Serum Lp(a) as a Discriminant Marker of Early Atherosclerotic Plaque at Three Extracoronary Sites in Hypercholesterolemic Men


To investigate the role of lipoprotein (a) (Lp(a)) as an atherogenic condition related to hypercholesterolemia, we studied the serum concentration of Lp(a) as measured by immunonephelometry in relation to the presence of asymptomatic echographic plaques in the peripheral arteries of 103 untreated hypercholesterolemic, normotensive, middle-aged men. Plaque was found at carotid, aortic, and femoral sites in 36%, 51%, and 53% of subjects, respectively. The Lp(a) level was higher in the group with carotid plaques than in the group without (0.29±0.20 versus 0.17±0.14 g/l, p<0.01), not significantly higher in the group with aortics plaque than in the group without (0.24±0.19 versus 0.19±0.16 g/l), and not different between groups with and without femoral plaques (0.21±0.18 versus 0.22±0.17 g/l). A logistic regression analysis confirmed that Lp(a) was associated with carotid plaques (p=0.004), independent of other risk factors. However, in patients with low density lipoprotein cholesterol values above the group median value (4.7 mmol/l), Lp(a) was associated not only with carotid plaques (p<0.01) but also with aortic plaques (p<0.05), as well as with the number of diseased sites (p=0.02). In contrast, in patients with low density lipoprotein cholesterol levels below or equal to 4.7 mmol/l, Lp(a) only remained associated with carotid plaques (p<0.05). Thus, in symptom-free, hypercholesterolemic men, early atherosclerosis was influenced by serum Lp(a), particularly in the carotid arteries, as well as by the presence of a higher level of low density lipoprotein cholesterol. (Arteriosclerosis and Thrombosis 1992;12:1346-1352)

KEY WORDS • B-mode ultrasonography • atherosclerotic plaque • cardiovascular disease risk factors • hypercholesterolemia

Several retrospective and prospective studies have shown that a high serum level of lipoprotein (a) (Lp[a]) may be an independent risk factor for atherothrombotic disease.1 These studies were mainly concerned with coronary heart disease, including premature myocardial infarction,2 clinical coronary disease,3 angiographically assessed coronary lesions,4-6 and restenosis of coronary bypass grafts.3 Moreover, the presence of Lp(a) has been described in atheromatous and venous coronary grafts.8,9 In contrast, little is known about the relation of serum Lp(a) to extracoronary disease,10-12 and even less is known about early atherosclerosis before the appearance of advanced arterial lesions. Thus, the purpose of our work was to determine the serum Lp(a) concentration in hypercholesterolemia, a powerful risk factor for atherosclerotic disease,13 and to analyze its relation to early extracoronary atherosclerosis in subjects free from any clinical cardiovascular disease. Early atherosclerosis was assessed on the basis of the presence of arterial plaques detected by high-resolution B-mode ultrasonography at three different sites: the carotid arteries, the femoral arteries, and the abdominal aorta.14,15

Methods

Study Subjects

All of the study subjects were men 28–60 years of age (Table 1). They were selected from an ongoing cholesterol screening program in occupational medicine that is being conducted on employees of several companies within the Paris area.14,15 They were screened for their total blood cholesterol level at their worksites by a group of occupational health physicians, the PCVMETRA group (Prevention Cardiovasculaire en médecine du Travail).14,15 Total blood cholesterol level was measured by the classic enzymatic method15 in biochemistry laboratories close to the worksites. In 5,758 of the men screened in this way, the worksite cholesterol value was, on average, 5.80±1.10 (mean±SD) mmol/l. Only those subjects whose total cholesterol level was above 6.2 mmol/l when measured at the worksite were referred to the hospital, where a second measurement of blood cholesterol level was
performed in our hospital laboratory. Subjects whose hospital cholesterol level was below 5.2 mmol/l, a threshold classically admitted as defining "desirable blood cholesterol,"\textsuperscript{13} were sent back to their occupational health physicians. The others were considered hypercholesterolemic and underwent complementary investigations, including blood lipid measurements, evaluation of nonlipid risk factors, and ultrasonic detection of arterial plaques.\textsuperscript{14,15} From these subjects, a group of 103 randomly selected men underwent the determination of serum Lp(a) concentration, on the condition that they fulfilled several selection criteria as defined below. All of these investigations were performed during a single day of hospitalization.

