The Effects of Physical Exercise on Plasma Prebeta-1 High-Density Lipoprotein

Mahtab Jafari, David Alexander Leaf, Holden MacRae, Julie Kasem, Patricia O'Conner, Clive Pullinger, Marry Malloy, and John P. Kane

The impact of physical exercise on high-density lipoprotein (HDL) metabolism is recognized as a major mechanism of coronary artery disease (CAD) risk reduction. Prebeta-1 HDL subparticle species play a pivotal role in initiating reverse cholesterol transport (RCT). We examined the effect of acute physical exercise on plasma prebeta-1 HDL levels. Nineteen nonsmoking, healthy men (n = 11) and women (n = 8) not receiving lipid-altering medications completed dietary surveys, and had percent body fat determinations, and fasting blood drawn for measurements of plasma lipids, lipoproteins, apolipoprotein A-I (Apo A-I), and absolute and percent prebeta-1 HDL. Each subject completed cardiopulmonary exercise stress testing to Vo_{2max} followed by a 4-km course of run-jogging. Laboratory measurements were repeated from blood drawn immediately after exercise. Mean ± SD values were determined for age, percent body fat, dietary calories, dietary cholesterol, dietary fat, and plasma lipids, lipoproteins, Apo A-I, and absolute and percent prebeta-1 HDL using 1-way analysis of variance (ANOVA). One-way ANOVA comparisons were made for measurements of plasma lipids, lipoproteins, Apo A-I, and absolute and percent prebeta HDL measurements taken before and after exercise for all subjects combined. Entry characteristics showed the following (mean ±SD): age, 24 ± 5.8 years; body mass index (BMI), 22.4 ± 2.6; percent body fat, 13 ± 5.7; and Vo_{2max}, 49.1 ± 7.9 mL O_2/kg /min. Exercise significantly increased absolute plasma prebeta HDL (0.10 ± 0.05 to 0.130 ± 0.07 μg/mL, $P = .039$) and decreased plasma HDL-triglycerides (23.3 ± 10.8 to 12.5 ± 5.6 mg/dL, $P = .012$). Our findings indicate that prebeta-1 HDL and HDL-triglyceride metabolism are significant components of the effect of acute exercise on RCT. These findings have important relevance for studies pertaining to exercise-related effects on HDL metabolism as pertains to CAD risk reduction.

PARTICIPATION IN REGULAR physical exercise pursuits is highly recommended for the prevention of coronary artery disease.[1] Among the major mechanisms by which regular physical exercise and physical exercise training mitigate coronary artery disease risk is by its impact on high-density lipoprotein (HDL) metabolism.[2-4] HDL compromises a collection of different molecular lipoprotein species containing triglycerides, cholesterol, apolipoproteins, and phospholipids that vary in composition and function. Plasma HDL plays a pivotal role in the reverse cholesterol transport (RCT) process.[5] RCT is comprised of a series of HDL-mediated steps whereby cholesterol is removed from peripheral tissues and brought to the liver where it is processed for excretion.[6] The initial step in this process involves cholesterol efflux from peripheral cells.[7,8] Gupta et al[9] have shown that the net mass of free cholesterol transport out of cultured human fibroblasts into athlete's serum was greater than that of sedentary controls. This indicates that physical exercise may promote RCT by increasing cholesterol efflux from peripheral tissues. Because specific subfractions of HDL, such as the prebeta-1 HDL fraction,[10] may be especially efficient at mediating cholesterol removal from peripheral cells, physical exercise would be anticipated to increase plasma prebeta-1 levels yet this has not been previously reported.

Prebeta-1 HDL is a molecular species of HDL that was not recognized until 1985.[11] Because of its high modal density, it was not included in HDL recovered by serum by ultracentrifugation in the traditional density interval of 1.063 to 1.21 g/mL. In addition, its rapid conversion to HDL species of larger diameter, ex vivo, by lecithin:cholesterol acyltransferase (LCAT), impeded its recognition by other techniques. The advent of a minimally perturbing chromatographic technique, selected affinity immunosorption[12] that recovers apolipoprotein A-I (Apo A-I)–containing particles quantitatively from human plasma, has permitted the subsequent recognition of HDL species of prebeta mobility, distinguishing them from the predominant mass of HDL that has alpha mobility (ie, alpha HDL).[11] Prebeta-1 HDL is a 67-kd species of plasma HDL that contains 2 copies of Apo A-I. Prebeta-1 HDL appears to be generated from both alpha HDL lipoproteins (A-I + A-II) (Lp [A-I + A-II]) and (A-I − A-II) (Lp [A-I − A-II]).[13] The measurement of prebeta-1 HDL in human plasma by an ultrafiltration-isotope dilution technique permits the methodology to examine the metabolic transitions among the native molecular species of HDL.[13,14] The evaluation of prebeta-1 HDL metabolism is may be of value in identifying mechanisms by which physical exercise-induced effects on HDL particles exert a protective action against coronary artery disease (CAD).[5]

The purpose of this study was to evaluate the effect of a single bout of protracted aerobic exercise on plasma prebeta-1 HDL levels.

