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Associations of lecithin: cholesterol acyltransferase (LCAT) mass concentrations with exercise, weight loss, and plasma lipoprotein subfraction concentrations in men

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Abstract

The relationships between plasma 1ecithin:cholesterol acyltransferase (LCAT) mass concentrations and lipids, apolipoprotein, and lipoprotein subfraction concentrations were studied in men assigned at random to a one-year exercise program (n = 48) and to a sedentary control condition (n = 31). Exercise training did not significantly affect mean concentrations of LCAT-mass. Moreover changes in LCAT within the exercise group were unrelated to distance run and weight loss. The baseline data and the one-year change data showed consistent positive correlations between LCAT concentrations and total cholesterol, low density lipoprotein cholesterol, very low density lipoprotein cholesterol, and apolipoprotein B concentrations, and consistently weak correlations between LCAT concentrations and high density lipoprotein (HDL)-cholesterol, HDL_2, and apolipoprotein A-I concentrations. The strong correlation between LCAT and total cholesterol may account for LCAT's relationships with lipoprotein subfractions, apolipoprotein B and other lipoprotein cholesterol concentrations.

INTRODUCTION

Lecithin:cholesterol acyltransferase (LCAT) is thought to play an essential role in cholesterol removal [1,2]. Free cholesterol resides primarily on the surface of lipoprotein particles. When catalyzed by LCAT to form cholesteryl ester, surface cholesterol is sequestered into the hydrophobic core of lipoprotein particles. The removal of free cholesterol from the lipoprotein surface creates a concentration gradient that favors the net transfer of cholesterol from cell membranes to the lipoprotein surface. Particles within the high density lipoprotein$_3$ (HDL_3) density range are the preferred substrate for LCAT [3], and the newly synthesized esterified cholesterol is primarily incorporated into HDL [4]. Most of the cholesteryl ester formed by LCAT on HDL is transferred to the apolipoprotein B containing lipoproteins [4,5], which are then cleared by receptors for LDL or triglyceride-rich lipoprotein remnants [6].

Long-distance runners have higher HDL-cholesterol concentrations than sedentary men [7,8]. Marneimi et al. [9,10] have speculated that an increase in the runners' LCAT activity may produce their high HDL-cholesterol levels. Marneimi et al. found LCAT activity was significantly higher in active men than sedentary men; that LCAT activity correlated positively with aerobic capacity in a cross-sectional sample of both active and inactive men, that LCAT activity was increased significantly after 2 months of military training, and that change in LCAT correlated significantly and positively with HDL-cholesterol during training [9]. Another study by Marneimi and Hietanen [10] purported to show a 2-fold increase in LCAT activity after 15 weeks of training [10].

To better understand LCAT's role in promoting lipoprotein changes during exercise and weight loss we (1) compare mean changes in LCAT-mass concentrations in men who participated in a one-year running program and in nonexercising controls; (2) correlate l-year changes in LCAT-mass concentrations with distance run, improved fitness and weight loss within the exercise group. Associations of LCAT with lipids, lipoprotein and apolipoproteins at baseline and during the experiment are also examined.

SUBJECTS AND METHODS

Subjects and laboratory measurements

Eighty-one sedentary men, 30–55 years old, were assigned at random to either a supervised running group of 48 persons or to a sedentary control group of 33 persons [8,11]. Recruitment, selection criteria, and experimental design are described elsewhere [8]. Body compositions were estimated from hydrostatic weighing and maximal oxygen uptakes (VO_2max) were determined from treadmill tests to exhaustion [8]. Diaries maintained by the runners showed they ran an average of 12.7 km/wk during the last seven months of the study [8,11].

Lipoproteins were measured by analytic ultracentrifugation of fasting serum samples, and concentrations of total lipoprotein mass were estimated using computer techniques for small low-density lipoproteins (small LDL, S_f 0–7), large low density lipoproteins (large LDL, S_f 7–12), intermediate density lipoproteins (IDL, S_f 12–20), very low density lipoproteins (VLDL, S_f 20–400), HDL_2 ($F_{1.20}$3.5–9) and HDL_3 ($F_{1.20}$0–3.5). Results are also described for the peak flotation rate (S_f) of the LDL-mass distribution [12,13]. Plasma lipoprotein cholesterol concentrations were measured directly by the methods of the Lipid Research Clinics [14], plasma apolipoprotein B concentrations were assessed by radioimmunoassay [15], apolipoprotein A-I and A-II concentrations were measured by radialimmunodiffusion [16], and LCAT mass was measured by double antibody radioimmunoassay [17]. Assays of apolipoproteins and LCAT were made on all samples at the end of the study using plasmas that had been stored at −80°C.

Statistics

The differences between the exercise and control groups are expressed as mean ±1 SD and evaluated using the significance levels assigned by 2-sample t-tests. Pearson correlation coefficients are used to assess pairwise associations between LCAT, lipoprotein mass concentrations, body mass index (BMI, kg/m^2), distance run per week and VO_2max.