**Blood Lipid Measurements**

Lipid measurements (Table 1) were performed at the hospital after a 14-hour fast on venous blood samples that were withdrawn after the subjects had been in the supine position for at least 10 minutes.\textsuperscript{13} Serum total cholesterol and triglyceride values were measured by using classic enzymatic methods.\textsuperscript{16} High density lipoprotein (HDL) cholesterol was measured by the enzymatic method after selective precipitation of low (LDL) and very low (VLDL) density lipoproteins by phosphotungstic–magnesium chloride acid.\textsuperscript{17} LDL cholesterol was calculated according to the classic formula\textsuperscript{18} (in millimoles per liter):

\[
LDL \text{ cholesterol} = \text{total cholesterol} - \text{HDL cholesterol} - (\text{triglyceride}/2.2)
\]

The study's selection criteria required all subjects to have a triglyceride level below or equal to 4.6 mmol/l. In addition, we verified that the subjects had no diseases or factors causing secondary hypercholesterolemia\textsuperscript{13} and no current or previous treatments with lipid-lowering drugs. Finally, for all subjects, electrophoresis of lipids was performed to verify the absence of hyperchylomicronemia.

The serum Lp(a) concentration was determined by immunonephelometry\textsuperscript{19,20} 1–5 days after the blood withdrawal. Once the patient's serum was isolated, it was stored at 4°C. Shear antisepser to apolipoprotein (a) (AG, Vienna, Austria), a reference human serum standard containing 58.6 mg/100 ml Lp(a), and normal human control serum containing 26.6 mg/100 ml Lp(a) were used. It has already been shown that the use of this polyclonal antibody does not induce a cross-reaction with plasminogen.\textsuperscript{21} The reference standard was diluted 1:5, 1:10, 1:20, 1:40, and 1:80 with a 0.15 M NaCl solution containing sodium azide (1 g/l) to obtain a calibration scale. The sample and control sera were diluted 1:5 with a sodium chloride solution. Samples that were too concentrated or too turbid to be read at a dilution of 1:5 were measured at 1:20 so that the reading would fall within the calibration scale. Lp(a) concentrations were determined in the presence of polyethylene glycol at 40%. The measurements were automatically performed by means of a nephelometric analyzer (Behring, Rueil Malmaison, France). A double determination of serum Lp(a) concentration in the same sample was performed in a random subgroup of 10 subjects, which resulted in a coefficient of variation of ±3%. The coefficient of variation between samples taken from the same individual at different occasions was determined as 14±12% (±SD) in a random subgroup of 23 subjects. Finally, to assess the possible confounding effects of triglyceride-rich particles, 34 samples of serum with triglyceride values ranging from 0.67 to 4.10 mmol/l (mean±SD, 1.83±0.84 mmol/l) were assayed for Lp(a) before and after ultracentrifugation for 17 hours at 100,000 g in a TPT 45.6 rotor (TG A50, Kontron Instruments, Montigny le Bretonneux, France) to eliminate VLDL particles. The mean concentrations of Lp(a) before and after VLDL elimination were 0.18±0.17 and 0.14±0.15 g/l, respectively. The values of the two measurements were closely correlated \((r=0.94)\) (Figure 1, upper panel). The intercept of the correlation as well as the comparison before and after ultracentrifugation shows that the ultracentrifugation introduced an underestimation of the actual Lp(a) level. We accounted for this phenomenon by means of a statistical approach for assessing agreement between two methods of biological measurement.\textsuperscript{22} The plot of the difference between the Lp(a) values before and after ultracentrifugation against their mean values (Figure 1, lower panel) shows that the underestimation induced by ultracentrifugation was higher than the correlation expressed in the upper panel of Figure 1. However, this underestimation was poorly correlated with the level of triglyceride \((r=0.36, p=0.05)\).