MATERIALS AND METHODS

Design

The study was designed to examine the effects of a bout of protracted physical exercise on fasting plasma lipids, lipoproteins, Apo A-I, and prebeta-1 HDL levels.

Subjects

Nineteen nonsmoking men and women volunteers in self-reported good health and not taking medications that would effect their plasma

From the Department of Medicine, University of California, Irvine, Irvine, CA; UCLA School of Medicine and VA Greater Los Angeles Healthcare System, Los Angeles, CA; Department of Sports Medicine, Pepperdine University, Malibu, CA; and the Department of Medicine, University of California, San Francisco, CA.

Submitted May 13, 2002; accepted October 25, 2002.

Address reprint requests to David Alexander Leaf, MD, MPH, Division of General Internal Medicine, 111G, Greater Los Angeles VA Healthcare System, Wilshire & Sawtelle Blvds, Los Angeles, CA 90073.

0026-0495/03/5204-0024$30.00/0
doi:10.1053/meta.2003.50086

lipids (including lipid-lowering agents and oral contraceptives), maintaining their usual diets, and able to complete the required exercise protocol signed informed consent that was approved by the Pepperdine University Institutional Review Board.

Methods

Subjects refrained from participation in physical exercise and consumption of ethanol-containing beverages 3 days prior to the testing session. They reported following a 12-hour (overnight) fast to the exercise laboratory. A history and physical examination were performed to confirm each subject's health status (D.A.L.) and pre-exercise laboratory collection included the following measurements: (1) fasting plasma lipids, lipoproteins, Apo A-I, and prebeta-1 HDL; (2) percent body fat; and (3) dietary fat and cholesterol intake. Subjects were classified as exercise-trained (ET) if they reported regular participation in physical exercise of at least 45 minutes of vigorous, aerobic physical exercise training 3 times per week, or sedentary (SED) if they reported no regular physical exercise behavior. Subjects then underwent a bout of protracted physical exercise consisting of maximal cardiopulmonary exercise (CPX) stress testing followed by a 4-km run-jog (total exercise time, 45 to 60 minutes). Following the exercise bout measurements of fasting plasma lipids, lipoproteins, Apo A-I, and prebeta-1 HDL were repeated.

Procedures

Body composition. Prior to undergoing CPX testing, body composition was determined via skinfold thickness measurements at specific sites (chest, abdomen, and thigh for men; tricept, suprailliac, and thigh for women) using standard procedures.[15] Measurements at each site and on each subject were made by an experienced investigator using Harpenden skinfold calipers (British Indicators, Dover, England). Each skinfold site was measured using the thumb and index finger of the left hand to elevate a double fold of skin, with subcutaneous tissue approximately 1 cm proximal to the site being measured. Each skinfold was raised perpendicular to the surface of the body at the measurement site, with the long axis of the skinfold parallel to the natural cleavage lines of the skin. The skinfold was kept elevated until the measurement was completed, and the jaws of the caliper were placed so that the thicknesss of the skinfold was measured perpendicular to its long axis when the pressure of the caliper was released and the caliper jaws moved toward each other. A reading of the skinfold thickness, in millimeters, was made 2 seconds after the caliper was released at the skinfold site. All sites on each subject were measured once, and then each site was measured a second time. A third skinfold measurement was made if the second measurement at a particular site exceeded the first by more than 1 mm. The skinfold thickness at a particular site was taken as the average of the 2 closest measurements. Intrameasurer reliability coefficients for experienced investigators using this technique are 0.97 (tricept), 09.6 (chest), 0.98 (abdomen), 0.97 (suprailliac), and 0.98 (thigh).

CPX testing. CPX testing was conducted using a standard Bruce protocol.[16] Heart rate was continuously monitored during CPX testing by telemetry (Polar Vantage XL, Polar USA, Hartford, CT), with heart rates recorded at one-minute intervals for 10 minutes following exercise. Metabolic measurements for determination of maximal aerobic capacity (Vo_{2max}) were made using a MedGraphics CardioO_2 system (Medical Graphics, St Paul, MN). Expired gas measurements were recorded at 30 second intervals, and Vo_{2max} was determined by the following criteria: (1) $<$ 100 mL increases in Vo_2 in consecutive 30 second sampling periods prior to exhaustion, (2) respiratory exchange ratio (RER) in excess of 1.10, and (3) attainment of predicted maximal heart rate $\pm$15 bpm.

4-km exercise bout. Approximately 5 to 10 minutes after the CPX test, when subjects' heart rates had recovered to $<$ 100 bpm, they engaged in a run-jog exercise bout covering 4 km on a running track adjacent to the laboratory, at a self-selected pace. This distance was selected such that, when combined with the CPX test, the subjects would expend approximately 300 to 350 kcal in aerobic exercise. Upon completion of the run-jog, the subjects underwent a final venipuncture.

