

33. Lipids

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Summary

The studies conducted thus far on physical activity and blood fats (lipids) have studied the effect of aerobic fitness training and strength training. There is no evidence today to suggest that strength training has a positive effect on blood lipids, whereas fitness training has an impact on triglycerides, HDL cholesterol (High Density Lipoprotein or alpha-lipoprotein) and to some degree also LDL cholesterol (Low Density Lipoproteins). The activity, which must be regular, 30–45 minutes most days of the week, should be of an intensity equivalent to 40–70 per cent of maximal capacity (after a gradual warm-up). The duration of each training session is dependent on the individual's possibilities and capacity, but should include a minimum of 30 minutes per session. To achieve maximal blood lipid-lowering effect, the training volume should be between 24–32 km per week, for example, a brisk walk or jogging, corresponding to 1200–2000 kcal per week. This calorie expenditure per week is associated with a 5–8 per cent increase in HDL cholesterol and a decrease in triglycerides of approximately 10 per cent.

Suitable activities include jogging, running, skiing, fitness classes, brisk walks, cycling, swimming, and racquet and ball sports.

Background

“The alpha-lipoprotein fraction is smaller and is more constant in amount, practically independent of the diet, and is considered to be non-atherogenic or even protective because its concentration in the serum is higher in premenopausal women than in men and tends to be reduced in CHD patients” (1).

The above was stated by Ancel Keys and Henry Blackburn almost 50 years ago, and they were the first to suggest that alpha-lipoprotein, or what we now call HDL cholesterol, had a protective effect with respect to cardiovascular disease. The interest in HDL cholesterol was weak for many years, overshadowed by studies that concentrated on total cholesterol, triglycerides and lipoproteins of a lower density. The reason for this is that researchers had not observed an ecological connection between alpha-lipoprotein levels and cardiovascular disease in Hawaii, Japan and Finland, three countries with large variations in the risk for heart diseases (2, 3). It was not until the brothers George and Norman Miller published their hypothesis that HDL had an anti-atherogenic effect, and the results of two prospective studies, from Tromso and Framingham, became known in 1977, that HDL cholesterol received attention as an interesting intermediary risk factor (4–6).

Functional mechanisms

What kind of a causal relationship is there?

What lies behind the reasoning of the relation between physical activity and blood lipids (HDL cholesterol fraction) is that it is HDL that has been shown to have the strongest relation to physical activity.

Figure 1 shows a simplified model of the relationship between physical inactivity and the risk for cardiovascular disease.

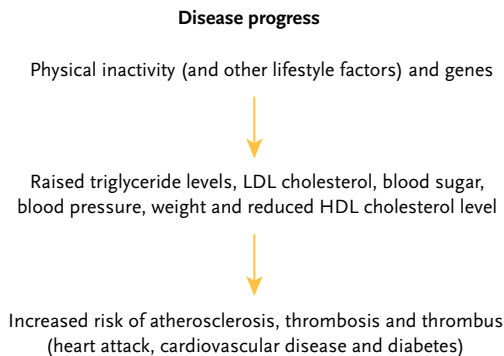


Figure 1. Model of the relation between physical inactivity and the risk for cardiovascular disease.

An individual's behaviour with regard to physical activity (such as frequency, intensity and duration) is assumed to affect different biological factors that play a part in one or more pathogenic mechanisms, for example, hardening of the arteries, risk of blood clots, or development of high blood pressure. After a certain time, the cells alter their function and thereby also the organ's function, which later yields clinical symptoms as a result of this. The above model gives a general picture of the disease mechanism that forms the basis for discussion about the relation between physical activity and blood lipids.

