Serum Lipid Concentrations in Patients with Coronary Arteriosclerosis Demonstrated by Coronary Arteriography

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The frequency of abnormal serum lipid concentrations in patients with coronary artery disease demonstrated by coronary arteriography was compared with that for normal control subjects and arteriographically normal patients. Triglycerides were supranormal in over half of the patients with demonstrable coronary artery disease, compared with only about a quarter of the subjects in the control group. Incidence of enhanced serum cholesterol was not significantly different in the two groups. These data support the observations of others who found that triglycerides are elevated more frequently than cholesterol in patients with coronary artery disease. Coronary arteriography enables the more precise diagnosis of coronary arteriosclerosis when attempting a correlation of serum lipid concentrations with coronary artery disease. Selection of subjects in this manner avoids the problem of the falsely low incidence of lipid abnormalities seen when patients are included who have normal coronary arteries. Of the subjects in this series in whom coronary arteriography was performed, 23% were found not to have coronary arteriosclerosis. However, patients who have undergone angiocardiographic studies are a highly selected group with special characteristics, and cannot be considered a representative sample of patients with coronary artery disease.

Additional Keyphrases serum cholesterol • serum triglycerides • myocardial infarction • angina pectoris • diagnostic aids

It is well established that the presence of abnormally high concentrations of blood lipids is one important factor in the pathogenesis of coronary arteriosclerosis. However, opinions differ as to whether enhanced cholesterol or enhanced triglycerides is of greater significance. Some investigators indicate that blood cholesterol concentrations correlate best with coronary artery disease (1). Others suggest that triglycerides are elevated more frequently than cholesterol (2, 3). Still others find that enhanced triglycerides without enhanced cholesterol is not associated with an increased risk of coronary arteriosclerosis (4, 5).

In most studies attempting to correlate blood lipids with coronary arteriosclerosis, the presence of coronary artery disease is based on clinical and electrocardiographic criteria. However, not all patients with angina pectoris actually have disease of the coronary arteries. Some patients may have chest pain of the coronary type, even associated with an abnormal electrocardiogram, but are shown to have normal coronary arteries when studied by coronary arteriography (6–8). In one study, about a third of the patients examined by coronary arteriography was found to have normal coronary vessels. Therefore, it was suggested that a more reliable correlation of lipid abnormalities with coronary artery disease is possible when the presence of coronary arteriosclerosis is demonstrated by coronary arteriography (9). Coronary arteriography usually cannot detect early small atheromatous plaques; however, the method is capable of defining the extent and location of larger plaques that cause narrowing or irregularity of the coronary arteries and that are likely to be clinically significant.

This study was undertaken to determine the
frequency and type of lipid abnormalities in a group of patients in whom coronary arteriosclerosis was demonstrated by selective coronary cineangiography.

Method

In an initial pilot study, serum lipids were evaluated in 70 patients with angiocardiographically demonstrated coronary artery disease who were admitted to St. Mary's Hospital (10). This group was compared with a control group of 50 subjects, mostly physicians on the hospital staff. This study was subsequently expanded to include an investigation of all patients who were admitted to the hospital for coronary arteriography during a two-year period (from July 1968 to July 1970). All specimens were obtained from subjects after an overnight fast of 12 to 14 h. Cholesterol and triglyceride were considered supranormal if they exceeded the age-adjusted normal limits proposed by Fredrickson et al. (11). Upper limit for normal cholesterol varied from 240–330 mg/100 ml, upper limit for normal triglyceride from 140–190 mg/100 ml, depending on the age of the subject. Cholesterol was measured by an automated direct method based on the Liebermann–Burchard reaction (12). This method has been shown to correlate well with extraction methods (13). Triglycerides were determined by the methods of Kessler et al. (14).

During the two-year period, 456 patients had coronary arteriographic studies. Of these patients, 106 or about 23% of the total group, had normal coronary arteries. One hundred and four patients had abnormal coronary arteriograms, but lipid data were either absent or incomplete, and this group was excluded from evaluation. Two hundred forty-six patients had abnormal arteriograms and complete lipid data were available; this group was used for analysis. Two control groups were used for comparison. One control group consisted of the 50 subjects from the original pilot study, 45 men and five women. Complete lipid data were available on 80 of the 106 patients who were shown to have normal coronary arteries by arteriography, and these 80 patients, 31 men and 49 women, were used as a second control group. The preponderance of women in this second control group probably reflects the greater frequency in women of the anginal syndrome with normal coronary arteries. There were 76 men and 54 women in the pooled control group. Because of the relatively large number of women in the second control group, the proportion of men in the pooled control group was somewhat lower than in the coronary group.

The group with demonstrable coronary artery disease consisted of 197 men and 49 women. Of these patients, 114 had sustained previous myocardial infarction.

Complete dietary information was not available for the subjects on whom coronary arteriography was performed; some may have been on lipid-lowering diets or received other treatment, but this information was not available.

It is known that serum lipid concentrations are unstable, and fluctuate for a variable period of time after an episode of myocardial infarction (15, 16). In this evaluation, when a patient had sustained a myocardial infarct, the catheterization and lipid studies were done after an interval of several months to several years, which minimized the possible effect of the previous infarct on the lipid data.

