High density lipoprotein cholesterol concentration as a predictor of coronary heart disease in West Indian men

G J Miller, G L A Beckles, G H Maude, D C Carson, S G L Price

Abstract

Study objective—The aim of the study was to determine whether the inverse association between high density lipoprotein cholesterol concentration and risk of coronary heart disease described in people of European stock was also present in other racial groups.

Design—The study was a prospective population survey. Cardiovascular risk factors were examined, including fasting serum lipid estimation (obtained at recruitment).

Setting—This was a community based study within a defined survey area in Trinidad.

Participants—All men aged between 35 and 69 years within the survey area were identified and followed between 1977 and 1986. Analysis was confined to those of African, Asian Indian, and mixed descent who were free of coronary heart disease at entry (n = 960, 69% of age eligible men in the survey population).

Measurements and main results—64 men developed coronary heart disease during the study period. A strong inverse curvilinear relation was found between high density lipoprotein cholesterol and coronary heart disease incidence (p < 0.005), independent of age or other relevant characteristics including low density lipoprotein cholesterol.

Conclusions—A low serum concentration of high density lipoprotein cholesterol is a risk factor for coronary heart disease in non-whites as well as in whites.

A strong and inverse relation between plasma high density lipoprotein cholesterol concentration and risk of coronary heart disease exists in many countries of European stock. The evidence that high density lipoprotein protects against atheroma suggests that its association with coronary heart disease will apply similarly to other racial groups. To test this possibility, a prospective survey was undertaken in Trinidad, West Indies.

Methods

The population and recruitment methods have been described. Briefly, all men aged 35–69 years within the defined survey area in Trinidad were identified by household census and followed between 1977 and 1986. Previous medical history (including angina pectoris) and smoking habit were recorded. Ethnic origin was assessed from the family history. Those judged to be at least 75% African, Asian Indian, European, Chinese, Lebanese or Syrian by descent were grouped accordingly, and others were designated “Mixed”. Fasting blood samples were taken at the time of recruitment. Separate aliquots of fasting serum were used to prepare high density lipoprotein by a heparin-manganese method, and very low density lipoprotein free serum by a sodium lauryl sulphate procedure. All preparations and a sample of whole serum were subsequently analysed for cholesterol and triglyceride by enzymatic procedures. Low density lipoprotein cholesterol concentration was derived by difference. Fasting blood glucose was measured by the Nelson-Somogyi method.

Blood pressure was recorded on two occasions on the left arm with a random zero sphygmomanometer and the average used in the analysis. A resting electrocardiogram (ECG) was recorded with a Cambridge VS 4S instrument, read against a reticle scale (Edmund Scientific, New Jersey), and coded to Minnesota criteria. Biceps, triceps, subscapular and suprailiac skinfolds were measured in duplicate and summed for statistical analysis.

Follow up

All men were visited annually and those with a history suggestive of recent cardiovascular disease were examined clinically. Survivors were offered an ECG at 5 years. Deaths were traced through family informants, death registers and hospital records. The underlying cause of morbidity or mortality was reached after independent review of all documentation by two physicians without reference to baseline status, with a third as arbiter when necessary. Events in which coronary heart disease was considered to be the underlying cause (coronary events) were grouped by mode of presentation according to ICD codes 410–4 (ischaemic heart disease), 427 (dysrhythmias), 428 (heart failure), 429.1 (myocardial degeneration), 798.1–2 (sudden death), or a new major Q wave (code 1J) in V5 of the 5 year ECG (silent myocardial infarction).

Statistical analysis

The analysis was confined to men of African, Asian Indian, and Mixed descent, since its purpose was to search for an association between high density lipoprotein cholesterol and coronary heart disease in non-Europeans. Small numbers of Chinese, Lebanese and Syrians were also excluded. Men with coronary heart disease at baseline (a positive history of angina pectoris or acute myocardial infarction, or a major Q wave...
HDL cholesterol as predictor of coronary heart disease in non-whites

35-74

424 23

321 38

215 3

960 64

Table I
Numbers of participants by age and ethnic group, with number of coronary events

Age group (years) | African | Indian | Mixed | Total
<table>
<thead>
<tr>
<th>n</th>
<th>Events</th>
<th>n</th>
<th>Events</th>
<th>n</th>
<th>Events</th>
<th>n</th>
<th>Events</th>
</tr>
</thead>
<tbody>
<tr>
<td>35-44</td>
<td>94</td>
<td>2</td>
<td>109</td>
<td>7</td>
<td>75</td>
<td>2</td>
<td>278</td>
</tr>
<tr>
<td>45-54</td>
<td>113</td>
<td>5</td>
<td>105</td>
<td>16</td>
<td>64</td>
<td>1</td>
<td>282</td>
</tr>
<tr>
<td>55-64</td>
<td>137</td>
<td>11</td>
<td>86</td>
<td>11</td>
<td>57</td>
<td>0</td>
<td>280</td>
</tr>
<tr>
<td>65-74</td>
<td>80</td>
<td>5</td>
<td>21</td>
<td>4</td>
<td>19</td>
<td>0</td>
<td>120</td>
</tr>
<tr>
<td>35-74</td>
<td>424</td>
<td>23</td>
<td>321</td>
<td>38</td>
<td>215</td>
<td>3</td>
<td>960</td>
</tr>
</tbody>
</table>