Dietary surveys. A 3-day dietary record was dispensed to all subjects within 1 week prior to the run-jog exercise session.[17,18] Subjects were instructed to list all daily food and drink intake for 2 days of the week and one day of the weekend. Portion sizes were estimated using household measures, and adherence to typical dietary intake was strongly recommended.[19] Daily caloric intake, dietary cholesterol, and fat were calculated using food composition tables.[20]

Plasma lipoproteins and apoproteins. Laboratory analysis was performed in a laboratory that participates in the standardization procedure for the National Heart Lung and blood Institute–Centers for Disease Control Lipid Standardization Program coordinated by the Centers for Disease Control, Atlanta, GA, and is certified. Two 20-mL fasting blood samples were obtained in EDTA-containing vacutainers from each subject before and immediately after exercise. The samples were stored immediately on wet ice for transport to the analytic laboratory. Each sample was cold centrifuged to collect the plasma and harvested on -60°C until assayed. Three major classes of plasma lipoproteins were separated by preparative ultracentrifugation, followed by measurement of the content of cholesterol and triglycerides in each.[21] The content of Apo A-I was measured by enzyme-linked immunoassay (ELISA).[22] The content of prebeta-1 HDL in plasma was measured by an ultrafiltration-isotope dilution technique, in which both the relative percentage of plasma Apo A-I that is present as prebeta-1 HDL and the absolute amount of prebeta-1 HDL in plasma are determined.[23] The ELISA used to measure prebeta-1 HDL was demonstrated to react with Apo A-I equivalently in prebeta-1 HDL and in larger HDL species of alpha electrophoretic mobility.

Analysis

Data were manually entered and analyzed using EXCEL software (Microsoft, Seattle, WA) in an Intel Pentium computer (Intel, Santa Clara, CA). Means $\pm$ SD were determined for the following entry characteristics: age, percent body fat, Vo_{2max}, dietary caloric intake, dietary cholesterol intake, and percentage dietary fat intake. As an internal validity check, 1-way analysis of variance (ANOVA) was conducted between ET and SED subjects' Vo_{2max} and pre-exercise plasma levels of plasma HDL-cholesterol, and between male and female subjects' pre-exercise plasma levels of HDL-cholesterol. Paired *t* tests were conducted for all subjects (N = 19) between pre- and post-exercise plasma levels of fasting plasma lipids, lipoproteins, Apo A-I, and prebeta-1 HDL.

RESULTS

All subjects completed the exercise protocol. Group characteristics are shown in Table 1. It is notable that subjects no. 2 and 18 reported zero cholesterol and very low fat diets. These subjects were young women who where using commercial very-low-fat meal replacements for weight management. Most subjects (N = 13) did not consume ethanol-containing beverages and the remainder consumed fewer than 5 ethanol-containing beverages per week. Subjects refrained from consuming ethanol-containing beverages during the 3 days preceding the exercise session. The comparisons made between ET and SED subjects as an internal validity check showed that Vo_{2max} was greater in ET than in SED subjects (52.8 $\pm$ 6.8 *v* 45.0 $\pm$ 7.3 mL O_2/kg/min, $P = .026$), and HDL-cholesterol levels were greater in ET than in SED subjects (54.8 $\pm$ 11.2 *v* 43.3 $\pm$ 8.7 mg/dL,

Table 1. Entry Characteristics (Mean ± SD) of Subjects (N = 19)

Subject	Age (yr)	Gender	Height (cm)	Weight (kg)	BMI	% Body Fat	Dietary Calories (kcal/d)	Dietary C (mg/d)	Dietary Fat	Vo_{2peak}	HDL-C	Exercise
1	20	F	175	71.623.9	23.9	11.0	3,221	132	21.5	55.0	44	PT
2	19	F	168	62.6	22.3	23.8	599	0	6.0	50.3	53	PT
3	21	M	170	74.4	25.7	5.3	1,881	252	12.2	47.8	41	PT
4	21	M	162	43.1	16.6	4.7	1,019	112	24.6	62.2	66	PT
5	22	F	183	79.8	24.2	17.2	1,475	158	31.5	49.7	45	PT
6	21	F	183	79.4	24.1	13.6	2,415	50	32.9	52.6	67	PT
7	20	M	183	72.6	22.0	5.2	1,702	123	19.3	64.8	74	PT
8	21	F	173	72.6	24.2	18.3	2,212	122	34.8	41.2	59	PT
9	29	M	178	83.9	26.2	15.3	1,916	359	39.2	51.9	51	PT
10	31	M	196	78.7	20.7	10.5	1,459	127	32.3	52.7	48	PT
11	41	M	185	74.6	21.9	13.8	2,118	215	38.0	40.7	35	SED
12	21	F	163	60.8	22.5	17.2	2,315	28	20.3	36.2	50	SED
13	21	M	164	54.4	20.1	7.0	1,342	36	5.6	56.9	44	SED
14	24	M	191	73.9	20.5	5.2	1,633	176	35.0	47.8	45	SED
15	28	M	162	44.9	17.3	14.5	1,081	364	48.9	35.7	32	SED
16	33	M	170	62.1	21.4	21.0	2,018	321	34.8	40.0	35	SED
17	21	M	171	68	23.4	11.6	1,337	192	20.4	49.9	40	SED
18	21	F	173	77.6	25.9	13.6	1,446	0	25.8	51.7	58	SED
19	31	M	168	64.1	22.3	17.9	1,614	281	39.7	45.7	51	SED
Mean ± SD	24.0 ± 5.8			68.4 ± 11.5	174.6 ± 9.9	22.4 ± 2.6	13.0 ± 5.7	1,733 ± 592	160.4 ± 114.9	28.0 ± 10.80	49.1 ± 7.9	49.3 ± 11.8