**Nonlipid Risk Factor Evaluation**

Systemic blood pressure was determined as the mean of at least three measurements taken by standard sphygmomanometric procedures in the arm while the subject was in the supine position and after a 10-minute rest.\textsuperscript{23} The study's selection criteria called for subjects whose diastolic blood pressure (Korotkoff phase V) was less than 95 mm Hg and who had never been treated with any antihypertensive drug. The body mass index (weight/height\(^2\)) was used as a measure of obesity.\textsuperscript{14,15} To define smoking status, a subject was considered to be a current daily smoker if he had regularly smoked at least five cigarettes per day for the previous 3 months.\textsuperscript{23} The lifelong smoking dose was also calculated by mul-
multiplying the mean number of cigarettes smoked daily and the number of years of smoking (pack-years, i.e., smoking one pack each day for 1 year). Blood glucose level was measured after an overnight fast. All subjects were required to have a fasting glucose level equal to or below 6.7 mmol/l and/or to have never undergone antidiabetic treatment. Blood glucose level was measured after an overnight fast. All subjects were required to have a fasting glucose level equal to or below 6.7 mmol/l and/or to have never undergone antidiabetic treatment. Finally, a complete clinical examination verified the absence of any apparent history or sign of cardiovascular complications, such as cerebral artery disease, coronary heart disease, and arteritis of the legs. Any of these signs constituted an exclusion criterion of the study.

Arterial Investigations

The carotid arteries, the abdominal aorta, and the femoral arteries of each subject were screened for atherosclerotic disease by real-time B-mode ultrasonography (radius CF, General Electric, CGR France, Issy les Moulineaux, France) with a 3.75-MHz probe for the aorta and a 7.5-MHz probe for the carotid and femoral arteries. A pulsed Doppler was incorporated into each probe to analyze the presence of vascular flow velocity. Examination of carotid arteries was performed by placing the probe on the neck along the vessel axis while the subject was lying in the supine position, with the neck extended in mild rotation. The examination included the common, internal, and external carotid arteries and the carotid bifurcation of both sides. Examination of the abdominal aorta was performed by placing the probe to the left of the subumbilical medial line while the patient was in the dorsal decubitus position. The examination included that part of the aorta located just under the diaphragm down to its lower end. Examination of the femoral arteries was performed by moving the probe over the length of the artery with the lower limb in slight external rotation while the patient was in the dorsal decubitus position. Examination included the common, superficial, and deep femoral arteries as well as the femoral bifurcation. The ultrasonic images were magnified and projected in real time on a television monitor. Hard copies of real-time images were made for longitudinal and axial sections of the arteries. An echo structure encroaching into the vessel lumen was considered to be a plaque when a distinct area with more than 50% greater intimal plus medial thickness compared with that of neighboring sites could be identified. A sound beam was adjusted perpendicularly to the arterial surface, intimal plus medial thickness was evaluated as the distance from the edge of the first echogenic bright line (corresponding to the lumen-intima interface) to the edge of the second echogenic line (corresponding to the media-adventitia interface). In practice, the minimal defining thickness of a plaque was considered to be 2 mm, and the presence of a plaque at each site was considered positive regardless of number. This classifi-
cation of atherosclerosis into two classes according to the absence or presence of plaque gave a high reproducibility rate, as previously demonstrated by an agreement of 90% or more between the original assessment and blinded reassessments.14,15

Statistical Analysis

At each site investigated, univariate comparisons of variables were performed according to the presence or absence of plaque. The independent sample t test for quantitative variables or the χ² test for qualitative variables was used. For variables with a nonnormal distribution (e.g., lifelong smoking status and Lp[a] level), a nonparametric Mann-Whitney U test was used. At each site, a multivariate logistic-regression analysis was performed between plaque (absence=0, presence=1) as the dependent variable and risk factors as independent variables.26 A logistic-regression analysis was also performed between the number of arterial sites with plaques (0, 1, 2, or 3), which were considered ordinal dependent variables, and risk factors, which were considered independent variables.26 As the distribution of Lp(a) values was skewed (Figure 2), a logarithmic transformation (ln Lp[a]) was applied for multivariate analysis to produce an approximate but not strictly normal distribution. Statistical analysis was carried out on an Apple Macintosh computer with the use of JMP (SAS Institute, Cary, N.C.) and EXCEL (Microsoft, Les Ulis, France) software.