Lipids and their relation to cardiovascular disease

Lipid is a collective term that includes a "diverse range of compounds, like fatty acids and their derivatives, carotenoids, terpenes, steroids and bile acids, which are all soluble in organic solvents such as diethyl ether, benzene, chloroform or methanol" (7). There are also a number of shorter water-soluble fatty acids, but for the sake of discussion it suffices to know that fat molecules ingested with food or produced by the body are included in the term "lipid". The terms *lipid* and *fat* will be used synonymously in this chapter. Fat is a necessary part of our diet, containing the fat-soluble vitamins A, D, E and K, as well as being an energy source. In order to be transported in the blood, fat molecules must bind to proteins and form water-soluble complexes such as lipoproteins.

Lipoproteins transport triglycerides and cholesterol in the blood. Triglycerides are made up of three fatty acids and one glycerol molecule. They make up the body's energy stores and are also an integral part of the cell membrane. 95 per cent of the body's energy is stored as triglycerides. Cholesterol is a complex substance that is produced in the liver or supplied via the animal products in our diet and absorbed in the intestine. Cholesterol is also a crucial part of the cell membrane and is a precursor to sex hormones such as testosterone and progesterone.

Lipoproteins are distinguished according to size and density into different classes (see Table 1): chylomicrons, very low density lipoprotein (VLDL), low density lipoprotein (LDL) and high density lipoprotein (HDL). These can be broken down according to particle size and intermediary groups such as intermediate-density lipoprotein (IDL) and lipoprotein (a) or Lp(a). Lp(a) is a variant of LDL with the addition of a glycoprotein, Apo(a), attached to the LDL core, which is related to LDL and strongly associated with an increased risk of cardiovascular disease.

Table 1. Some physical characteristics and mean composition of lipoprotein fractions from normal triglycerides.

	Chylomicrons ¹	VLDL ²	IDL ³	LDL ⁴	HDL ⁵
Density (g/ml)					
Lower limit	–	0.96	1.006	1.019	1.063
Upper limit	0.96	1.006	1.019	1.063	1.21
Size (nm)	75–1200	30–80	25–35	19–25	5–12

1. Chylomicrons = belong to the lipoprotein group. After meals, cholesterol and triglycerides are transported via chylomicrons from the intestine.

2. VLDL = Very Low Density Lipoprotein.

3. IDL = Intermediate Density Lipoprotein.

4. LDL = Low Density Lipoprotein.

5. HDL = High Density Lipoprotein.

All of these lipoprotein complexes have been shown to be associated with cardiovascular disease at increased levels of LDL cholesterol. VLDL cholesterol, IDL cholesterol and Lp(a) are associated with a higher risk, while increased HDL cholesterol shows a lower risk. The sum of LDL-, VLDL-, IDL- and HDL cholesterol is what is measured as *total cholesterol*.

HDL cholesterol levels are higher in women than in men, and lower among diabetic patients, smokers, and in people who are overweight or physically inactive (8).

Alcohol intake also increases the level of HDL cholesterol (9).

Effects of physical activity

The studies that are of interest are either observation studies, in which physical activity is recorded and serum lipid levels in otherwise healthy individuals are measured, or investigations where the individual exercises at different intensities and the effect of blood fats is studied.

The relation between blood lipids and physical activity is known from observation studies from the 1970s, where individuals who reported low physical activity had 8 per cent higher total cholesterol than the very physically active subjects (10). Correspondingly, physically active men had 7 per cent- and physically active women 6 per cent higher HDL cholesterol than the inactive subjects (8). Findings from observation studies are, however, not the same as proof of a relation. Smaller trials have, however, been able to confirm the relation from epidemiological studies. Table 2 shows the effects of fitness training on blood lipids in women and men. After a programme lasting 12 weeks, HDL cholesterol increased by up to 16 per cent and was directly associated with the amount of exercise training (11–13). Shorter periods of training do not yield the same effect as longer ones. The effect on HDL cholesterol is more pronounced if the initial level is low. The increase in HDL cholesterol is related to the reduction in triglyceride levels, where HDL cholesterol and triglycerides have an inverse relationship (14), that is, the higher the triglycerides, the lower the HDL cholesterol. Physical activity has a direct effect on triglyceride

levels, with close to 30 per cent reduction if the initial value is high. At lower levels, the reduction will be approximately 10 per cent. The effect on LDL cholesterol is less impressive than the effect on triglycerides and HDL cholesterol.