NOTE. Dietary fat in % fat of total daily calories; Vo_{2peak} in mL O_2/kg/min.
Abbreviations: C, cholesterol, PT, physical exercise-trained; SED, sedentary.

$P = .024$). Pre-exercise plasma HDL-cholesterol levels were not significantly different between male (n =12, 48.0 ± 13.3 mg/dL) and female (n = 7, 51.1 ± 9.4 mg/dL) subjects.

Table 2 summarizes mean ± SD values of fasting lipids, lipoproteins, Apo A-I, and prebeta HDL before and after exercise. Paired *t* tests conducted for all subjects (N = 19) between pre- and post-exercise plasma levels of fasting lipids, lipoproteins, Apo A-I, and prebeta-1 HDL showed a significant decrease in plasma HDL-triglyceride levels (23.3 ± 10.8 to 12.5 ± 5.6 mg/dL, $P < .012$) and an increase in absolute prebeta-1 HDL (0.10 ± 0.05 to 0.13 ± 0.07, $P = .039$) before and after exercise. Table 3 shows individual subjects' plasma

Table 2. Effects of Physical Exercise on Fasting Levels of Plasma Lipids, Lipoproteins, Apo A-I, and Prebeta HDL

Total cholesterol (mg/dL)	
Pre-	183.1 ± 42.7
Post-	177.8 ± 38.7
LDL-cholesterol (mg/dL)	
Pre-	112.9 ± 37.8
Post-	104.6 ± 31.2
Triglycerides (mg/dL)	
Pre-	95.7 ± 36.8
Post-	92.4 ± 36.5
HDL-cholesterol (mg/dL)	
Pre-	49.3 ± 11.8
Post-	55.2 ± 21.8
HDL-triglycerides* (mg/dL)	
Pre-	23.3 ± 10.8
Post-	12.5 ± 5.6
Apo A-I (mg/dL)	
Pre-	1.36 ± 0.19
Post-	1.31 ± 0.19
Absolute prebeta† (μg/mL)	
Pre-	0.10 ± 0.06
Post-	0.13 ± 0.07
Percent prebeta	
Pre-	7.90 ± 3.82
Post-	8.88 ± 4.08

*Pre- *v.* post-exercise, $P = .012$.
†Pre- *v* post-exercise, $P = .039$.

Table 3. Individual Subjects' Plasma Prebeta-1 HDL Values (μg/mL) Before and After Exercise

Subject No.	Before Exercise	After Exercise
1	0.08	0.06
2	0.12	0.12
3	0.05	0.05
4	0.11	0.12
5	0.17	0.17
6	0.03	0.03
7	0.13	0.15
8	0.16	0.16
9	0.10	0.11
10	0.08	0.28
11	0.04	0.05
12	0.07	0.10
13	0.25	0.24
14	0.09	0.13
15	0.11	0.19
16	0.09	0.18
17	0.12	0.17
18	0.12	0.11
19	0.03	0.03
Mean ± SD	0.10 ± 0.05	0.13 ± 0.07

prebeta-1 HDL levels before and after exercise. The response was heterogeneous but favored increased plasma prebeta-1 HDL levels (n = 11). Plasma prebeta-1 HDL levels were unchanged in 6 subjects and decreased slightly in 3 subjects.

DISCUSSION

Our findings confirm the expected result that young adults' level of regular habitual exercise status is related to increased VO_{2max} and plasma HDL-cholesterol levels in ET subjects compared with SED counterparts. To our knowledge the effect of physical exercise on plasma prebeta-1 HDL levels has not been previously reported. Plasma prebeta-1 HDL levels increased and plasma HDL-triglyceride levels were lowered following physical exercise.

The study was conducted in young, healthy adults, and hence the findings may not extend to older persons. Although the study did not include an nonexercising control group, we do not regard this as a major design flaw because the substantial physiological impact from the protracted intervention resulted in changes in plasma lipoprotein levels that we cannot ascribe as artifact. In addition, we did not measure specific enzymes involved in prebeta-1 HDL metabolism. Acute exercise has generally been shown to increase plasma HDL-cholesterol levels by 4% to 43%.[24] The lack of acute exercise-induced increase in plasma HDL-cholesterol noted in our study may reflect a "masking effect" of exercise-induced offsetting reciprocal changes in plasma HDL_2-cholesterol (increased) and HDL_3-cholesterol (decreased) subparticle levels.[25] Our study did not measure HDL subparticle composition.