Results

The selected characteristics of the study group are given in Table 1. No significant correlations were observed between Lp(a) and age, body mass index, smoking status, and other blood lipids. Table 2 shows that the prevalence of the presence of plaque at the carotid, aortic, and femoral sites was 36%, 51%, and 53%, respectively. Age was significantly higher in subjects with plaque than in those without at the carotid (p<0.05), aortic (p<0.05), and femoral (p<0.01) sites (Table 2). The frequency of current smokers was significantly higher in subjects with aortic plaque than in those without (p<0.05) but was not significantly higher in subjects with plaque than in those without at the carotid and femoral sites (Table 2). The lifelong smoking dose was significantly higher in subjects with aortic plaque than in those without (p<0.05) and in subjects with femoral plaque than in those without (p<0.01) but was not significantly different among subjects with carotid plaque and those without (Table 2). Body mass index and blood lipid levels other than Lp(a) were not different among subjects with plaque and those without, regardless of site (Table 2). Finally, the serum Lp(a) level was significantly higher in subjects with carotid plaque than in those without (p<0.01) but was not significantly different among subjects with plaque and those without at the aortic and femoral sites (Figure 3).

A multivariate logistic-regression analysis was carried out to investigate risk factors influencing the presence of plaque at each site and the number of diseased sites (Table 3). The presence of carotid plaque was associated with Lp(a) (p=0.004) and to a nearly significant extent with age (p=0.06) (Table 3). The presence of aortic plaque was not associated with any factor (Table 3). The presence of femoral plaque was associated only with age (p=0.001) (Table 3). The number of diseased sites was associated with age (p=0.001) and the lifelong

### Table 2. Plaque Prevalence and Univariate Comparison of Traditional Risk Factors* at Three Extracoronary Sites

<table>
<thead>
<tr>
<th>Variable</th>
<th>Carotid plaque</th>
<th>Aortic plaque</th>
<th>Femoral plaque</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Absent</td>
<td>Present</td>
<td>Absent</td>
</tr>
<tr>
<td>Percentage of subjects</td>
<td>64</td>
<td>36</td>
<td>49</td>
</tr>
<tr>
<td>Age (years)</td>
<td>44±7</td>
<td>47±7†</td>
<td>44±7</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>25±2</td>
<td>25±2</td>
<td>25±3</td>
</tr>
<tr>
<td>Smokers (% current)</td>
<td>38</td>
<td>43</td>
<td>29</td>
</tr>
<tr>
<td>Lifelong smoking (pack-years)</td>
<td>13±16</td>
<td>18±18</td>
<td>12±16</td>
</tr>
<tr>
<td>Total cholesterol (mmol/l)</td>
<td>6.77±0.81</td>
<td>6.95±0.81</td>
<td>6.75±0.76</td>
</tr>
<tr>
<td>LDL cholesterol (mmol/l)</td>
<td>4.80±0.78</td>
<td>4.87±0.80</td>
<td>4.75±0.76</td>
</tr>
<tr>
<td>HDL cholesterol (mmol/l)</td>
<td>1.17±0.32</td>
<td>1.25±0.25</td>
<td>1.21±0.32</td>
</tr>
<tr>
<td>Triglycerides (mmol/l)</td>
<td>1.75±0.86</td>
<td>1.84±0.88</td>
<td>1.75±0.92</td>
</tr>
</tbody>
</table>

LDL, low density lipoprotein; HDL, high density lipoprotein. Values are mean±SD or as a percentage of the number of subjects in each subgroup.

*Comparison between those with (present) and without (absent) plaques was performed with a nonparametric test (see “Methods”) and were significantly different from each other at tp<0.05 and tp<0.01.
smoking dose ($p=0.04$) but not significantly with Lp(a) ($p=0.08$) (Table 3).

A univariate comparison of risk factors according to the presence or absence of plaque at each site was performed after dividing the overall population into two subgroups according to the median of LDL cholesterol concentration (4.7 mmol/l): a lower LDL cholesterol subgroup of 52 subjects and a higher LDL cholesterol subgroup of the 51 remaining subjects (Table 4). In the lower LDL cholesterol subgroup, the Lp(a) level was higher in subjects with carotid plaque than in those without ($p<0.05$), age was higher in subjects with aortic plaque than in those without ($p<0.05$), and age and lifelong smoking dose were higher in subjects with femoral plaque than in those without ($p<0.05$) (Table 4). In the higher LDL cholesterol subgroup, the Lp(a) level was higher in subjects with carotid and aortic plaques than in those without ($p<0.01$ and $p<0.05$, respectively), and age was higher in subjects with femoral plaques than in those without ($p<0.001$) (Table 4). Finally, a multivariate logistic-regression analysis of risk factors influencing the number of arterial sites affected by plaque showed that in the lower LDL cholesterol subgroup, only age was associated with the number of diseased sites ($p=0.004$), whereas in the higher LDL cholesterol subgroup both Lp(a) and age were associated with the number of diseased sites ($p=0.02$ and $p=0.04$, respectively) (data not shown).

