Lipids and Other Risk Factors Selected by Discriminant Analysis in Symptomatic Patients With Supra-Aortic and Peripheral Atherosclerosis

G.B. Vigna, MD; M. Bolzan, PhD; F. Romagnoni, MD; G. Valerio, MD; E. Vitale, MD; G. Zuliani, MD; and R. Fellin, MD

Background. Different patterns of risk factors might be related to the involvement of specific vascular districts by atherosclerosis. In this sense, many investigations have addressed coronary artery disease, whereas extracoronary atherosclerosis has received less extensive attention.

Methods and Results. Vascular risk factors, with particular attention to lipid parameters (total cholesterol [TC]; triglycerides; high density lipoprotein cholesterol [HDL-C], HDL₂ and HDL₃ cholesterol [HDL₂-C, HDL₃-C]), were evaluated by means of univariate and multivariate (discriminant) analysis in a group of 169 patients (128 men and 41 women; mean ages, 58±7 and 62±7 years, respectively) with clinically and angiographically demonstrated atherosclerosis of the supra-aortic trunk and/or lower limbs. Patients with coronary artery disease were excluded from this study. The control group consisted of 140 age- and sex-matched individuals. By univariate analysis, smoking was more closely associated with peripheral atherosclerosis, whereas blood pressure was higher in patients with supra-aortic disease. Unrecognized diabetes mellitus was a frequent finding in patients with peripheral disease. The percentage of hyperlipidemias was fourfold higher in patients than in control subjects, with differences consisting of higher triglycerides and lower HDL-C, HDL₂-C, and HDL₃-C concentrations. By discriminant analysis, high correct classification (CC) rates were achieved in the various patient subgroups on the basis of variables selected from the statistical function. In male patients with peripheral disease, the variables HDL-C, smoking, diastolic blood pressure, uric acid, and glucose, in that order, yielded a CC in 90.4% of the cases; in female patients, smoking, TC/HDL-C, and body mass index gave a CC rate of 95.9%. In men with cerebral disease, the selected variables TC/HDL-C, diastolic blood pressure, and TC yielded a CC of 90.7%; in women, uric acid, TC/HDL-C, and fibrinogen levels produced a CC rate of 89.2%.

Conclusions. Risk profiles in atherosclerosis of the supra-aortic trunks and lower limbs seem to differ in relation to gender and circulatory district involved. The importance of lipid parameters, in particular HDL-C, HDL₂-C, and TC/HDL-C, as extracoronary risk factors is further confirmed. (Circulation 1992;85:2205–2211)

KEY WORDS • atherosclerosis • supra-aortic • peripheral vasculature • lipids • risk factors • analysis, discriminant

Among the clinical manifestations of atherosclerosis, ischemic heart disease (IHD) is the most studied from both epidemiological and pathogenetic points of view, whereas carotid or vertebral and peripheral atherosclerosis have received less attention. Subsequent investigations into risk factors (RFs) associated with extracoronary atherosclerosis were in part influenced by IHD studies, but findings nonetheless indicated that a different risk pattern is related to the predominant and occasionally exclusive involvement of a specific vascular district.¹⁻⁴

We examined patients with atherosclerosis of the supra-aortic trunk or lower limbs with the aim of evaluating the relation between the two forms of the disease and some lipid parameters and other cardiovascular RFs; particular attention was given to the high density lipoprotein (HDL) subfractions. Results were elaborated by univariate analysis and stepwise multiple discriminant analysis; with the latter procedure, we searched for variables that allowed the best correct classification (CC) of patients with vascular disease compared with healthy control subjects.