Physical exercise is recognized to have a triglyceride-lowering effect[26] that is prominent following acute[27] and chronic exercise in hypertriglyceridemics.[28] The lack of an acute exercise response on total plasma triglyceride lowering may be reconciled by the relatively low pre-exercise triglyceride levels among these subjects as exercise-induced triglyceride lowering occurs more prominently among those with increasing triglyceride levels.[29]

Prebeta-1 HDL behaves as the quantum HDL particle in the initial phase of the pathway for cholesterol retrieval from peripheral cells to the liver.[6] It is the first acceptor of unesterified cholesterol, becoming a substrate for LCAT. As the cholesterol is esterified, the prebeta particles are ultimately subsumed into larger, spherical alpha HDL particles.[7] As cholesteryl esters are then transferred, under the influence of cholesteryl ester transfer protein (CETP), to acceptor lipoproteins that contain the B apolipoproteins, prebeta-1 particles are regenerated. Thus the circulating level of prebeta-1 HDL reflects the relative activities of LCAT and CETP, in what is now recognized as a cyclic process. Increased LCAT activity increases alpha HDL formation and has been shown to be greater in athletes than sedentary counterparts,[9,30,31] and is increased immediately after acute exercise.[32,33] Decreased CETP activity increases alpha HDL levels by increasing cholesterol ester content, and concomittently reduces HDL-triglyceride content by triglyceride transfer to non-HDL lipoprotein species. On the other hand, increased CEPT activity could facilitate alpha HDL turnover and promote prebeta HDL formation. In some studies CETP activity is greater among athletes than sedentary individuals,[9] while it has also been shown to decrease following physical exercise training.[34] Following acute exercise CEPT activity is shown to decrease[35] or be unchanged.[36]

Our findings showing that acute exercise increases prebeta-1 HDL without increasing plasma Apo A1 levels are consistent with studies showing that prebeta-1 HDL is derived from alpha HDL particles rather from de novo Apo A-I synthesis.[13] Both HDL particle species Lp (A-I − A-II) and Lp (A-I + A-II) contribute Apo A-I that is dissociated from these particles in the formation of prebeta HDL.[13] Prebeta HDL particles are generated from alpha HDL during cholesterol clearance by several pathways, including: (1) CETP-mediated exchange of cholesterol esters from HDL to the very–low-density lipoprotein (VLDL)/low-density lipoprotein (LDL) particle series which then provides cholesterol removal by the LDL receptor pathway[6,37]; and (2) direct HDL-mediated receptor pathways that include (a) cubulin[38,39,40] that mediates HDL holoparticle endocytosis, and (b) the scavenger receptor, type BI (SR-BI) that binds HDL and selectively mediates the uptake or removal of HDL cholesterol esters without the uptake/degradation of HDL–Apo A-I.[38,41] The SR-BI receptor appears to act as a "docking" site where cholesterol esters can be removed and subsequently the HDL particle (depleted of cholesterol esters) "undocks" and recirculates to pick up more cholesterol esters from peripheral tissues. Exercise-induced modulation of these HDL catalytic pathways could potentially play an important role in regulating plasma prebeta-1 HDL levels. Hepatic lipase has been shown to play a major role in HDL catabolism by hydrolyzing both triglycerides and phospholipids within HDL particles.[42,43]

LP A-I particles appear to be the most efficient in facilitating cholesterol ester uptake by SR-BI receptors: Hep G_2 cell uptake of [^{3}H] cholesterol ester is approximately 75% greater from LP A-I than LP A-I + A-II particles.[44] Niacin has been shown to selectively inhibit plasma LP A-I removal without affecting cholesterol ester uptake.[45] Niacin inhibition of plasma LP A-I removal may promote prebeta-1 HDL regeneration. It is conceivable that physical exercise could exert a similar effect to increase plasma LP A-I levels by reducing LP A-I removal. Indeed Herbert et al[46] found that the mean biological half-life of HDL proteins was longer in runners (6.2 days) than in sedentary controls (3.8 days). Tracer studies of radioiodinated autologous HDL demonstrated that runners did not produce more HDL protein but rather catabolized less. These studies have been more recently corroborated by Thompson et. Al,[47] who showed that participation in 8 to 11 months of aerobic-based PET increased the biological half-life of Apo A-I by 10% (P = .07) by decreasing the fractional catabolic rate by a corresponding amount and not affecting Apo A-I synthetic rate. A similar finding was noted for Apo A-II. Some[48,49,50] but not other[51,52] studies indicate that physical exercise training raises plasma Apo A-I levels. We found no difference in plasma Apo A-I levels between entry and Apo A-I levels following acute exercise. These findings are consistent with the possibility that physical exercise promotes alpha HDL recycling and regeneration of HDL.

