Atherosclerotic Changes in the Femoral and Carotid Arteries in Familial Hypercholesterolemia

Ultrasonographic Assessment of Intima-Media Thickness and Plaque Occurrence

Inger Wendelhag, Olov Wiklund, John Wikstrand

B-mode ultrasound is increasingly used in clinical research to study the atherosclerotic process in the carotid arteries. The present investigation evaluated the feasibility of measuring intima-media thickness in the common femoral artery and assessed whether such measurement might provide further information on the extent of the atherosclerotic process in patients with familial hypercholesterolemia. A further aim was to study the relationship between the intima-media thickness of the common carotid artery and the occurrence of plaque in the carotid and femoral arteries. The results showed an increased intima-media thickness in the far wall of the common femoral artery in patients with familial hypercholesterolemia compared with the control subjects (P<.01). The results also showed a clear relationship between the thickness of the intima-media complex in the common carotid artery and the prevalence of plaque in the carotid and femoral arteries. This may be interpreted as an indication that an increase in intima-media thickness in the common carotid artery at least partly expresses a generalized atherosclerotic process. The atherosclerotic changes appeared to be more advanced in the femoral artery compared with the carotid artery. In future studies, therefore, valuable information on different stages of atherosclerotic changes may be achieved by combining information from B-mode recordings from both the carotid and femoral arteries. (Arterioscler Thromb. 1993;13:1404-1411.)

KEY WORDS • arterial wall thickness • B-mode imaging • surrogate variable • familial hypercholesterolemia

Subjects with familial hypercholesterolemia (FH) inherit a defectively functioning low-density lipoprotein (LDL) receptor, resulting in elevated LDL cholesterol (LDL-C) levels. The disease is associated with an increased risk for premature coronary atherosclerosis. Atherosclerotic disease may progress for many years before coronary symptoms occur, and little is known about the clinically silent phase of disease development.

B-mode ultrasound is increasingly used in epidemiological and clinical research to noninvasively study the atherosclerotic process in the carotid artery. It is assumed that the atherosclerotic changes in the carotid artery mirror general atherosclerosis, and ultrasound measurements of intima-media thickness in the carotid artery are partly used as surrogate variables for coronary atherosclerosis.

An increased thickness of the intima-media complex in the common carotid artery has previously been reported in patients with FH compared with a sex- and age-matched control group. The aim of the present investigation was to evaluate the feasibility of measuring the intima-media complex in the common femoral artery and to assess whether such measurement might provide further information on the extent of the atherosclerotic disease in FH patients. A further aim was to assess the occurrence of plaque in the femoral and carotid arteries in the two studied groups and to evaluate the relationship between plaque prevalence in these arteries and far wall intima-media thickness of the common carotid artery.

Methods

Study Groups

Patients (n=53) with heterozygous FH were recruited from the lipid clinic of the Sahlgrenska Hospital, Gothenburg, Sweden, to participate in the present study. This group is referred to as the “hypercholesterolemic group.” The diagnosis of FH was made using specific criteria. These criteria as well as patient characteristics for the total study group have been described in detail previously. Premenopausal women and patients with diabetes, hepatic dysfunction, severe hypertension, or excessive obesity were excluded.

A control group (n=53) with serum cholesterol levels below 6.5 mmol/L was recruited from a representative population sample in Gothenburg. To each patient with hypercholesterolemia a subject was matched with re-
Biochemical Analysis

Blood samples for serum cholesterol, serum triglycerides, and lipoprotein fractions were drawn after a fast of 10 to 12 hours. Cholesterol and triglyceride levels were determined by fully enzymatic techniques by using a Gilford System 3500 Autoanalyzer (Gilford Instruments Inc, Oberlin, Ohio). Apolipoprotein cholesterol (HDL-C) was determined after precipitation of apolipoprotein (apo) B–containing lipoproteins with manganese chloride and heparin. LDL-C was calculated as described by Friedewald et al.

Apolipoproteins A-I, B, and E were analyzed by using frozen samples stored at -80°C. ApoA-I concentrations were measured by a rate-nephelometric method. ApoB and apoE levels were determined by electroimmunoassay. Levels of lipoprotein(a) (Lp[a]) were determined by radioimmunoassay (Pharmacia Diagnostics, Uppsala, Sweden).

Ultrasonography

Examination was performed with an ultrasound scanner (Acuson 128, Mountain View, Calif) equipped with a linear 5- or 7-MHz transducer. The transducer aperture was 38 mm. Subjects were examined in the supine position. During the carotid scanning the head was turned to the left. The ECG signal (lead II) was simultaneously recorded to synchronize the image capture to the top of the R wave (end diastole).