Methods

Patients

In the period from 1986 to 1989, we studied 169 patients (128 men and 41 women; mean age, 58±7 and 62±7 years, respectively) with supra-aortic or peripheral atherosclerosis. All were symptomatic and were

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Received October 18, 1990; revision accepted March 11, 1992.
referred to our department for the evaluation of episodes of intermittent claudication or transient ischemic attacks (TIAs) in the carotid and/or vertebral-basilar vascular districts. These patients were studied during hospitalization, and in every case the clinical diagnosis was confirmed by angiography. Angiographic examination of both the supra-aortic and peripheral vascular trees was performed only in patients with clinical symptoms (TIAs, previous stroke, intermittent claudication) or signs (vascular bruits, reduction or disappearance of one or more arterial pulses) in both arterial districts. Patients with TIA or previous stroke without symptoms and/or physical signs of lower limb atherosclerosis underwent supra-aortic angiographic examination only. In patients with intermittent claudication and those in whom supra-aortic vascular involvement could be excluded by clinical assessment, only lower limb angiography was performed. Moreover, noninvasive vascular assessment excluded clinical underestimates of vascular territory involvement in all patients: real-time B-mode imaging was performed in the supra-aortic vascular district by use of a Biosound real-time imager and an 8-MHz transducer probe; transcutaneous Doppler with analog waveform recording permitted the evaluation of femoral and posterior tibial arteries and the determination of the ankle/arm index.

Hemodynamically significant atherosclerotic lesions (stenosis >50% in one or more vessels) were localized in the lower limbs in 102 subjects (76 men, 26 women) and in the supra-aortic trunk in 46 (31 men, 15 women) (Table 1).

Abdominal aorta and iliac arteries were affected in 20% of patients, femoral/popliteal involvement was present in 49%, and combined aorto/femoral/iliac disease was detected in 31%. Among subjects with supra-aortic trunk atherosclerosis (46 patients; 31 men and 15 women), 63% had internal carotid disease, 15% common carotid, and 22% different combinations of common carotid, brachiocephalic trunk, vertebral, and subclavian artery involvement.

Isolated aneurysmatic dilatations were not detected (most likely because this lesion is uncommon or rarely symptomatic with regard to claudication or TIA). Abdominal aortic aneurysm was associated with more distally located stenosis in six patients.

Both supra-aortic and lower limb vascular sites were involved in 21 men (Table 1); common carotid and femoral/popliteal artery involvement were the most common associations (75%).

Patients with history of myocardial infarction, clinical symptoms, or ECG signs of IHD were excluded from this study. Other exclusion criteria were secondary hyperlipidemia and a documented history of diabetes mellitus. However, patients in whom the diagnosis of diabetes mellitus was formulated during the study were included and considered as having unrecognized diabetes. At the time of this investigation, no patient was taking drugs known to interfere with lipid metabolism.

A group of 140 age- and sex-matched healthy persons (84 men and 56 women; mean ages, 58±7 and 59±9 years, respectively) living in the same geographical area (northeastern Italy) served as control subjects. Eligibility for control group enrollment was determined by the absence of clinical symptoms and signs of vascular and other severe systemic disease (neoplastic and hematological disease; chronic infections). Exclusion criteria also included endocrinopathies and other disorders implicated in secondary hyperlipidemia, as well as extreme paraphysiological conditions (strenuous physical training, incongruous diet). A specific questionnaire and a complete physical examination ruled out the presence of symptoms or signs ascribable to intermittent claudication, TIA or previous stroke, angina pectoris, and myocardial infarction. Palpation of arterial pulses (carotid, subclavian, radial, ulnar, femoral, popliteal, posterior tibial, and pedal) was routinely performed, with normal results in every case. No bruits were heard in the main vascular districts (neck, abdomen, subclavian, and femoral regions). ECG records were examined in all subjects according to the revised Minnesota code and enabled exclusion of IHD. Control subjects were recruited over a 3-year period among healthy subjects who came to our medical attention in a variety of ways (relatives of noncardiovascular patients, medical staff, direct invitation). Every group of 10 patients investigated was followed by another group of 10 normal subjects with a similar age range. Every subject was carefully evaluated for the presence of coronary, cerebrovascular, or peripheral atherosclerosis; history, ECG, full physical examination, and routine analysis permitted a sufficiently accurate recruitment. Twenty presumably normal persons were excluded after this examination because unrecognized disease was found (anemia in eight, moderate renal insufficiency in three,
### Table 2. Blood Glucose, Uric Acid, Fibrinogen, Body Mass Index, Systolic and Diastolic Blood Pressures, and Smoke in Patients and Control Subjects