Results

Table 1 compares the lipid data for the group of 246 patients having coronary disease with that for the control groups. Serum lipid concentrations were normal in 39% of the patients with coronary artery disease, whereas serum lipids were normal in a much higher percentage of the control groups (P <0.001). The frequency of enhanced cholesterol without enhanced triglyceride was low in both the coronary artery disease group and the control groups; the differences are not statistically significant. Enhanced triglycerides without enhanced cholesterol was found in about half of the coronary artery disease group and in about a quarter of the control groups (P <0.001). Both lipids were enhanced in 11% of the coronary artery disease group, and a smaller percentage of the two control groups. This difference is also significant (P <0.01).

Table 2 compares the frequency of enhanced cholesterol and triglycerides in the coronary artery disease group with that in the control

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<th>Table 1. Frequency of Abnormal Serum Lipid Concentrations in Patients with Coronary Artery Disease as Compared with Two Control Groups</th>
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<th>Table 2. Frequency of Supranormal Concentrations of Serum Lipids in Patients with Coronary Disease as Compared with Two Control Groups</th>
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groups. The frequency of hypercholesterolemia with or without hyperglyceridemia was 13% in the coronary artery disease group, which was not significantly different from that found in the control groups. However, triglycerides were abnormally high in 58% of the coronary group, but in only about a quarter of the subjects in the control groups (P <0.001).

Table 3 compares the results for the coronary artery disease group by sex and age in decades with those for the control group of 80 patients in whom coronary arteriography had been performed with no evidence of disease. The number of subjects in each group is indicated; mean cholesterol and triglycerides are tabulated by sex and decade. In male patients, the mean cholesterol in the third and fourth decades was higher than the mean for either control group, but this difference was not observed in the older subjects. The mean triglyceride concentration of the male coronary patients in the third and fourth decades was also greater than that for the controls. In women with coronary disease, mean cholesterol concentration was greater than the controls in all decades, and their mean triglyceride concentration also tended to be somewhat greater than that of controls in the fourth, fifth, and sixth decades.

There is some evidence that supranormal cholesterol concentrations correlate better with coronary artery disease in the younger patient (17).

We found that the mean cholesterol concentration in the younger patients appeared to be greater than the mean for the control subjects. Table 4 indicates how frequently cholesterol was abnormally high in coronary disease patients of both sexes in the third and fourth decades (18%), as compared with 10.5% of the corresponding control groups. Because of the small numbers of patients involved in the comparison, the difference is not statistically significant. However, triglycerides were more frequently supranormal in the coronary disease group than in the control groups (P <0.01).

**Discussion**

Our data support the observation of others—that serum triglycerides are enhanced more frequently than serum cholesterol in patients who have coronary artery disease. This study also demonstrates that coronary arteriography is a much more precise method for defining the presence of coronary arteriosclerosis when attempting any correlation of serum lipid levels with coronary artery disease. The selection of patients in this manner avoids the problem of a false low incidence of lipid abnormalities because patients have been included who have normal coronary arteries. In this study, 23% of patients suspected of coronary disease were shown not to have coronary arteriosclerosis demonstrable by arteriography. This
incidence of normal coronary arteries is comparable to the experience of Proudfit et al. (18), who found that 17% of their 700 patients considered clinically to have coronary artery disease had normal coronary arteries. In other studies, an even greater frequency of normal coronary arteriograms has been observed (9). Because patients with suspected coronary arteriosclerosis often have angiographically normal coronary arteries, standard clinical and electrocardiographic criteria evidently are subject to considerable error in defining patients with disease of the major coronary arteries. A possible error of this magnitude may introduce considerable bias into a study relating coronary artery disease to change in serum lipids.

However, patients who have undergone angiographic studies are not a representative sample of patients with coronary artery disease for several reasons.

First, many patients studied by arteriography have had myocardial infarctions. Approximately half of the patients in this study had sustained a previous myocardial infarction. Since mortality after myocardial infarction is about 15 to 20%, the postinfarction patients studied are survivors of a larger group. In the Framingham study (1), it was found that the mortality within the first three weeks after myocardial infarction was related to the antecedent cholesterol level. Patients with high concentrations of serum cholesterol before their infarction had a higher mortality than patients whose concentrations were normal or low. Therefore, the number of patients with elevated cholesterol would be expected to be disproportionately low in survivors of myocardial infarction because of the excessive mortality in the patients with hypercholesterolemia.

Secondly, the patient who has coronary arteriography—with its concomitant expense, discomfort, and slight risk of coronary arteriography—is probably very highly motivated, and not representative of the typical patient. He is more likely to maintain his ideal weight, exercise moderately, not eat or drink excessively, and to adopt other habits and activities tending to promote more normal serum lipids.

Thirdly, the patient with established coronary artery disease is likely to have made some attempt at modification of his diet, either of his own accord or under his physician’s supervision, and it is well known that both cholesterol and triglyceride can be influenced by altering the diet.

These factors may account for the fact that the frequency of hypercholesterolemia in the coronary disease group was not significantly higher than in the control groups in this study.

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References