**Discussion**

The purpose of the present work was to investigate the connections between Lp(a) levels and early atherosclerotic plaques in asymptomatic hypercholesterolemia. We defined atheroma by the presence of plaque because, as we have previously shown, such a definition gives the best interobserver and intraobserver reproducibility. However, more sophisticated ultrasonic measurements should be undertaken in further studies to obtain more informative and quantitative evaluation of aspects of atherosclerosis, such as the arterial wall thickness. To avoid possible atherogenic influences of major nonlipid risk factors, which could interfere with the potential relations between Lp(a) level and plaque, subjects with hypertension and/or diabetes mellitus were excluded from the study. Smokers were included in the study because smoking is very common among male employees included in this study group. We also excluded any subject who had ever taken a lipid-lowering drug, a factor that can alter the arterial structure. Thus, we found that the influence of age and smoking on arterial plaque was similar to that observed in our previous study on carotid and aortic plaques in normotensive hypercholesterolemic men. In contrast, the present work was slightly discrepant with another study that we performed on atherosclerotic plaques at three sites in 208 hypercholesterolemic men, in whom we found that carotid plaque was not significantly related to age but significantly related to LDL cholesterol. This discrepancy could be accounted for the fact that, unlike the present normotensive population, 25% of our previous 208 men were hypertensive. Our major objective was to analyze the level of serum Lp(a) in relation to the presence of extracoronary

**Table 3. Logistic-Regression Analysis of Risk Factors Influencing the Site of Arterial Plaque and Number of Arterial Sites Affected by Plaque**

<table>
<thead>
<tr>
<th>Dependent variable</th>
<th>Independent variable</th>
<th>$\chi^2$</th>
<th>$P$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carotid arterial plaque</td>
<td>ln (Lp[a])</td>
<td>8.3</td>
<td>0.004</td>
</tr>
<tr>
<td></td>
<td>Age</td>
<td>3.4</td>
<td>0.06</td>
</tr>
<tr>
<td>Aortic arterial plaque</td>
<td>Lifelong smoking</td>
<td>2.1</td>
<td>0.14</td>
</tr>
<tr>
<td></td>
<td>Age</td>
<td>3.1</td>
<td>0.08</td>
</tr>
<tr>
<td>Femoral arterial plaque</td>
<td>Age</td>
<td>10.8</td>
<td>0.001</td>
</tr>
<tr>
<td></td>
<td>Lifelong smoking</td>
<td>2.6</td>
<td>0.11</td>
</tr>
<tr>
<td>Number of diseased sites</td>
<td>Age</td>
<td>10.2</td>
<td>0.001</td>
</tr>
<tr>
<td></td>
<td>Lifelong smoking</td>
<td>4.1</td>
<td>0.04</td>
</tr>
<tr>
<td></td>
<td>ln (Lp[a])</td>
<td>3.1</td>
<td>0.08</td>
</tr>
</tbody>
</table>

Lp(a), lipoprotein (a).
plaque at different sites. The immunonephelometric assay used to measure Lp(a) level has a high capacity and is easy to perform but can be inaccurate for samples containing triglyceride-rich particles. For this reason we excluded subjects with a triglyceride level above 4.6 mmol/l. Nevertheless, in a random subsample of 34 subjects, we found that when we eliminated VLDL fractions through ultracentrifugation, triglyceride-rich lipoproteins interfered slightly with the immunonephelometric assay of Lp(a). However, this interference was minimally dependent on the increase in triglycerides for values below 4.6 mmol/l. In this way we found that the Lp(a) concentration was, on average, 71% higher in subjects with carotid plaques than in those without but not significantly different between subjects with aortic or femoral plaques and those without. Moreover, the strong association between elevated serum Lp(a) level and the presence of carotid plaque was independent of age, the only other risk factor related to carotid plaque. These findings agree with previous studies reported in the literature that show that serum Lp(a) level is a reliable indicator for cerebrovascular disease and is strongly correlated with carotid lesions scored from Doppler analysis of patients with clinical cerebrovascular disease. However, unlike these studies, the subjects of the present work were asymptomatic and exempt from any clinical cardiovascular disease. Finally, our findings suggest that aortic and femoral sites were less sensitive to the atherogenic effect of Lp(a) than were the carotid arteries.

