 ± 0.030	−0.010 ± 0.016*
Apo A-I	0.230 ± 0.031	0.212 ± 0.032	−0.017 ± 0.019†
Apo A-II	0.203 ± 0.024	0.190 ± 0.036	−0.013 ± 0.030
Biological half-life (d)			
HDL	4.87 ± 0.57	5.17 ± 0.74	0.30 ± 0.38†
Apo A-I	4.76 ± 0.95	5.20 ± 0.89	0.44 ± 0.79*
Apo A-II	5.41 ± 0.83	5.71 ± 1.31	0.30 ± 1.39
Synthetic rate (mg/d)			
Apo A-I	825.0 ± 116.2	931.2 ± 109.2	106.2 ± 142.2†
Apo A-II	215.8 ± 36.9	220.3 ± 48.0	4.5 ± 56.6
Synthetic rate (mg/kg/d)			
Apo A-I	9.0 ± 1.5	10.1 ± 1.5	1.1 ± 1.5
Apo A-II	2.3 ± 0.4	2.4 ± 0.6	0.1 ± 0.6

*$P < .05$.
†$P < .01$.
‡$P < .001$.

increased 11% with exercise ($P > .05$), whereas HTGLA decreased 12% ($P < .05$). Intravenous fat clearance rates increased slightly but not significantly.

HDL Kinetic Studies

Baseline catabolic rates were similar to values previously reported for sedentary subjects.[2,5] The FCR of HDL decreased 5% ($P < .05$) with exercise training (Table 3 and Fig 2). Catabolic rates of apo A-I and apo A-II decreased by 6% to 7% with training, but changes in apo A-II catabolism did not achieve statistical significance ($P = .08$). Actual decay curves are not presented, because these changes are small and were not apparent from visual inspection alone. Reductions in HDL and apo A-I catabolism with exercise training were associated with comparable increases in HDL and apo A-I half-life values. The synthetic rate of apo A-I increased 13% after exercise training ($P < .01$), whereas the synthetic rate of apo A-II was unchanged.

Table 4. Spearman Correlation Coefficients Between Variables at Baseline and Change (Δ) at 1 Year of Exercise Training (N = 17)

	ΔHDL	ΔHDL_2	ΔHDL_3	ΔTG	ΔApo A-I	ΔApo A-II	$\Delta\dot{V}O_2max$ L	$\Delta\dot{V}O_2max$ mL
HDL	.13	.78†	−.25	−.15	−.26	.14	.23	.45
HDL_2	.26	.36	.18	−.08	−.33	.24	.46	.59*
HDL_3	−.04	.76†	−.58*	−.17	−.15	−.05	−.05	.09
TG	−.18	−.70†	.17	−.59*	.02	−.04	−.40	−.41
Apo A-I	−.11	.29	−.12	−.19	−.68†	.12	.36	.60*
Apo A-II	.37	.54*	−.07	−.35	.14	.06	.17	.19

Abbreviation: TG, triglycerides.
*$P < .05$.
†$P < .01$.

Correlations Between Baseline Values and Change With Training

The change in HDL-C with exercise training was not related to any baseline parameter of lipid metabolism, body composition, or $\dot{V}O_2max$ (data not shown). Baseline HDL-C ($r = .78$) and HDL_3 ($r = .76$) were directly correlated with the change in HDL_2 ($P < .01$ for both), indicating that men with the highest initial HDL-C and HDL_3 levels experienced the greatest HDL_2 increment with training (Table 4). In contrast, baseline triglycerides were inversely related to the change in HDL_2 ($r = -.70$, $P < .01$), indicating that increases in HDL_2 were greatest in men with initially low triglyceride levels. Baseline triglyceride levels were also negatively related to the change in triglycerides ($r = -.59$, $P < .05$), demonstrating that triglycerides decreased the most in men with the highest baseline values. Similarly, pretraining apo B levels were inversely related to the subsequent change in apo B levels ($r = -.56$, $P < .05$) and to the change in triglycerides ($r = -.49$, $P < .05$; data not shown). Changes in LPLA after exercise training were directly related to baseline HDL-C ($r = .56$), HDL_2 ($r = .62$), and apo A-I ($r = .53$, $P < .05$ for all), indicating that increases in LPLA were greatest in subjects with higher baseline HDL levels.