It is likely that intravascular lipolysis is a further contributor to the levels of prebeta-1 HDL in plasma. As lipoprotein

lipase–mediated lipolysis proceeds, phospholipid, and some small molecular weight apolipoproteins move from the surface monolayers of triglyceride-rich lipoproteins to HDL. Exercise-induced lipoprotein lipase activity may account for exercise-related reductions in plasma HDL-triglyceride levels.[53,54] Lipoprotein lipases are a family of tissue-specific hydrolytic enzymes that are rate-limiting for the removal of circulating lipoprotein triglycerides and have been implicated in atherogenesis.[55,56] Adipose lipoprotein lipase activity, involved in triglyceride storage of acyl groups derived primarily from the hydrolysis of plasma lipoproteins, increases with physical exercise training.[57] Acute exercise also increases lipoprotein lipase activity and fat tolerance.[58,59] This has been most widely shown in fit individuals performing at high levels of protracted physical exertion, but also has been shown to occur in sedentary individuals exercising for as little as 1 hour at 80% of maximal heart rate.[60] These observations have lead to the hypothesis that exercise acutely depletes intramuscular triglycerides, a finding that has recently been confirmed.[61] This stimulates the synthesis or translocation of lipoprotein lipase, which hydrolyzes triglycerides from lower-density lipoproteins with transfer of the excess surface cholesterol to the HDL particle.[62] Skeletal muscle lipoprotein lipase has become the recent focus of exercise-related effects on plasma lipids and lipoproteins.[63] Exercise raises skeletal lipoprotein lipase activity in the capillary beds of skeletal muscles where fatty acids are hydrolyzed from circulating lipoproteins for energy utilization. This could influence plasma HDL-triglyceride metabolism as we have previously shown acute exercise to reduce plasma HDL-triglycerides by 30% in hypertriglyceridemics.[27]

In conclusion, both acute physical exercise and regular physical exercise training are recognized for their effects of HDL metabolism that can mitigate coronary artery disease risk. Our findings indicate that the effect of acute physical exercise on plasma HDL particles involves increasing prebeta-1 HDL particles. Additional studies are warranted to further evaluate the role of exercise-related effects upon plasma prebeta HDL relating to coronary artery disease risk reduction.