Another aim of our work was to determine whether the influence of serum Lp(a) on arterial plaque was dependent on the level of LDL cholesterol. It has been reported that the relative risk for myocardial infarction is significantly increased in subjects with high Lp(a) concentrations when LDL concentrations are also high. As our study group was characterized by a wide variation in LDL cholesterol level, we divided the group into two subgroups of higher and lower LDL cholesterol values. The association between carotid plaque and elevated Lp(a) level persisted in the higher LDL cholesterol subgroup but disappeared in the lower LDL cholesterol subgroup. Moreover, a significant association appeared between aortic plaque and Lp(a) level as well as between the number of diseased sites and Lp(a) level in the higher LDL cholesterol subgroup but not in the lower LDL cholesterol subgroup. In contrast, oral plaque was not associated with Lp(a) level in any subgroup. These findings suggest an interaction between Lp(a) and LDL cholesterol when they are considered as two independent risk factors for both carotid and aortic plaques and the number of diseased sites. However, a discussion regarding such an interaction is limited by methodological problems. Thus, the possibility that the high LDL group may have larger plaques that are more easily detected has not been investigated in the present study, and this would affect the analysis.

In conclusion, our analysis suggests that serum Lp(a) level has a clear influence on extracoronary atherosclerosis, in particular in the carotid arteries and in the presence of a high level of LDL cholesterol. However, the hypercholesterolemic population chosen for the present work did not allow us to draw the conclusion that Lp(a) has a better discriminative power than the conventional lipids, such as total, HDL, and LDL cholesterol and triglycerides. Further studies incorporating a normocholesterolemic control group are needed to clarify this point.

Appendix


Acknowledgments

We thank Christine Beuzet for her excellent secretarial assistance and Muriel Del Pino, Nelly Poulain, and Suzanne Goiny for their helpful technical assistance.

References


Table 4. Univariate Comparison of Risk Factors According to the Presence or Absence of Plaque at Each Site in Lower and Higher LDL Cholesterol Subgroups

<table>
<thead>
<tr>
<th>Arterial site</th>
<th>Variable</th>
<th>Plaque absent</th>
<th>Plaque present</th>
<th>Plaque absent</th>
<th>Plaque present</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carotid arteries</td>
<td>Lp(a) (g/l)</td>
<td>0.20±0.16</td>
<td>0.33±0.22‡</td>
<td>0.15±0.11</td>
<td>0.26±0.20‡</td>
</tr>
<tr>
<td>Age (years)</td>
<td>43±7</td>
<td>48±7†</td>
<td>45±7</td>
<td>46±8</td>
<td></td>
</tr>
<tr>
<td>Lp(a) (g/l)</td>
<td>0.21±0.19</td>
<td>0.22±0.20</td>
<td>0.14±0.10</td>
<td>0.25±0.19†</td>
<td></td>
</tr>
<tr>
<td>Femoral arteries</td>
<td>Age (years)</td>
<td>43±7</td>
<td>47±7†</td>
<td>41±7</td>
<td>48±7‡</td>
</tr>
<tr>
<td>Lifelong smoking</td>
<td>9±16</td>
<td>15±15‡</td>
<td>14±14</td>
<td>22±19</td>
<td></td>
</tr>
</tbody>
</table>

LDL, low density lipoprotein; Lp(a), lipoprotein (a). Only parameters with significant differences in at least one subgroup are given. Data are mean±SD. Comparisons between those with and without plaque in each subgroup were performed with a nonparametric test (see "Methods") and were found to be significantly different from each other at $p<0.05$, $p<0.01$, and $p<0.001$. 

§p<0.001.
1352 Arteriosclerosis and Thrombosis Vol 12, No 11 November 1992

Serum Lp(a) as a discriminant marker of early atherosclerotic plaque at three extracoronary sites in hypercholesterolemic men. The PCVMETRA Group.
M Cambillau, A Simon, J Amar, P Giral, V Atger, P Segond, J Levenson, I Merli, J L Megnien and M C Plainfosse

doi: 10.1161/01.ATV.12.11.1346

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://atvb.ahajournals.org/content/12/11/1346

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Arteriosclerosis, Thrombosis, and Vascular Biology can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Arteriosclerosis, Thrombosis, and Vascular Biology is online at:
http://atvb.ahajournals.org/subscriptions/