The increase in $\dot{V}O_2max$ was directly related to baseline HDL_2 and apo A-I levels. These relationships were significant only when the change in $\dot{V}O_2max$ was expressed relative to body weight. Baseline estimated percent body fat was inversely related to the increase in $\dot{V}O_2max$ ($r = -.41$, P = NS for

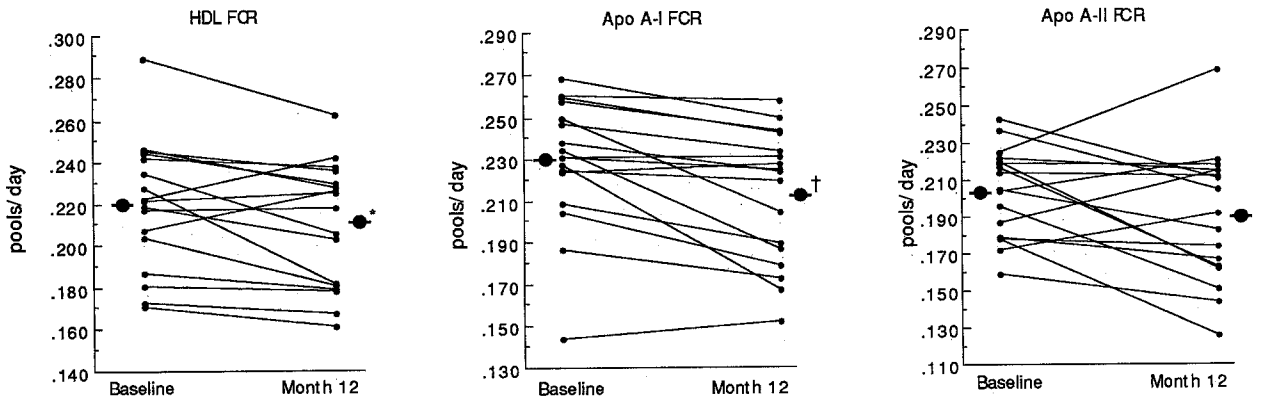

Fig 2. Individual and mean HDL, apo A-I, and apo A-II FCRs at baseline and after 1 year of exercise training. *$P < .05$; †$P < .001$.

L/min; $r = -.50$, $P < .05$ for mL/kg/min; Fig 3), although the baseline waist to hip ratio and body weight were not related to subsequent $\dot{V}O_2$ change. This suggests that fatter men at baseline obtained a less robust cardiovascular adaptation to exercise training when weight loss was not permitted.

Correlations Between Changes With Training

Changes in HDL-C correlated directly with changes in apo A-I ($r = .55$, $P < .05$) and negatively with changes in FCRs for apo A-I ($r = -.74$, $P < .01$) and apo A-II ($r = -.48$, $P < .06$). Changes in HDL were not importantly related to changes in apoprotein synthetic rates, lipase activites, fat tolerance, or exercise capacity. Changes in both apo A-I ($r = .55$, $P < .05$) and apo A-II ($r = .76$, $P < .01$) were positively related to changes in apo A-I and apo A-II synthetic rates, respectively.

