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High-density lipoprotein and other risk factors for coronary artery disease assessed by angiography

Total blood cholesterol and low-density lipoprotein cholesterol concentrations are well-established risk factors for the development of coronary artery disease,¹ whereas high-density lipoprotein cholesterol constitutes a negative risk factor for coronary disease²—that is, may exert a protective effect. The Framingham study¹ showed that the ratio of high-density lipoprotein cholesterol to total cholesterol may be an even more powerful negative risk factor. As neither the presence nor severity of coronary artery disease can be determined accurately by clinical or electrocardiographic examination, our study compared the serum total cholesterol and total high-density lipoprotein cholesterol concentrations and the ratio of high-density lipoprotein cholesterol to total cholesterol with the degree of coronary artery disease assessed angiographically.

Patients, method, and results

We studied 160 consecutive patients undergoing coronary angiography for the investigation of chest pain or assessment of valvular heart disease. The angiograms were reported independently by a consultant radiologist. Lesions were graded visually from 0 to 4: 0=normal, 1=25% stenosis, 2=50% stenosis, 3=75% stenosis, and 4=total occlusion.

A coronary index was calculated using the method designed by Balcon *et al*³ which takes into account the site, severity, and effect of multiple lesions in the coronary circulation. The index ranges from 0 to 1, where 0=total occlusion of all vessels and 1=normal coronary circulation. Twenty-four hours before catheterisation the serum total cholesterol and high-density lipoprotein cholesterol concentrations were measured after a 12-hour fast. Cholesterol and triglyceride concentrations were measured by semiautomated fluorometric techniques, Technicon method N77 and Liebermann-Burchard's reagent being used for cholesterol and Cramp and Robertson's method for triglyceride. High-density lipoprotein cholesterol was measured as for plasma cholesterol after precipitation with heparin (250 units in 50 μ l) and manganese chloride (50 μ l 1M solution).

Clinical details, lipid measurements, and coronary indices (expressed as means $\pm$ SD) of patient groups analysed by quartiles

Patient group	Sex		Age (years)	Blood pressure (mm Hg)		No of smokers	Mean No of cigarettes smoked daily	Plasma cholesterol (mmol/l)	Plasma high-density lipoprotein cholesterol (mmol/l)	High-density lipoprotein cholesterol: total cholesterol	Coronary index
	M	F		Systolic	Diastolic						
Cholesterol:											
Upper quartile	33	7	54.4 $\pm$ 8.8	144 $\pm$ 23	89 $\pm$ 12	16	22.9	8.0 $\pm$ 0.88			0.5 $\pm$ 0.31
Lower quartile	27	13	54.9 $\pm$ 8.4	144 $\pm$ 22	85 $\pm$ 12	18	20.0	4.8 $\pm$ 0.51			0.71 $\pm$ 0.32†
High-density lipoprotein cholesterol:											
Upper quartile	23	17	57.4 $\pm$ 8.4	141 $\pm$ 22	85 $\pm$ 12	15	15.6		1.4 $\pm$ 0.51		0.71 $\pm$ 0.33
Lower quartile	34	6	53.4 $\pm$ 7.7*	136 $\pm$ 23	85 $\pm$ 12	20	26.9		0.67 $\pm$ 0.09		0.58 $\pm$ 0.32
High-density lipoprotein cholesterol: total cholesterol:											
Upper quartile	26	14	55.7 $\pm$ 8.6	141 $\pm$ 23	85 $\pm$ 14	15	18.5			0.24 $\pm$ 0.04	0.78 $\pm$ 0.34
Lower quartile	36	4	52.9 $\pm$ 8.8	140 $\pm$ 24	86 $\pm$ 13	23	22.1			0.1 $\pm$ 0.01	0.52 $\pm$ 0.28§
Patients with coronary index of:											
1	33	23	52.9 $\pm$ 9.9	136 $\pm$ 22	85 $\pm$ 13	27	18.0	5.9 $\pm$ 1.2	1.05 $\pm$ 0.28	0.18 $\pm$ 0.06	1.0
< 0.42	49	7	56.1 $\pm$ 6.3*	145 $\pm$ 25†	89 $\pm$ 13	36	26.0	6.7 $\pm$ 1.6‡	1.0 $\pm$ 0.29	0.15 $\pm$ 0.05‡	0.25 $\pm$ 0.1

Significance of differences (Mann-Whitney U test): *p=0.04; †p=0.02; ‡p<0.01; §p<0.001.
Conversion: SI to traditional units—Cholesterol: 1 mmol/l $\approx$ 38.7 mg/100 ml.

The 160 patients were divided into quartiles on the basis of mean serum cholesterol and high-density lipoprotein cholesterol concentrations and the ratio of high-density lipoprotein cholesterol to total cholesterol. The coronary indices of the patients in the top and bottom quartiles for the respective lipid profiles were determined for comparison. Also, patients with normal coronary arteries were compared with an equivalent number of patients with the severest coronary artery disease for differences in lipoprotein concentrations. Other risk factors such as age, the number of cigarettes smoked daily, and systolic and diastolic blood pressures were also considered. The Mann-Whitney U non-parametric test was applied in all statistical analyses.

The table gives clinical details of the patients and the coronary indices, and shows significant differences between the groups.

Comment

Jenkins *et al*,⁴ in a study similar to ours, showed a significant inverse relation between high-density lipoprotein concentrations and the severity of coronary artery disease assessed angiographically. This association was not found in the present study (p<0.11). Total cholesterol, however, was significantly associated with severity of coronary artery disease, and the ratio of high-density lipoprotein cholesterol to total cholesterol was inversely related to the severity of coronary disease. Of these two variables, the inverse relation of the ratio was slightly stronger (p<0.001 and p=0.01 respectively).

Apart from a significant age difference between the two quartiles with high and low concentrations of high-density lipoprotein cholesterol (p=0.05), there were no significant differences in age, number of cigarettes smoked daily; and systolic and diastolic blood pressures between the upper and lower quartiles. When the data were analysed by comparing patients with the severest coronary occlusion (coronary index <0.42) with those with no occlusion, however, those with the severest occlusion were found to be older (p=0.04) and heavier smokers and to have higher blood pressure (p=0.02), as well as having a lower ratio of high-density lipoprotein to total cholesterol (p<0.01).

These results support the suggestion of Williams *et al*⁵ that the ratio of high-density lipoprotein cholesterol to total cholesterol should be included in any coronary risk screening profile.

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