Earlier ultrasound studies have focused on the carotid arteries. The present study investigated both carotid and femoral arteries, but to avoid prolonging the examination time only the right sides of the carotid and femoral arteries were examined. The carotid artery was scanned at the level of the bifurcation. The examination included approximately 2 cm of the common carotid artery, the carotid bulb, and 1 cm each of the internal and external arteries. The femoral artery was examined distal to the inguinal ligament at the site where the artery divides into the superficial femoral artery and the profound femoral artery. The femoral artery was scanned approximately 4 cm proximal and 1 cm distal to the flow divider. These regions were scanned both longitudinally and transversely to assess the occurrence of plaque. Three “frozen” B-mode images of plaques from the longitudinal view were recorded on videotape, and a short sequence of real-time images was also recorded. Pulsed Doppler was used to provide information on blood flow velocity.

In addition, the common carotid artery was scanned longitudinally for the recording of images for intima-media thickness measurements. At the position of the thickest part of the far wall, three B-mode images were captured in end diastole and recorded on videotape. Images for the measurement of intima-media thickness in the femoral artery were captured in end diastole at the position of the thickest part of the far wall of the common femoral artery. The vessel was scanned both longitudinally and transversely when determining the optimal transducer position. The goal was to have a projection in which the ultrasound beam crossed perpendicularly to the thickest part of the far wall. A short sequence of real-time images was also recorded on videotape.

Measurement of Wall Thickness and Lumen Diameter

The ultrasound images from the videotape were analyzed in a computerized analyzing system. Analyses were performed in a blinded manner with regard to the group to which the images belonged. Intima-media thickness was defined as the distance from the leading edge of the intima-intima interface to the leading edge of the media-adventitia interface of the far wall. The measurement of intima-media thickness in the common

<table>
<thead>
<tr>
<th>TABLE 1. Availability of Wall Thickness Measurements and Plaque Assessments in FH Patients and Control Subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>No. of Control Subjects</strong></td>
</tr>
<tr>
<td><strong>Carotid artery</strong></td>
</tr>
<tr>
<td>Wall thickness measurement, CCA</td>
</tr>
<tr>
<td>Plaque occurrence assessment</td>
</tr>
<tr>
<td><strong>Femoral artery</strong></td>
</tr>
<tr>
<td>Wall thickness measurement, CFA</td>
</tr>
<tr>
<td>Plaque occurrence assessment</td>
</tr>
<tr>
<td><strong>Carotid and femoral arteries</strong></td>
</tr>
<tr>
<td>Plaque occurrence assessment</td>
</tr>
</tbody>
</table>

FH Indicates familial hypercholesterolemia; CCA, common carotid artery; CFA, common femoral artery.

*Readable recordings had to be available from both the carotid and femoral arteries.

Smoking

Information on smoking habits was obtained by a self-administered questionnaire. The total number of years of smoking was multiplied by the average number of cigarettes smoked daily. The product was called "cigarette-years."

Blood Pressure

Resting blood pressure was measured phonographically in the right arm after about 30 minutes of supine rest at the time of the ultrasound examination. A heart-sound microphone was placed over the brachial artery, and an automatically inflated and deflated standard cuff (Bouche-Brecht, FRG) was used. Cuff pressure, Korotkoff sounds, and an electrocardiographic (ECG) signal (lead II) were simultaneously recorded on a Mingograph (Siemens-Elema, Sweden). Blood pressure, Korotkoff sounds, and an electrocardiographic (ECG) signal (lead II) were simultaneously recorded in end diastole.

Regarding to sex, age, height, and weight, as described previously.4

For technical reasons it was not possible to achieve high-quality ultrasound images from both the carotid and femoral arteries in all subjects investigated. The scanning of the femoral artery was somewhat more difficult to perform, partly due to the curved form of the common carotid artery, which explains why more images from the femoral artery were missing compared with the carotid artery. The numbers of subjects included in the different analyses are given in Table 1.

Blood Pressure

Resting blood pressure was measured phonographically in the right arm after about 30 minutes of supine rest at the time of the ultrasound examination. A heart-sound microphone was placed over the brachial artery, and an automatically inflated and deflated standard cuff (Bouche-Brecht, FRG) was used. Cuff pressure, Korotkoff sounds, and an electrocardiographic (ECG) signal (lead II) were simultaneously recorded on a Mingograph (Siemens-Elema, Sweden). Blood pressure, Korotkoff sounds, and an electrocardiographic (ECG) signal (lead II) were simultaneously recorded in end diastole.

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carotid artery was made along a 10-mm-long section just proximal to the carotid bulb. In the common femoral artery measurements were made along a 15-mm-long section proximal to the bifurcation. This section was defined by two reference lines in the analyzing program (Fig 1). The distal line was set at the point where the far wall of the common femoral artery started to bend to form the profound femoral artery. This transition was used as an internal marker, as the femoral artery lacks a bulb like the carotid artery. The computer program calculated the maximum and mean values of intima-media thickness of the far wall from three analyzed images.