<table>
<thead>
<tr>
<th>Site</th>
<th>Sex</th>
<th>Glucose (mg/dl)</th>
<th>Uric acid (mg/dl)</th>
<th>Fibrinogen (mg/dl)</th>
<th>Body mass index (kg/m²)</th>
<th>Systolic blood pressure (mm Hg)</th>
<th>Diastolic blood pressure (mm Hg)</th>
<th>Smoke (cigarettes per day)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lower limb M</td>
<td>101±29*</td>
<td>6.2±1.4†</td>
<td>400±114*</td>
<td>25.2±2.9</td>
<td>152±18*</td>
<td>87±9†</td>
<td>19±13‡</td>
<td></td>
</tr>
<tr>
<td>Supra-aortic M</td>
<td>106±46</td>
<td>5.6±1.9†</td>
<td>341±99</td>
<td>25.5±3.1</td>
<td>156±26*</td>
<td>89±11†</td>
<td>16±11†</td>
<td></td>
</tr>
<tr>
<td>Both sites M</td>
<td>98±24</td>
<td>6.2±2.0*</td>
<td>398±56</td>
<td>25.7±3.5</td>
<td>154±20*</td>
<td>83±10</td>
<td>16±17</td>
<td></td>
</tr>
<tr>
<td>Total M</td>
<td>102±33†</td>
<td>6.1±1.7†</td>
<td>383±107</td>
<td>25.4±3.0</td>
<td>153±21‡</td>
<td>87±10†</td>
<td>18±14‡</td>
<td></td>
</tr>
<tr>
<td>Control subjects M</td>
<td>89±14</td>
<td>4.9±1.0</td>
<td>350±50</td>
<td>25.7±3.0</td>
<td>140±15</td>
<td>82±9</td>
<td>8±11</td>
<td></td>
</tr>
<tr>
<td>Lower limb F</td>
<td>106±26†</td>
<td>5.3±1.1†</td>
<td>397±117</td>
<td>22.0±3.1</td>
<td>141±13</td>
<td>83±7</td>
<td>12±7‡</td>
<td></td>
</tr>
<tr>
<td>Supra-aortic F</td>
<td>92±10</td>
<td>5.6±1.3†</td>
<td>316±43*</td>
<td>25.6±4.5</td>
<td>155±21*</td>
<td>86±7†</td>
<td>5±8</td>
<td></td>
</tr>
<tr>
<td>Total F</td>
<td>101±23†</td>
<td>5.4±1.2‡</td>
<td>370±105</td>
<td>23.4±4.1</td>
<td>146±18</td>
<td>84±7</td>
<td>9±8‡</td>
<td></td>
</tr>
<tr>
<td>Control subjects F</td>
<td>87±9</td>
<td>4.4±0.9</td>
<td>359±39</td>
<td>24.2±3.9</td>
<td>146±14</td>
<td>80±7</td>
<td>2±5</td>
<td></td>
</tr>
</tbody>
</table>

Values are mean±SD.

*tp<0.05, †tp<0.01, ‡tp<0.001, patients vs. control subjects.

abnormal increase of transaminases in eight, and hypothyroidism in one).

### Blood Lipid Analysis and Detection of Other Risk Factors

Each patient was interviewed concerning diseases preceding or concomitant with the current atherosclerotic pathology, and a drug inventory was made; blood pressure was measured, and body mass index (BMI) (weight in kilograms divided by the square of height in meters) was determined. Smokers were identified; a subject who smoked two or more cigarettes daily for at least 1 year was defined as a current smoker. This variable was quantified as follows: if a person did not smoke, the number of cigarettes smoked per day was listed as zero; for a smoker or ex-smoker, the rough mean number of cigarettes smoked daily in the last 5 years was recorded.