Studies of physical activity in the population

A number of studies have demonstrated the relation between physical activity and lower blood fat levels, and individuals who are physically active have lower total cholesterol and higher HDL cholesterol. Data from a number of studies has shown that there is a break-point regarding the amount of physical activity needed to achieve a beneficial effect on blood lipids, corresponding to 24 to 32 km of brisk walking or jogging per week, that is, a calorie expenditure of 1200 to 2200 kcal is required to gain the desired effect. This weekly calorie expenditure is associated with an increase in HDL cholesterol of 0.5–0.8 mmol per litre and a decrease of triglycerides of 0.1–0.2 mmol per litre (15). Physical activity has a certain lowering effect on total cholesterol and LDL cholesterol.

After menopause, women have higher total cholesterol and higher LDL cholesterol. Physical activity has a beneficial effect in both older men and women, possibly with a greater reduction in LDL compared to younger individuals, as well as a reduction in total cholesterol (16, 17). Even individuals with a physically strenuous job or who are very active in daily life have higher HDL and total cholesterol (18).

Prescription

The studies conducted to date have looked at the effect of fitness training and strength training (resistance training). At present, there is no evidence to suggest that strength training has any particular positive effect on lipids, whereas fitness training has a positive effect on triglycerides, HDL cholesterol, and to a certain extent also LDL cholesterol (see Table 2).

Table 2. Expected protective effect of blood lipids and lipoproteins after a fitness training programme for men, women and seniors.

Lipid/Lipoprotein	Relation to CHD*	Effects of physical activity
Chylomicrons	Positive	↔
VLDL ¹	Somewhat positive	↔
IDL ²	Somewhat positive	↔
LDL ³	Positive	↔
Lp(a) ⁴	Clearly positive	↔
HDL ⁵	Clearly reverse	↑
Total cholesterol	Clearly positive	↔
Triglycerides	Somewhat positive	↓

*CHD = Coronary Heart Disease.

1. VLDL = Very Low Density Lipoprotein.

2. IDL = Intermediate Density Lipoprotein.

3. LDL = Low Density Lipoprotein.

4. Lp(a) is a variant of LDL with the addition of a glycoprotein, Apo(a), attached to the LDL core.

5. HDL = High Density Lipoprotein.

↑ = Increased levels in blood, ↓ = Reduced levels in blood, ↔ = Little or no change in blood levels.

Increased physical activity is a supplement to other interventions, such as changes in diet and/or drugs, aimed at improving the blood lipid profile. The activity, which must be regular and carried out most days of the week, should be of an intensity equivalent to 40–70 per cent of maximal capacity (after a gradual warm-up). The duration of each exercise session is dependent on the individual’s possibilities and capacity, but should include a minimum of 30–45 minutes per day, and can likely be broken up into several shorter sessions throughout the day, though no shorter than 10 minutes per session.

There is currently an ongoing discussion as to the true meaning of HDL cholesterol as a causal factor or simply as a risk marker for coronary artery disease. Thus far, one clinical trial has been conducted with HDL-raisers, but without the expected positive result (19, 20). The only known method of actively raising HDL cholesterol without side-effects is physical activity.