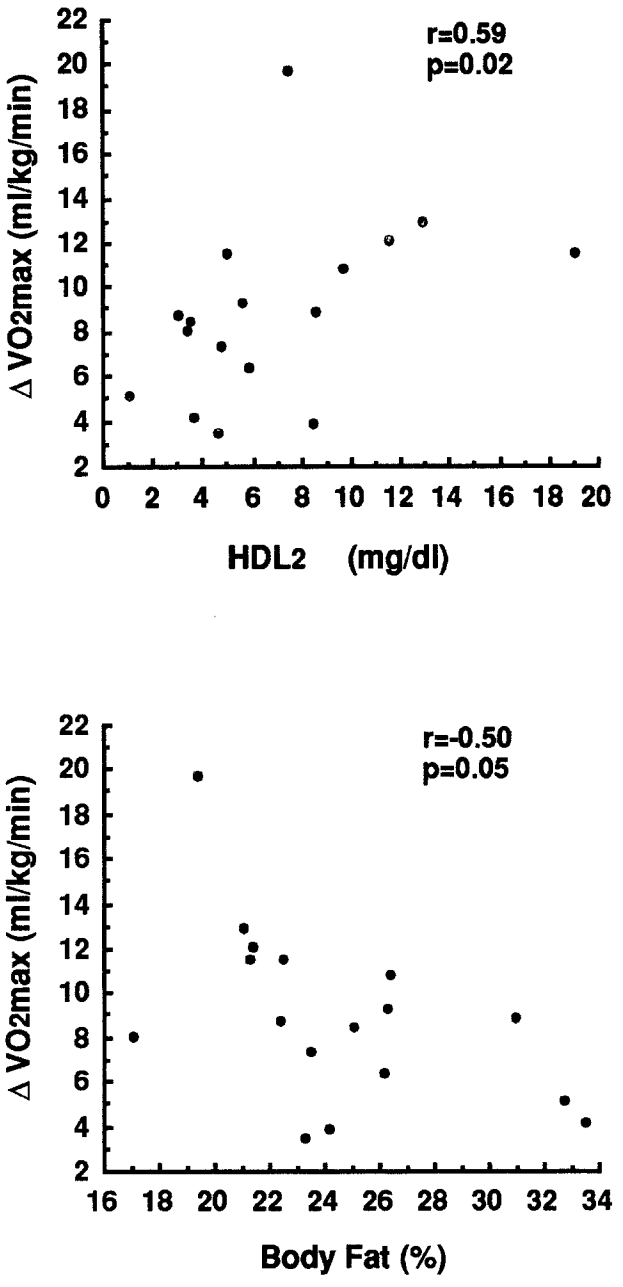

Fig 3. Correlations between baseline HDL_2 and estimated body fat and change (Δ) in $\dot{V}O_2$max (mL/kg/min) after 1 year of exercise training.

DISCUSSION

The present study examined the effects of exercise training without weight loss on HDL metabolism. Dietary variation was eliminated by measuring lipid levels while subjects consumed defined diets provided by a metabolic kitchen. Lipid levels before and after training were the mean of nine measurements in each subject. Participants exercised under supervision for at least 4 hours weekly for 1 year. Subjects were financially reimbursed for their efforts to ensure adherence to the exercise training protocol. Body weight was maintained to isolate the independent effects of exercise training on serum lipids.

Increases in HDL-C in the present study were associated with 5% to 7% reductions in FCRs for radiolabeled total HDL protein and for apo A-I and apo A-II. The synthetic rate for apo A-I (milligrams per day) also increased 13% with exercise training. The reduction in HDL protein catabolic rates and the increase in the apo A-I synthetic rate suggest that exercise training decreases HDL particle clearance and increases apo A-I synthesis. This agrees with reports that HDL catabolic rates are 20% lower in endurance athletes than in sedentary men[2] and that apo A-I synthetic rates are 10% higher in athletes.[21] Apo A-II synthetic rates are also slightly lower in endurance athletes,[2,21] but were not changed by 1 year of training in the present study. Consequently, it appears that prolonged exercise training both decreases HDL protein catabolism and increases apo A-I synthesis with little effect on the apo A-II synthetic rate.

Nevertheless, the overall effect of intense exercise training on serum lipids was small. Total and LDL cholesterol did not change. Triglycerides decreased only 9 mg/dL (0.10 mmol/L), or 7%, but baseline triglyceride levels were low and triglycerides decreased the most in men with the highest baseline values. The mean HDL-C level increased 4 mg/dL (0.10 mmol/L), or 10%.

These changes in HDL-C, although small, are among the larger increments reported with exercise training. A meta-analysis of 59 exercise training studies reported an average increase in HDL-C concentrations of approximately 2 mg/dL (0.05 mmol/L).[22] However, even such modest changes, if applied to a sufficient number of subjects, could have important effects on coronary heart disease incidence, since each 1-mg/dL (0.026-mmol/L) increment in HDL-C theoretically confers a 2% to 4% reduction in heart disease risk.[23] Nevertheless, the present report and prior reports[4,5,24] of prolonged exercise demonstrate smaller mean increases in HDL-C and other serum lipids than are expected by most clinicians.