Morning venous blood samples were obtained after a 12-hour fast; 10 ml was left at room temperature for 1 hour and then centrifuged at 2,000 rpm for 10 minutes to separate serum; 5 ml was collected in test tubes containing 7 mg EDTA, immediately centrifuged, and used to determine plasma fibrinogen, uric acid, and glucose.

Blood lipids were assayed in serum. Lipoprotein electrophoretic separation was carried out in agarose gel. Total HDL and HDL₃ fractions were isolated by selective lipoprotein precipitation with polyanions (sodium heparin and dextran sulfate) according to a modification of the procedure described by Gideon et al.⁶,⁷ Total cholesterol (TC) as well as HDL and HDL₃ cholesterol (HDL-C and HDL₃-C, respectively) were determined enzymatically according to the method of Allain et al.⁸; HDL₂ cholesterol (HDL₂-C) was obtained by subtraction (HDL-C minus HDL₃-C). Triglycerides (TGs) were evaluated according to Wahlefeld.⁹

### Statistical Analysis

Mean values in the male and female patient and control groups were compared by Student's t test or Cochran and Cox's W test (for significantly heteroscedastic groups); frequency distributions were compared by the χ² test.¹⁰ Stepwise discriminant analysis¹¹ was first performed in the men as a whole, considering case patients and control subjects as classification groups, and then in a similar manner in the women. The analysis was then conducted separately in each subgroup of the case patients and in the control subjects grouped according to sex.

### Results

A comprehensive examination of the RFs studied confirmed the importance of smoking, hypertension, diabetes mellitus, and hyperlipidemia in patients with extracoronary atherosclerosis (Table 1). Cigarette smoking as well as the number of cigarettes smoked daily (Table 2) were significantly associated with peripheral atherosclerosis (p<0.001) in both men and women. Patients with atherosclerosis of the supra-aortic trunks instead were more frequently hypertensive (systolic blood pressure >160 mm Hg and/or diastolic blood pressure >95 mm Hg) than were patients with peripheral disease and controls and had significantly higher systolic and diastolic blood pressures (p<0.05 and p<0.01, respectively). Male patients in whom both vascular districts were involved had the highest frequency of hypertension (57%, p<0.001) (Tables 1 and 2).

Plasma glucose levels were significantly higher in male (p<0.01) and female (p<0.01) patients considered together than in control subjects (Table 2). Uric acid concentrations were significantly higher in patients than in control subjects (p<0.01 in men and p<0.001 in women); plasma fibrinogen was increased in men with peripheral atherosclerosis (p<0.05) and reduced in women with supra-aortic disease (p<0.05). Overweight, expressed by BMI, was not clearly associated with extracoronary atherosclerosis by univariate analysis (Table 2). The overall percentage of hyperlipidemias that were classified on the basis of plasma lipoprotein electrophoresis was about fourfold higher in patients than in control subjects; the most frequent World Health Organization (WHO) phenotypes were type IV in men (18%) and type IIA in women (22%) (Table 3). Mean values of lipid parameters are reported in Table 4. TGs were significantly higher (p<0.05), and HDL-C
was reduced ($p<0.001$), in all the groups compared with the control group. This last finding is explained by a simultaneous reduction in HDL$_2$-C and HDL$_3$-C. TC levels were significantly increased only in female patients with peripheral atherosclerosis (252±49 mg/dl, $p<0.01$), although the TC/HDL-C ratio was invariably higher ($p<0.01$) in all the patient groups than in the control group.

The results of multivariate analysis (stepwise discriminant analysis) are shown in Figure 1. In male patients, a set of five variables was selected that allowed a CC of 87.4% of the subjects. HDL-C alone was the determining factor in 73.7%; for the others, it was necessary to add smoking, diastolic blood pressure, uric acid, and plasma glucose levels. Analysis of the single subgroups increased discriminating capacity; the main variables were the TC/HDL-C ratio in patients with atherosclerosis of the supra-aortic trunk and combined supra-aortic and lower limb involvement (in whom this ratio alone produced a CC rate of 80.4% and 82.2%, respectively) and once again HDL-C in patients with peripheral disease (in whom it correctly classified 69.9% of these cases). In women, three variables alone (TC/HDL-C, smoking, and uric acid levels, in this order) allowed a CC of 83.6% of the patients. Uric acid concentrations (79.3%) and smoking (83.3%) predominated in the supra-aortic and peripheral groups, respectively, but the TC/HDL-C ratio in both groups was the second most important variable identified.