REFERENCES

1. Pate RR, Pratt M, Blair SN, et al: Physical activity and public health. A recommendation from the Centers for Disease Control and Prevention and the American College of Sports Medicine. JAMA 273:402-407, 1995
2. Wood PD, Stephanick ML: Exercise, fitness, and atherosclerosis, in Bouchard C, Shephard RJ, Stephens T, et al (eds): Exercise, Fitness, and Health: A Consensus of Current Knowledge. Champaign, IL, Human Kinetics, 1990, pp 407-424
3. Leaf DA, Parker DL, Schaad D: Changes in VO_{2max}, physical activity, and body fat with chronic exercise: effects of plasma lipids. Med Sci Sports Exerc 29:1152-1159, 1997
4. Leon AS, Sanchez OA: Response of blood lipids to exercise training alone or combined with dietary interventions. Med Sci Sports Exerc 33:S502-S515, 2001 (suppl 6)
5. Tall AR, Jiang X, Luo Y, et al: 1999 George Lyman Duff Memorial Lecture. Lipid transfer proteins, HDL metabolism, and atherogenesis. Arterioscler Thromb Vasc Biol 20:1185-1188, 2000
6. von Eckardstein A, Nofer J-R, Assman G: High density lipoproteins and arteriosclerosis. Role of cholesterol efflux and reverse cholesterol transport. Arterioscler Thromb Vasc Biol 21:13-27, 2001
7. Phillips MC, Gillote KL, Haynes MP, et al: Mechanisms of high-density lipoprotein-mediated efflux of cholesterol from cell plasma membranes. Atherosclerosis. 137:S13-S17, 1998 (suppl)
8. Dean M, Hasmon Y, Chimini G: The human ATP-binding cassette (ABC) transporter superfamily. J Lipid Res 42:1007-1017, 2001
9. Gupta AK, Ross EA, Myers JN, et al: Increased reverse cholesterol transport in athletes. Metabolism 42:684-690, 1993
10. Fielding CJ, Fielding PE: Molecular physiology of reverse cholesterol transport. J Lipid Res 36:211-228, 1995
11. Kunnitake S, La Sada K, Kane J: Apolipoprotein A-I-containing lipoproteins with per-beta electrophoretic mobility. J Lipid Res 26:549-555, 1985
12. McVicar JP, Kunnitake ST, Hamilton RI, et al: Characteristics of human lipoproteins isolated by selected affinity immunosorption of apolipoprotein A-I. Proc Natl Acad Sci USA 81:1356-1360, 1984
13. Hennessy LK, Kunitake ST, Kane JP: Apolipoprotein A-I-containing lipoproteins, with or without apolipoprotein A-II, as progenitors of pre-B high-density lipoprotein particles. Biochemistry 32:5759-5765, 1993
14. O'Connor PM, Naya-Vigne JM, Duchateau PN, et al: Measurement of prebeta-1 HDL in human plasma by an ultracentrigfugation-isotope dilution technique. Anal Biochem 251:234-240, 1997
15. Jackson AS, Pollock ML: Practical assessment of body composition. Phys Sports Med 13:76-90, 1985
16. Bruce RA: Methods of exercise testing. Am J Cardiol 33:715-720, 1974
17. Posner BM, Martin-Munley SS, Smigelski C, et al: Comparison of techniques for estimating nutrient intake: The Framingham Study. Epidemiology 3:171-177, 1992
18. Crawford PB, Obarzanek E, Morrison J, et al: Comparative advantage of 3-day food records over 24-hour recall and 5-day food frequency validated by observation of 9 and 10-year-ol girls. J Am Diet Assoc 94:626-630, 1994
19. Luhrmann PM, Herbetr BM, Gaster C, et al: Validation of a self-administered 3-day estimated dietary record for use in the elderly. Eur J Nutr 38:235-240, 1999
20. Grodner TK: Foundation and Clinical Applications of Nutrition: A Nursing Approach (ed 4).. Philadelphia, PA, Mosby-Yearbook, 1996, pp 638-726
21. Kane JP, Malloy MJ, Ports TA, et al: Regression of coronary atherosclerosis during treatment of familial hypercholesterolemia with combined drug regimens. JAMA 264:3007-3012, 1990
22. Kunitake ST, O'Connor P, Naya-Vigne J: xxx, in Bradley G, Segrest J (eds): Methods in Enzymology. San Diego, CA, Academic Press, 1996, pp 260-267
23. O'Connor PM, Naya-Vigne J, Duchateau PN, etal: Measurement of prebeta-1 HDL in human plasma by an ultrafiltration-isotope dilution technique. Anal Biochem 251:234-240, 1997
24. Thompson PD, Crouse SF, Goodpaster B, et al: The acute versus the chronic response to exercise. Med Sci Sports Exerc 33:S438-S445, 2001 (suppl 6)
25. Nye ER, Carlson K, Kirstein P, et al: Changes in high density lipoprotein subfractions and other lipoproteins induced by exercise. Clin Chim Acta 113:51-57, 1981
26. Leaf DA, Parker DL, Schaad D: Changes in VO_{2max}, physical activity, and body fat with chronic exercise: effects on plasma lipids. Med Sci Sprots Exerc 29:1152-1159, 1997
27. Leaf DA, Kuehl K: Acute prolonged subanaerobic exercise on hypertriglyceridmics: Effect on plasma lipids, lipoproteins, and respiratory exchange ratio slope. Ann Sports Med 3:242-246, 1988

28. Lampman RM, Santiaga JT, Hodge MF, et al: Type IV hyperlipidemia: Effects of a caloric restricted diet versus physical training plus isocaloric type IV diet. Am J Clin Nutr 33:1233-1243, 1980

29. Crouse SF, O'Brien BC, Rohack JJ, et al: Changes in serum lipids and apolipoproteins after exercise in men with high cholesterol: Influence of intensity. J Appl Physiol 79:279-286, 1995

30. Tsopanakis C, Kotsarellis D, Tsopanakis A: Plasma lecithin: cholesterol acyltransferase activity in elite athletes from selected sports. Eur J Appl Physiol 58:262-265, 1988

31. Lopez-S A, Vial R, Balart L, et al: Effect of exercise and physical fitness on serum lipids and lipoproteins. Atherosclerosis 20: 1-9, 1974

32. Dufaux B, Order U, Muller R, et al: Delayed effects of prolonged exercise on serum lipoproteins. Metabolism 35:105-109, 1986

33. Frey I, Baumstark MW, Berg A, et al: Influence of acute maximal exercise on lecithin:cholesterol acyltransferase activity in healthy adults of differing aerobic performance. Eur J Appl Physiol 62:31-35, 1991

34. Seip RL, Moulin P, Cocke T, et al: Exercise training decreases plasma cholesteryl exter transfer protein. Arterioscler Thromb 13:1359-1367, 1993

35. Foger B, Wohlfarter T, Ritsch A, et al: Kinetics of lipids, apolipoproteins, and cholesteryl ester transfer protein in plasma after a bicycle marathon. Metabolism 43:633-639, 1994

36. Grandjean PW, Crouse SF, Rohak JJ: Influence of cholesterol status on blood lipid and lipoprotein enzyme responses to aerobic exercise. J Appl Physiol 89:472-480, 2000

37. Willnow TE, Nykjaer A, Herz J: Lipoprotein receptors: New role of ancient proteins. Nat Cell Biol 1:E157-E162, 1999

38. Acton S, Rigotti A, Landschultz K, et al: Identification of scavenger receptor SR-B1 as a high density lipoprotein receptor. Science 271:518-520, 1996