After allowance for age at entry, the log transformed value of high density lipoprotein cholesterol was more strongly associated with coronary heart disease hazard (log likelihood $\chi^2 = 7.99; p < 0.005$) than the untransformed value ($\chi^2 = 4.20; p = 0.04$). Thus $\log_{10}$ high density lipoprotein cholesterol was used in further analyses. There was a significant reduction in coronary heart disease hazard of $30\%$, per standard deviation increase in $\log_{10}$ high density lipoprotein cholesterol ($p = 0.003$). The curvilinear relation between high density lipoprotein cholesterol concentration and age adjusted coronary heart disease hazard is shown in the figure.

The relation between high density lipoprotein (HDL) cholesterol concentration and age-adjusted coronary heart disease hazard relative to that at a concentration of 1 mmol/litre (hazard ratio).

Table II gives the standardised hazard ratios for high density lipoprotein cholesterol when account had been taken of age at entry and one or more additional risk factors. For example, after adjustment for age and low density lipoprotein cholesterol, a one standard deviation increase in $\log_{10}$ high density lipoprotein cholesterol was associated with a $27\%$ reduction in coronary heart disease hazard ($p = 0.01$). In a further analysis in which age group at entry, low density lipoprotein cholesterol, serum triglyceride concentration, fasting blood glucose, four summed skinfolds, systolic and diastolic blood pressure, and ethnic group were taken into account, high density lipoprotein cholesterol remained significantly, inversely and independently associated with coronary heart disease risk (log likelihood $\chi^2 = 5.00; p = 0.025$). When total serum cholesterol was substituted for low density lipoprotein cholesterol in this further analysis, the $\chi^2$ value increased to 7.38 ($p < 0.01$), and a one SD increase in $\log_{10}$ high density lipoprotein cholesterol was associated with a $32\%$ reduction in coronary heart disease hazard. The associations did not differ with ethnic group. Cigarette smoking was not considered in the analysis because it lacked any significant association with coronary heart disease in this community.

Discussion

This study has shown that the association between a low high density lipoprotein cholesterol and high coronary heart disease risk is not confined to populations of European descent but applies also to non-white communities. As elsewhere,1-3 the relation is independent of other coronary heart disease risk factors including low density lipoprotein cholesterol and serum triglyceride concentrations, blood glucose concentration and blood pressure. The
Table II  Standardised hazard ratio (SHR) for log_{10} high density lipoprotein (HDL) cholesterol after allowance for additional risk factors

<table>
<thead>
<tr>
<th>Additional risk factor</th>
<th>SHR for log HDL cholesterol</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age alone</td>
<td>0.70</td>
<td>0.003</td>
</tr>
<tr>
<td>Age + LDL cholesterol</td>
<td>0.73</td>
<td>0.01</td>
</tr>
<tr>
<td>Age + serum triglyceride</td>
<td>0.70</td>
<td>0.008</td>
</tr>
<tr>
<td>Age + blood glucose</td>
<td>0.72</td>
<td>0.01</td>
</tr>
<tr>
<td>Age + sum of 4 skinfolds</td>
<td>0.68</td>
<td>0.003</td>
</tr>
<tr>
<td>Age + systolic pressure</td>
<td>0.67</td>
<td>0.002</td>
</tr>
<tr>
<td>Age + diastolic pressure</td>
<td>0.69</td>
<td>0.003</td>
</tr>
<tr>
<td>Age + ethnic group</td>
<td>0.77</td>
<td>0.004</td>
</tr>
<tr>
<td>All of the above</td>
<td>0.73</td>
<td>0.025</td>
</tr>
</tbody>
</table>

The consistency of the findings across several ethnic groups is further evidence for a fundamental role of high density lipoprotein cholesterol in the disease process, with high concentrations affording protection.

Only one other study has sought an association between high density lipoprotein cholesterol and coronary heart disease in a non-white population. Equivocal results were given by an analysis of data for 465 black men randomised to “usual care” in the American Multiple Risk Factor Intervention Trial. This study was not designed to search for this relation, however, and lacked statistical power in this respect.

The predominantly non-white Trinidad population has a surprisingly high coronary heart disease mortality. In 1983 for example, the death rate from myocardial infarction in men aged 55–64 years was reported to be 394.3/100,000, as compared with 329.5/100,000 in the USA. Preventive measures to reduce the incidence of coronary heart disease in this population are therefore urgently required. As in other communities, high density lipoprotein cholesterol concentration should be included in the assessment of individual risk, using reference values established by the local laboratory. As an approximation, each decrement of 0.025 mmol/litre (1 mg/dl) in high density lipoprotein cholesterol between the mean and one standard deviation below the mean was associated with a 1–6% increase in coronary heart disease risk, which was similar to the 2%, increase reported in the USA.

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