RESULTS

Complete data were obtained for 77 men at baseline and for 42 exercisers and 30 controls at 1 year. Table 1 presents the baseline means and the 1-year mean change scores for LCAT, lipoprotein, and apolipoprotein concentrations. Baseline LCAT concentrations were well matched in exercisers and controls (mean ± SD: 5.8 ± 0.1 vs. 5.8 ± 0.2 μg/ml). Relative to controls, the exercisers increased their VO_2max (7.52 ± 8.38 vs. −1.43 ± 4.05 ml/kg/min, $P < 0.0001$) and reduced their total weight (−1.89 ± 3.84 vs. 0.56 ± 3.87 kg, $P < 0.01$). The training program did not significantly change the exercisers' mean lipoprotein or LCAT concentrations as compared to controls (Table 1).

Within the exercise group, distance run correlated significantly with changes in HDL-cholesterol, HDL_2, and small LDL concentrations, and weight loss correlated significantly with changes in HDL-cholesterol, HDL_2, small LDL-mass, IDL-mass, and VLDL-mass concentrations and LDL peak flotation rate (reported previously in refs. 8,11,18). Changes in

LCAT in exercisers were unrelated to distance run ($r = -0.10$) or changes in total weight ($r = 0.16$), VO_2max ($r = 0.23$), fat weight ($r = 0.19$) or BMI (Table 2).

Table 2 presents the correlations of LCAT with lipid, apolipoprotein, lipoprotein mass concentrations at baseline, and the correlations between changes in LCAT and changes in lipids, apolipoprotein, and lipoprotein mass concentrations after 1 year. One-year changes in plasma LCAT concentrations correlated significantly and strongly with 1-year changes in total cholesterol. Partial correlational coefficients suggest that most of the associations between LCAT and triglycerides, lipoproteins and apolipoproteins may be secondary to the LCAT-total cholesterol relationship.

DISCUSSION

Marneimi et al.'s report of an increase in LCAT with exercise and improved fitness are not corroborated by our data. We found no significant relationship between change in LCAT-mass concentrations and distance run, increased aerobic capacity, total weight lost, or HDL-cholesterol change. The effects of training on LCAT-mass concentration (measured in the present study) and LCAT-activity level (measured by Marneimi et al.) should agree since there is a strong correlation between LCAT-mass measurements by double-antibody radioimmunoassay and LCAT activity measurements by radioassay ($r = 0.98$) [19]. Moreover, all of the LCAT appears to be active. Marneimi et al.'s conclusion that LCAT is increased with exercise training also is not consistent with the low levels of total cholesterol, LDL-cholesterol and VLDL-cholesterol, triglycerides and small LDL that characterize long-distance runners [7,8]. Given the positive correlations cited above and elsewhere between LCAT and these lipoprotein concentrations [20–23], we would expect training to decrease LCAT concentrations. The positive correlation they report between changes in HDL-cholesterol and LCAT activity is also unexpected from the data presented by us and others. Possibly the LCAT assay developed by Alcindor et al. [24] and used by Marneimi et al. reflected the effects of exercise on LCAT substrates, activators, inhibitors and products rather than LCAT concentrations per se [25].

Others have observed the strong correlation between LCAT and total cholesterol levels [20–23]. We show that the correlation is also strong between changes in LCAT levels and total cholesterol measured over time (Table 2). While the major portion of plasma cholesterol is in the esterified form and most of the plasma cholesteryl ester is produced from free cholesterol by LCAT [1,2] it has been shown that total cholesterol concentrations are not primarily determined by LCAT concentrations [25]. The alternative, that LCAT levels may be regulated in response to plasma total cholesterol concentrations, warrants further study.

The correlations of Table 2 suggest that LCAT's associations with lipoprotein subfractions, apolipoprotein B and lipoprotein cholesterol concentrations are all secondary to the LCAT-total cholesterol relationship. Specifically, changes in LCAT levels correlated significantly with changes in triglycerides, LDL-cholesterol, VLDL-cholesterol, and apolipoprotein B concentrations, but not when adjusted for their correlations with total cholesterol. Moreover, the associations of LCAT with specific lipoprotein subfractions were weak and usually nonsignificant.

Exercise may change lipoprotein subfraction concentrations in part by reducing the level of cholesteryl ester-triglyceride exchange between HDL and triglyceride-enriched lipoproteins [18]. The rate of exchange appears to be affected by the availability of VLDL (in the fasting state) and chylomicrons (in the postprandial state). The reductions in VLDL and postprandial chylomicron levels in runners may be due to increased lipoprotein lipase activities in adipose

and muscle tissue [11,18,26–29]. It is possible that weight loss and exercise reduce cholesteryl ester-triglyceride exchange without altering plasma LCAT mass concentrations.