39. Hammad SM, Steingrimur S, Twal WO, et al: Cubulin, the endocytic receptor for factor-vitamin B12 complex, mediates high-density holoparticle endocytosis. Proc Natl Acad Sci USA 96:10158-10163, 1999

40. Kozyraki F, Fyfe J, Kristiansen M, et al: The intrinsic factor-vitamin B12, cubilin, is a high-affinity apolipoprotein A-I receptor facilitating endocytosis of high-density lipoprotein. Nat Med 5:656-661, 1999

41. Kreiger M: Scavenger receptor class B type I is a multiligand HDL receptor that influences diverse physiologic systems. J Clin Invest 108:793-797, 2001

42. Rader DJ, Ikewaki K: Unravelling high density lipoprotein-apolipoprotein metabolism in human mutants and animal models. Curr Opin Lipodol 7:117-123, 1996

43. Santamarina-Fojo S, Haudenschild CC, Shamburek RD, et al: The role of hepatic lipase in lipoprotein metabolism and atherosclerosis. Curr Opin Lipidol 9:211-219, 1998

44. Sakai T, Kamanna VS, Kashyap ML: Niacin, but not gemfibrozil, selectively increases LP-AI, a cardioprotective subfraction of HDL, in patients with low HDL-cholesterol. Arterioscler Thromb Vasc Biol 21:1783-1789, 2001

45. Fy-You J, Kamanna VS, Kashyap ML: Niacin decreases removal of high-density lipoprotein apolipoprotein A-I but not cholesterol ester by Hep G2 cells. Implication for reverse cholesterol transport. Arterioscler Thromb Vasc Biol 17:2020-2028, 1997

46. Herbert PN, Bernier DN, Cullinane EM, et al: High-density lipoprotein metabolism in runners and sedentary men. JAMA 252: 1034-1037, 1984

47. Thompson PD, Cullinanae EM, Sady SP, et al: Modest changes in high-density lipoprotein concentration and metabolism with prolonged exercise training. Circulation 78:25-34, 1988

48. Couillard C, Despres J-P, Lamarche B, et al: Effects of endurance exercise training on plasma HDL cholesterol levels depend on levels of triglycerides. Arterioscler Thromb Vasc Biol 21:1226-1232, 2001

49. Kiens B, Jorgensen I, Lewsi S, et al: Increased plasma HDL-cholesterol and apo A-I in sedentary middle-aged men after physical conditioning. Eur J Clin Invest10:203-209, 1980

50. Thompson PD, Yurgalevitch SM, Flynn MM, et al: Effect of prolonged training without weight loss on high-density lipoprotein metabolism in overweight men. Metabolism 46:, 1997217-223.

51. Thompson PD, Cullinane EM, Sady EP, et al: Modest changes in high-density lipoprotein concentration and metabolism with prolonged exercise training. Circulation 78:24-34, 1988

52. Wood PD, Stefanick WM, Dreon DM, et al: Changes in plasma lipids and lipoproteins in overweight men during weight loss through dieting as compared with exercise. N Engl J Med 319:1173-1179, 1988

53. Kantor MA, Cullinane EM, Herbert PN, et al: Acute increase in lipoprotein lipase following prolonged exercise. Metabolism 33;454-457, 1984

54. Sady SP, Thompson PD, Cullinane EM, et al: Prolonged exercise augments plasma triglyceride clearance. JAMA 256:2552-2555, 1986

55. Eckel RH: Lipoprotein lipase: A multifunctional enzyme relevant to common metabolic diseases. N Engl J Med 320:1060-1068, 1989

56. Goldber IJ: Lipoprotein lipase and lipolysis: Central roles in lipoprotein metabolism and atherosclerosis. J Lipid Res 37:693-707, 1996

57. Nikklia EA: Role of lipoprotein lipase in metabolic adaptation to exercise and training, in Borzensztajn J (ed): Lipoprotein Lipase. Chicago, IL, Evener, 1987, pp187-199

58. Kantor MA, Cullinane EM, Herbert PN, et al: Acute increase in lipoprotein lipase following prolonged exercise. Metabolism 33:454-457, 1984

59. Sady SP, Thompson PD, Cullinane EM, et al: Prolonged exercise augments plasma triglyceride clearance JAMA 256:2552-2555, 1986

60. Kantor MA, Cullinane EM, Sady SP, et al: Exercise acutely increases HDL-cholesterol and lipoprotein lipase activity in trained and untrained men. Metabolism 36:188-192, 1987

61. Rico-Sanz J, Moosavi M, Thomas EL, et al: In vivo evaluation of the effects of continuous exercise on skeletal muscle triglylcerides in trained humans. Lipids 35:1313-1318, 2000

62. Thompson PD, Cullinane E, Henderson L, et al: Acute effects of prolonged exercise on serum lipids. Metabolism 29:662-665, 1980

63. Thompson PD: What do muscles have to do with lipoproteins? Circulation 81:1428-1430, 1990