### Table 3. Prevalence of Hyperlipidemias Among Patients and Control Subjects

<table>
<thead>
<tr>
<th></th>
<th>Men Patients (n=128)</th>
<th>Controls (n=84)</th>
<th>Women Patients (n=41)</th>
<th>Controls (n=56)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n %</td>
<td>n %</td>
<td>n %</td>
<td>n %</td>
</tr>
<tr>
<td>Hyperlipidemic</td>
<td>48*</td>
<td>38 8 10</td>
<td>15†</td>
<td>37 5 9</td>
</tr>
<tr>
<td>Phenotype IIA</td>
<td>15 12 5 6</td>
<td>9 22 5 9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Phenotype IIB</td>
<td>10 8 3 4</td>
<td>4 10</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Phenotype IV</td>
<td>23*</td>
<td>18 . . . . . . .</td>
<td>2 5</td>
<td></td>
</tr>
</tbody>
</table>

*p<0.001, †p<0.01, patients vs. control subjects.

### Table 4. Total Cholesterol, Triglycerides, HDL, HDL$_2$, and HDL$_3$ Cholesterol in Patients Subdivided According to Lesion Distribution and Control Subjects

<table>
<thead>
<tr>
<th>Site</th>
<th>Sex</th>
<th>Total cholesterol (mg/dl)</th>
<th>Triglycerides (mg/dl)</th>
<th>HDL-C (mg/dl)</th>
<th>HDL$_2$-C (mg/dl)</th>
<th>HDL$_3$-C (mg/dl)</th>
<th>TC/HDL-C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lower limb</td>
<td>M</td>
<td>221±49</td>
<td>145±72*</td>
<td>38.9±9.5†</td>
<td>12.8±6.3†</td>
<td>26.1±6.1†</td>
<td>5.89±1.62†</td>
</tr>
<tr>
<td>Supra-aortic</td>
<td>M</td>
<td>226±48</td>
<td>158±84*</td>
<td>35.9±9.4†</td>
<td>10.6±5.7†</td>
<td>25.3±7.1†</td>
<td>6.66±2.03†</td>
</tr>
<tr>
<td>Both sites</td>
<td>M</td>
<td>217±46</td>
<td>155±76*</td>
<td>36.6±9.8†</td>
<td>10.5±4.4†</td>
<td>26.0±6.7†</td>
<td>6.24±1.78†</td>
</tr>
<tr>
<td>Control</td>
<td>M</td>
<td>217±32</td>
<td>117±40</td>
<td>51.2±11.2</td>
<td>19.2±7.8</td>
<td>32.0±5.6</td>
<td>4.39±1.00</td>
</tr>
<tr>
<td>Lower limb</td>
<td>F</td>
<td>252±49‡</td>
<td>153±87‡</td>
<td>45.5±11.3†</td>
<td>16.3±7.8†</td>
<td>29.5±7.1†</td>
<td>5.81±1.71†</td>
</tr>
<tr>
<td>Supra-aortic</td>
<td>F</td>
<td>209±34</td>
<td>105±37</td>
<td>44.7±12.6†</td>
<td>14.9±8.6†</td>
<td>29.1±6.6‡</td>
<td>5.04±1.65‡</td>
</tr>
</tbody>
</table>

Control subjects

<table>
<thead>
<tr>
<th>Sex</th>
<th>Total cholesterol (mg/dl)</th>
<th>Triglycerides (mg/dl)</th>
<th>HDL-C (mg/dl)</th>
<th>HDL$_2$-C (mg/dl)</th>
<th>HDL$_3$-C (mg/dl)</th>
<th>TC/HDL-C</th>
</tr>
</thead>
<tbody>
<tr>
<td>M</td>
<td>213±30</td>
<td>84±27</td>
<td>58.8±9.8</td>
<td>23.8±8.9</td>
<td>35.1±6.4</td>
<td>3.73±0.91</td>
</tr>
<tr>
<td>F</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Values are mean±SD. HDL-C, high density lipoprotein cholesterol; TC, total cholesterol; M, male; F, female.