References

1. Keys A, Blackburn H. Background of the patient with coronary heart disease. *Progr in Cardio Dis* 1963;6:14-44.
2. Keys A, Kimura N, Kusunokawa A, Bronte-Stewart B, Larsen N, Keys MH. Lessons from serum cholesterol studies in Japan, Hawaii and Los Angeles. *Ann Intern Med* 1958;48:83-94.
3. Karvonen M, Orma E, Keys A, Fidanza F, Brozek J. Cigarette smoking, serum-cholesterol, blood-pressure, and body fatness. Observations in Finland. *Lancet* 1959;1:492-4.
4. Miller GJ, Miller NE. Plasma-high-density-lipoprotein concentration and development of ischaemic heart disease. *Lancet* 1975;1:16-9.
5. Miller NE, Thelle DS, Førde OH, Mjos OD. The Tromso Heart Study. High-density lipoprotein and coronary heart disease. A prospective case-control study. *Lancet* 1977;1:965-8.
6. Gordon T, Castelli WP, Hjortland MC, Kannel WB, Dawber TR. High density lipoprotein as a protective factor against coronary heart disease. The Framingham Study. *Am J Med* 1977;62:707-14.
7. Christie WW. Lipid analysis. New York: Pergamon Press; 1982.
8. Førde OH, Thelle DS, Arnesen E, Mjos OD. Distribution of high density lipoprotein cholesterol according to relative body weight, cigarette smoking and leisure time physical activity. The Cardiovascular Disease Study in Finnmark 1977. *Acta Med Scand* 1986;219:167-71.
9. Schaefer EJ, Lamon-Fava S, Ordovas JM, Cohn SD, Schaefer MM, Castelli WP, et al. Factors associated with low and elevated plasma high density lipoprotein cholesterol and apolipoprotein A-I levels in the Framingham Offspring Study. *J Lipid Res* 1994; 35:871-82.
10. Thelle DS, Førde OH, Try K, Lehmann EH. The Tromso Heart Study. Methods and main results of the cross-sectional study. *Acta Med Scand* 1976;200:107-18.
11. Wood PD, Haskell WL, Blair SN, Williams PT, Krauss RM, Lindgren FT, et al. Increased exercise level and plasma lipoprotein concentrations. A one-year, randomized, controlled study in sedentary, middle-aged men. *Metabolism* 1983;32:31-9.
12. Dengel DR, Hagberg JM, Pratley RE, Rogus EM, Goldberg AP. Improvements in blood pressure, glucose metabolism, and lipoprotein lipids after aerobic exercise plus weight loss in obese, hypertensive middle-aged men. *Metabolism* 1998;47:1075-82.
13. Hagberg JM, Ferrell RE, Dengel DR, Wilund KR. Exercise training-induced blood pressure and plasma lipid improvements in hypertensives may be genotype dependent. *Hypertension* 1999;34:18-23.
14. Thelle DS, Cramp DG, Patel I, Walker M, Marr JW, Shaper AG. Total cholesterol, high density lipoprotein-cholesterol and triglycerides after a standardized high-fat meal. *Hum Nutr Clin Nutr* 1982;36:469-74.

15. Durstine JL, Grandjean PW, Davis PG, Ferguson MA, Alderson NL, DuBose KD. Blood lipid and lipoprotein adaptations to exercise. A quantitative analysis. *Sports Med* 2001;31:1033-62.
16. Boardley D, Fahlman M, Topp R, Morgan AL, McNevin N. The impact of exercise training on blood lipids in older adults. *Am J Geriatr Cardiol* 2007;16:30-5.
17. Pescatello LS, Murphy D, Costanzo D. Low-intensity physical activity benefits blood lipids and lipoproteins in older adults living at home. *Age Ageing* 2000;29:433-9.
18. Barengo NC, Kastarinen M, Lakka T, Nissinen A, Tuomilehto J. Different forms of physical activity and cardiovascular risk factors among 24–64-year-old men and women in Finland. *Eur J Cardiovasc Prev Rehabil* 2006;13:51-9.
19. Nicola P. Pfizer halts clinical trials of torcetrapib due to patients safety concerns. In: National Electronic Library of Medicines /<http://nelm.nhs.uk>); 2006.
20. Duriez P, Bordet R, Berthelot P. The strange case of Dr HDL and Mr HDL. Does a NO's story illuminate the mystery of HDL's dark side uncovered by Dr HDL's drug targeting CETP? *Med Hypotheses* 2007;69:752-7.