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Table 1

Lecithin:cholesterol acyltransferase (LCAT), Lipid, and Lipoprotein Concentrations in Exercisers and Controls. Values are means ± SD

	Baseline everyone	Change after one-year	
		Exercisers	Controls
LCAT-mass (μg/ml)	5.79 ± 0.98	−0.19 ± 0.64	0.08 ± 0.94
Plasma triglycerides (mg/dl)	119.59 ± 56.74	−10.79 ± 41.51	3.77 ± 37.91
Plasma cholesterol concentration (mg/dl)			
Total	214.17 ± 30.83	−5.51 ± 18.91	1.98 ± 25.85
HDL	48.75 ± 8.84	2.08 ± 8.25	0.22 ± 6.02
LDL	146.04 ± 27.31	−5.76 ± 17.10	1.72 ± 20.90
VLDL	19.38 ± 11.45	−1.83 ± 10.15	0.05 ± 10.29
Plasma apolipoprotein concentrations (mg/dl)			
A-I	129.21 ± 15.83	4.62 ± 12.86	2.97 ± 12.10
A-II	37.16 ± 5.15	−1.16 ± 6.32	− 0.71 ± 5.71
B	82.55 ± 17.31	−1.28 ± 12.87	0.04 ± 12.07
Serum mass concentrations (mg/dl)			
HDL_2 ($F_{1.20}$ 3.5–9)	40.59 ± 31.80	18.02 ± 37.18	3.25 ± 25.76
HDL_3 ($F_{1.20}$ 0–3.5)	231.73 ± 36.83	3.49 ± 31.30	0.22 ± 33.43
Small LDL (S_f 0–7)	226.63 ± 63.59	−6.81± 53.87	7.13 ± 39.47
Large LDL (S_f 7–12)	133.55 ± 41.69	12.97 ± 40.21	14.01 ± 41.26
IDL (S_f 12–20)	42.68 ± 18.92	0.85 ± 14.27	3.77 ± 13.98
VLDL (S_f 20–400)	101.94 ± 69.35	7.91 ± 47.04	16.38 ± 46.96
LDL-peak			
Floatation rate (S_f)	5.89 ± 0.85	0.17 ± 0.75	− 0.06 ± 0.65

Seventy-seven men had complete data at baseline, 42 exercisers and 30 controls with complete data at baseline and one year.

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Table 2

Pearson correlation coefficients between plasma LCAT mass concentrations and plasma lipid, lipoprotein, and apolipoprotein concentrations and body mass index.

	Cross-sectional at baseline			One-year change in controls			One-year change in exercisers		
	Cholesterol	**LCAT**	**LCAT adj. for cholesterol**	**Cholesterol**	**LCAT**	**LCAT adj. for cholesterol**	**Cholesterol**	**LCAT**	**LCAT adj. for cholesterol**
LCAT	0.32**	—	—	0.51**	—	—	0.53***	—	—
Triglycerides	0.49****	0.28**	0.15	0.30	0.31	0.19	0.20	0.38**	0.33*
HDL-chol.	−0.06	0.02	0.04	0.11	−0.10	−0.19	0.01	0.06	0.06
LDL-chol.	0.93****	0.25*	−0.14	0.93****	0.45**	−0.07	0.85****	0.31*	−0.31*
VLDL-chol.	0.52****	0.25*	0.10	0.56***	0.42*	0.19	0.43*	0.42**	0.25
HDL_2-mass	−0.16	−0.16	−0.12	−0.20	−0.13	−0.03	−0.15	0.01	0.11
HDL_3-mass	0.24*	0.29**	0.23*	0.16	−0.14	−0.26	0.35*	0.23	0.06
Small LDL-mass	0.66****	0.30**	0.13	0.35	0.21	0.03	0.56***	0.40**	0.15
Large LDL-mass	0.21	−0.13	−0.21	0.14	0.05	−0.03	0.04	−0.16	−0.21
IDL-mass	0.51****	0.14	−0.03	0.50**	0.27	0.02	0.47***	0.25	0.00
VLDL-mass	0.43****	0.16	0.02	0.23	0.29	0.21	0.11	0.22	0.20
LDL peak S_f rate	−0.39***	−0.27*	−0.16	−0.34	−0.17	0.01	−0.41**	−0.33*	−0.15
Apo A-I	0.17	0.14	0.09	−0.10	0.12	0.19	0.26	0.14	0.00
Apo A-II	0.15	0.21	0.17	0.49**	0.33	0.10	0.08	0.09	0.05
Apo B	0.70****	0.37***	0.21	0.76****	0.50**	0.21	0.50***	0.35*	0.12
BMI	0.21	0.24*	0.19	0.52**	0.31	0.06	0.16	0.14	0.07

Significance levels for Pearson correlations are coded:

* $P < 0.05$;

** $P < 0.01$;

*** $P < 0.001$;

**** $P < 0.00001$.