*p<0.05, †p<0.001, ‡p<0.01, patients vs. controls.

### Discussion

All the patients in this study were symptomatic. It is known, however, that the individuals who come to medical attention because of stroke, TIA, or intermittent claudication represent only a part of those with supra-aortic or peripheral vascular disease, whereas a larger group is asymptomatic or shows only limited or atypical findings. In fact, several reports indicate that the prevalence rate of intermittent claudication in populations with an average age similar to that of our study group is about 1–4%.

On the other hand, clinical evaluation of the reduction or disappearance of peripheral pulses (particularly in the dorsalis pedis artery) disclosed figures from 10% to 30%. The actual prevalence of peripheral artery disease has been variously assessed with noninvasive tests, and it seems to be about 11–15% for subjects about 60 years of age.

Similar considerations hold for cerebrovascular symptoms related to supra-aortic trunk involvement. The prevalence of TIA in selected studies was estimated at two to 18 per 1,000 in subjects over 40 years of age.

The incidence of stroke in men aged 55–64 years ranged from three to seven per 1,000 per year (lower figures in women). In this case as well, the prevalence of arterial stenosis by clinical (vascular bruises) or instrumental evaluation was clearly superior, with different figures according to the sex, age, and group characteristics of investigated subjects.

Our investigation, however, did not address these epidemiological aspects. This study was conducted in a large series of symptomatic patients with the specific aim of evaluating the relative significance of several risk factors in extracoronary atherosclerosis and identifying those variables that permitted the best discrimination from normal control subjects. Subjects with overt clinical symptoms of cerebral or peripheral atherosclerosis were selected in order to contribute to subgroup homogeneity (as further confirmed by the severe stenosis disclosed by angiographic study) as well as to investigate risk factors in a relevant clinical setting of disease. For this reason and because multivariate analysis requires a large sample number, any further patient stratification based on impairment in each vascular district was obviated.
It was reported that up to 10% of middle-aged subjects without symptoms of myocardial ischemia had clinically silent IHD.\(^2^\) Moreover, by means of \(^2^\)TI myocardial scintigraphy or ECG stress testing, other workers found a 23% incidence of silent myocardial ischemia among patients with cerebrovascular disorders.\(^3^\) Thus, even an accurate evaluation of the patient's history and standard ECG may not suffice to exclude coronary impairment in subjects manifesting atherosclerosis of the carotid, vertebro, or ilio-femoral arteries. Hence, in the light of these considerations, it is noteworthy that although the presence of extracoronary atherosclerosis was the main feature of vascular disease in our patients, it did not definitely exclude concomitant coronary involvement of slight or moderate degree.

By univariate analysis, smoking and the number of cigarettes smoked daily were closely associated with the presence of peripheral atherosclerosis (as generally recognized)\(^4^\); their importance was further confirmed by discriminant analysis. Nonetheless, the latter did not seem to indicate that the risk connected with smoking was ascribable to effects on fibrinogen levels, which were higher than in control subjects. Prospective studies found this association related to acute coronary and cerebral events.\(^5^\)\(^6^\)

Hypertension was more frequent in patients with supra-aortic atherosclerosis but not always at a significant level. Patients with carotid and vertebral atherosclerosis generally presented a closer association with diastolic blood pressure. Several epidemiological investigations found that hypertension was the main RF for acute cerebral atherothrombotic events,\(^7^\)\(^8^\) and yet it was associated in a weak and inconsistent manner with angiographically defined carotid atherosclerosis even by multivariate analysis.\(^9^\)\(^10^\) In this study, discriminant analysis identified diastolic blood pressure as a significant variable but only in male patients with supra-aortic disease.