The present study examined the effects of exercise training without weight loss on HDL metabolism, and neither body weight, estimated body fat, nor the waist to hip ratio changed. This is critical, because several studies suggest that weight loss is the primary physiologic mechanism by which exercise training increases HDL-C,[4,6] although few studies have examined this issue directly. Sopko et al[7] compared the independent and combined effects of exercise and weight loss on HDL-C levels in overweight men. Both exercise groups expended 3,500

kcal/wk by treadmill walking, and each weight loss group lost 6 kg over 12 weeks. The combination of exercise and weight loss increased HDL-C by 5.5%, or 2 mg/dL (0.05 mmol/L), whereas weight loss or treadmill walking alone increased HDL-C by only 2.0% to 2.4%, or 1 mg/dL (0.025 mmol/L). Similarly, the meta-analysis cited earlier reported a 3.3%, or 1.7-mg/dL (0.04-mmol/L), increase in HDL-C concentrations among 33 exercise training studies when body weight did not change, and a 4.9%, or 2.3-mg/dL (0.06-mmol/L), increment in HDL-C in 19 training studies when subjects lost weight.[22] These results suggest that the effects of exercise and weight loss on HDL-C are additive, but that even this cumulative effect generally produces only small mean increases in HDL-C.

Despite the small mean increase in HDL-C in the present study, some subjects demonstrated markedly higher HDL-C levels after training. Williams et al,[24] in a 1-year training study, noted that the largest increases in $\dot{V}O_2$max and HDL-C occurred in men induced to run the most miles. However, men running the most miles had the highest pretraining HDL-C and lowest triglyceride concentrations. Baseline HDL-C remained a significant predictor of miles run even after adjusting for baseline body fatness. The investigators suggested that initial lipid levels, or some unmeasured but associated factor, facilitate participation in endurance activities that further elevate HDL levels. The relationship between baseline HDL-C and the increase in $\dot{V}O_2$max was not presented.[24]

In the present study, baseline HDL-C ($r = .45$, P = NS), HDL_2 ($r = .59$, $P < .05$), and apo A-I ($r = .60$, $P < .05$) were directly related to the exercise-induced increase in $\dot{V}O_2$max expressed per kilogram body weight. However, baseline percent body fat was also inversely related to the subsequent increase in $\dot{V}O_2$max expressed relative to body weight ($r = -.50$, $P = .05$) and baseline HDL_2 and apo A-I were no longer significant predictors of the change in $\dot{V}O_2$max after controlling for baseline body fat. Consequently, the relationship between baseline HDL_2 and apo A-I and the change in $\dot{V}O_2$max is mediated through fatter men achieving less of a physiologic effect from exercise training. This may mean that fatter men exercised less, although we did not quantify the distance run by the subjects since our training regimen was based entirely on time spent exercising. Baseline body fat did not correlate with the change in any lipid level or parameter of HDL metabolism ($r \leq \pm .29$, P = NS).

The possibility that fatter men exercise less even in this supervised training program may explain the discrepancy between studies that do or do not conclude that weight loss is required for exercise to increase HDL-C. There is little doubt that exercise alone can increase HDL, since even a single exercise session increases HDL-C in sedentary men.[25] In supervised training programs, overweight men are more likely to exercise and thereby obtain an increase in HDL-C. However, in less structured programs, weight loss may be required either to increase HDL-C directly or to facilitate enough exercise to produce an HDL-C increase.

LPLA increased 11% with exercise training, although this change was not statistically significant. LPLA facilitates the catabolism of lower-density lipoproteins and the transfer of redundant surface material including free cholesterol to HDL.[26] LPLA is increased in endurance athletes,[1] enhanced by an isolated exercise session,[11,25,27] and increased with exercise training.[5] We have speculated that increased LPLA may be an adaptive reaction to replete intramuscular triglycerides used during endurance exercise.[28] HTGLA, in contrast, is often lower in endurance athletes,[2] and decreases after an isolated exercise session[18,25,27] and with exercise training.[5] HTGLA is thought to delipidate HDL particles and thereby facilitate their catabolism.[26] The physiologic explanation for why exercise affects HTGLA is not clear. Plasma volume expands with exercise training,[1] and lower HTGLA may result from the expansion of plasma volume that occurs after exercise.[5] Indeed, in the present study, the 12% reduction in HTGLA with exercise training is similar to the 11% increase in plasma volume. The expansion of plasma volume could have also obscured a larger increase in LPLA by diluting LPLA.

In summary, the present results demonstrate that prolonged exercise training without weight loss in overweight men reduces HDL catabolism and increases apo A-I synthesis. However, such an exercise regimen produces only small increases in the mean HDL-C level.

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