Serum C-Reactive Protein and Lipids in Ultra-Marathon Runners

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In this investigation, we compared lipid and inflammatory parameters in regular long distance runners with matched sedentary controls. Long distance runners had significantly lower low-density lipoprotein cholesterol and C-reactive protein levels than the control group. This exercise-induced reduction in low-density lipoprotein cholesterol was independent of the decrease in C-reactive protein levels. ©2004 by Excerpta Medica, Inc.

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Relations between inflammatory biomarkers and cholesterol metabolism in physically active subjects have not been extensively investigated. Therefore, it is not known whether subjects with exercise-induced suppression of chronic inflammation (as measured by low C-reactive protein [CRP] levels) also exhibit favorable lipid profiles. To address this issue, we analyzed serum lipid profiles in a cohort of regular ultra-marathon runners and demographically matched sedentary, healthy controls whose CRP levels had been previously evaluated.[1]

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Sixty-seven long distance runners participating in the Calissia 2000 Ultra-Marathon Study along with 63 sedentary, otherwise healthy controls were included in the present analysis. The details of the study design, recruitment strategy, and phenotyping have been previously described.[1] In brief, each participant was a nonsmoking, healthy male with no clinical history of any chronic disorders or medication. All ultra-marathon runners reported a very high level of regular physical activity (40 to 100 km of running per week for >2 years) and confirmed participation in ≥2 marathons. In contrast, control subjects represented a typical sedentary middle-aged male population with an average weekly physical activity of <2 hours. Fasting serum samples obtained from peripheral blood were stored at −70°C until the biochemical analysis. Circulating concentrations of CRP were measured by the previously validated high-sensitivity enzyme-linked immunosorbent assay, as described previously.[1] Serum concentrations of total cholesterol, high-density lipoprotein (HDL) cholesterol, and triglycerides were determined by enzymatic methods, as previously reported.[2] Low-density lipoprotein (LDL) cholesterol was calculated based on Friedewald's equation.

Data are shown as mean ± SDs or as medians (interquartile range). The distribution of CRP was skewed; therefore, these results were log-transformed. Quantitative variables were compared by parametric tests (Student's *t* test and analysis of variance) as well as nonparametric methods (Mann-Whitney test and Kruskal-Wallis test). Qualitative binary traits were analyzed using the chi-square test. Pearson's linear correlation and multiple regression analysis were used to test for associations among 2 and multiple quantitative variables, respectively. p Values <0.05 were considered significant.

Fifty-five lean ultra-marathon runners, 30 lean sedentary controls, 12 non-lean ultra-marathon runners, and 33 non-lean control subjects were included in the analysis. There were no statistically significant differences in age, body mass index, and mean arterial pressure between the ultra-marathon runners and the controls, either in the lean or non-lean category, as described previously.[1] As previously reported,[1] median CRP levels were significantly lower among the lean ultra-marathon runners (0.4; 0.2 to 0.9) than in the lean controls (0.9; 0.5 to 2.7) ($p = 0.0013$), and this difference was even more striking when non-lean runners (0.4; 0.3 to 0.8) were compared with the non-lean sedentary controls (1.5; 0.9 to 2.5) ($p = 0.0002$).

Comparative characteristics of lipid profile among ultra-marathon runners and sedentary control subjects are presented in Table 1. The difference in LDL between ultra-marathon runners and the sedentary controls remained statistically significant after adjustment for age, body mass index, and log CRP. Circulating concentrations of lipids did not differ among ultra-marathon runners, representing 4 quartiles of log CRP distribution (Table 2). Total cholesterol, LDL, HDL, triglycerides, and the triglyceride/HDL ratio did not correlate linearly with log CRP among ultra-marathon runners. There was a borderline negative linear correlation between HDL and log CRP among sedentary controls ($p = 0.045$). None of the other lipid fractions correlated with log CRP in the control group.

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TABLE 1 Circulating Concentrations of Lipids Among the Ultra-marathon Runners and Sedentary Controls

Lipid Fraction	Lean Runners	Lean Controls	p Value	Non-lean Runners	Non-lean Controls	p Value
Total cholesterol (mg/dl)	193.5 ± 34.8	220.6 ± 31.0	0.0007	216.7 ± 92.9	224.5 ± 46.4	NS
LDL cholesterol (mg/dl)	112.2 ± 27.1	174.2 ± 23.2	<0.0001	135.5 ± 42.6	170.3 ± 42.6	0.016
HDL cholesterol (mg/dl)	46.4 ± 11.6	42.6 ± 11.6	NS	42.6 ± 15.5	34.8 ± 11.6	NS
Triglycerides (mg/dl)	168.3 ± 88.6	141.8 ± 88.6	NS	194.9 ± 132.9	186.1 ± 106.3	NS
Triglycerides/HDL cholesterol ratio	4.1 ± 3.1	4.1 ± 3.9	NS	6.0 ± 6.3	6.4 ± 5.9	NS

TABLE 2 Serum Concentrations of Lipids Across the Percentile Distribution of Log C-reactive Protein (CRP) Among the Ultra-marathon Runners

	CRP			
Lipid Fraction	1 Quartile	2 Quartile	3 Quartile	4 Quartile
Total cholesterol (mg/dl)	197.4 ± 32.2	196.7 ± 29.1	205.9 ± 35.7	192.8 ± 51.9
LDL cholesterol (mg/dl)	116.3 ± 26.6	117.7 ± 26.7	124.7 ± 35.6	111.7 ± 38.0
HDL cholesterol (mg/dl)	50.8 ± 13.9	45.2 ± 13.1	48.3 ± 13.5	38.9 ± 7.7
Triglycerides (mg/dl)	152.5 ± 90.5	170.0 ± 85.8	166.6 ± 109.2	211.6 ± 131.0
Triglycerides/HDL cholesterol ratio	3.4 ± 2.8	4.6 ± 4.8	4.0 ± 3.4	5.9 ± 4.2

The major finding from this study is that regular long distance running lowers the LDL fraction independent of simultaneous reduction of CRP levels. Previous studies have implicated improvements in different lipoprotein fractions, including HDL,[3] LDL,[4] and triglycerides[3] after regular training, such as rugby[4] or tennis.[3] Together with these data, our results indicate that regular aerobic physical activities may differ significantly in terms of their qualitative influences on lipoprotein profiles in men. This implies that the type of exercise along with its amount[5] may be important when preventive or therapeutic decisions are made. Previous reports demonstrating the lack of association between reduction in LDL and CRP after pharmacologic and nonpharmacologic interventions[6–9] are supported by the results from this study. The lack of association between metabolic and inflammatory response to regular training mimics the antilipidemic effect of statins, which are believed to be independent of their anti-inflammatory influence.[8] Independent effects of statins on CRP and LDL may be explained, at least in part, by existence of 3-hydroxy-3-methylglutaryl coenzyme A reductase-dependent as well as -independent pathways.[10] Mechanisms responsible for anti-inflammatory and antilipidemic effects of exercise are not known. Weight loss, the most obvious pathway by which exercise could contribute to lowering of both inflammatory markers and cholesterol, can be excluded as the causative factor in the present analysis because the exercising subjects as well as the control group were well-matched for body mass index.[1] Moreover, our earlier investigations indicated that exercise-induced lowering of CRP is independent of markers of adiposity.[1] Finally, a case-control difference in LDL levels was more significant in lean subjects, whereas the magnitude of difference in CRP among the exercising subjects and sedentary controls was more striking in the non-lean category.

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