Hyperglycemia and, occasionally, clinically unrecognized diabetes mellitus were detected in particular in subjects with peripheral disease.

Increased uric acid levels compared with control subjects were a frequent finding and constituted the most significant classification variable by discriminant analysis in the subgroup of female patients with supra-aortic disease. The meaning of this parameter is uncertain; some workers find it correlated with stroke,\(^11^\) whereas others evidence an inverse relation.\(^12^\) It is possible that uric acid metabolism alterations are part of a more widespread metabolic disorder that includes
dyslipoproteinemia, hyperglycemia, hyperinsulinemia, and hypertension (polymetabolic syndrome).33,34

High TGs and low HDL-C levels were important features in patient groups of both sexes with supraaortic and peripheral atherosclerosis. This confirms results reported by other workers.24,35-43 In agreement with our previous observations,7,44 HDL-C (the most antiatherogenic HDL fraction45) was reduced percentagewise to levels equal to or higher than HDL-C concentration. Low serum HDL levels may be related to their decreased synthesis or an altered catabolism. As we previously described in detail,44 this finding could correspond to a reduced degradation of TG-rich lipoproteins (very low density lipoproteins) in these patients. On the other hand, the sex-related HDL pattern was maintained (HDL higher in female patients than in male), thus suggesting that other factors responsible for their plasma level (hormones, diet) are normally operating.

In male patients, multivariate analysis clearly selected lipoprotein parameters (HDL-C, TC/HDL-C) as the best classification discriminants. In female patients as a whole, once again the TC/HDL-C ratio was the most meaningful variable, despite the importance of smoking and high uric acid levels in peripheral and cerebral atherosclerosis, respectively.

Very few analyses similar to the one described in this study are available. Pilger et al41 evaluated a group of 49 male patients with peripheral atherosclerosis by discriminant analysis, addressing in particular the plasma apolipoproteins (apo A-I, apo A-II, apo B), which were considered better discriminators than plasma lipids or lipoproteins. These workers proposed an optimal model with 14 variables that gave a CC rate of 95.6%; the selected parameters included HDL-C, smoking, hyperuricemia, and diabetes mellitus, which also appear with varying significance in our analysis.

As shown in Figure 1, our model achieved a CC rate of 90.4% with five variables in men and 95.9% with only three variables in women. In a study of male and female patients with stroke, Kostner et al42 demonstrated that an optimal discrimination could be achieved using seven variables, among which were TC, HDL-C, and arterial blood pressure, in partial agreement with our findings (the other variables were apo A-I, apo A-II, plasma lecithin, and cholesterol).

In the present study, stepwise discriminant analysis was preferred to multiple logistic regression analysis to select useful parameters that could best identify subjects with prevalent atherosclerotic disease in extracranial vascular sites. This choice was justified by the types of variables collected, knowledge of the complex and limited resources inherent in a clinical epidemiological investigation, and the high classification levels we eventually reached. This analysis consistently selected a number of variables in women equal to or lower than that in men; in addition, risk profiles in the two sexes differed somewhat. Although these results on the whole confirm a distinct sensitivity to vascular RFs in different circulatory districts and in the two sexes, they also indicate the need for further study to explain residual differences. In this regard, a potentially confusing aspect of our investigation deserves comment. The exclusion criteria for enrolling both patients and control subjects were chosen to preclude disease that was previously shown to be highly atherogenic (diabetes mellitus) or in any case able to modify some variables under study (e.g., secondary hyperlipidemias). At the same time, however, this choice might preclude a broader application of our results to different groups or populations with such diseases. In addition, the main clinical basis of patient selection likewise could be said to limit the generalizability of our data to subjects with symptomatic disease only; however, this group in effect represents an epidemiologically significant unit of primary medical care.

Acknowledgment

The authors wish to thank Patricia Segato for her help in preparation of the manuscript.

References

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_Circulation_. 1992;85:2205-2211
doi: 10.1161/01.CIR.85.6.2205

_Circulation_ is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

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