Measurements of lumen diameter in the femoral artery could not be performed because the intima-lumen interface of the near wall was difficult to visualize in most of the images. Therefore, measurements were performed from the leading edge of the periadventitia-adventitia interface of the near wall to the leading edge of the lumen-intima interface of the far wall. This measurement includes lumen diameter and also the total thickness of adventitia-media-intima of the near wall. For further comments on this variable, which was used to indirectly assess the lumen diameter of the femoral artery, see “Discussion.”

Assessment of Plaque Occurrence

A semiquantitative subjective scale was used to grade the size of plaques. This analysis included plaques in the near as well as the far wall of the vessel. A plaque was defined as a distinct area with an intima-media thickness more than 50% thicker than neighboring sites and graded as follows: Grade 0: no plaque; Grade 1: one or more small plaques (each less than approximately 10 mm² in the carotid artery and less than approximately 20 mm² in the femoral artery); Grade 2: moderate to large plaques (the differentiation between Grades 1 and 2 was made subjectively in most cases, and quantitative measurements were made in the computerized analyzing system only when the correct classification was not obvious to the observer); Grade 3: large plaques that caused a hemodynamic change in blood flow as defined by the pulsed Doppler curve: in the carotid artery if peak systolic velocity was >1.2 m/s at a 60° Doppler angle; and in the femoral artery if there was a 100% increase in peak systolic velocity at the site of the plaque in relation to the segment proximal to the plaque concomitant with a loss of reverse flow.

One of the aims of this study was to analyze whether patients with plaques in the carotid or femoral artery regions also had a thicker intima-media complex in the
common carotid artery. If a plaque was present in the common carotid artery, this analysis was not performed (n=2).

Variability Studies

Thirty-five subjects, 17 from the hypercholesterolemic group and 18 control subjects, were examined on two different occasions within 7 to 14 days to estimate the intraobserver variability of recording and measurement of intima-media thickness in the common carotid and common femoral arteries. The two recordings and the measurements were performed by the same technologist, who was blinded with regard to the results of the first examination. The coefficient of variation was 10.6% (intraobserver error [s]=0.08 mm) for mean intima-media thickness in the common carotid artery and 10.4% (s=0.10 mm) for maximum intima-media thickness. For mean lumen diameter in the common carotid artery the coefficient of variation was 3.5% (s=0.22 mm). The results from a study of interobserver variability of the carotid measurements have been previously reported.4

The two independent measurements of mean and maximum intima-media thickness in the common femoral artery gave a coefficient of variation of 11.9% (s=0.16 mm) and 14.4% (s=0.26 mm), respectively (high-quality images from the femoral artery were missing for three of the subjects in the variability study). For mean near-wall plus lumen diameter the coefficient of variation was 2.8% (s=0.26 mm).

Statistical Analysis

All statistics were analyzed on a personal computer connected to a VAX/VMS system using SPSS FOR WINDOWS 5.0 (Chicago, Ill). In the variability study, means and standard deviations (SDs) for differences between the two examinations were calculated. The SD of the intraobserver error(s) was then calculated according to the formula $s=SD/V.2$. The coefficient of variation (CV) describes the difference as a percentage of the pooled mean values (X) and was calculated according to the formula

$$CV = \frac{s \times 100}{X}$$

The Mann-Whitney U test was used for comparisons between the groups, and 95% confidence intervals (CIs) for differences were also calculated. Because by definition the two groups differed in serum lipids, these were not formally tested, but 95% CIs for each of these variables in the two groups have been given.

A trend in the contingency table test was used to analyze the differences in distribution of plaque occurrence between the two groups. The same test was used to compare the number of cigarette-years in the two groups. The proportions of smokers (never, past, or current) were compared by testing with a $x^2$ test. Two-sided probability values less than .05 were regarded as statistically significant. The limit for abnormality of mean intima-media thickness of the common femoral artery was arbitrarily set at the second highest value of the control group.

### Table 2. Anthropometric Data, Blood Pressure, Heart Rate, and Smoking Habits of Femoral Analysis Study Participants

<table>
<thead>
<tr>
<th>Variable</th>
<th>Control Group (n=36)</th>
<th>Familial Hypercholesterolemia Group (n=34)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male/female</td>
<td>20/16</td>
<td>18/16</td>
</tr>
<tr>
<td>Age, y</td>
<td>53.4±11.6</td>
<td>50.9±11.5</td>
</tr>
<tr>
<td>Body height, cm</td>
<td>173±7</td>
<td>172±10</td>
</tr>
<tr>
<td>Body weight, kg</td>
<td>72.8±11.3</td>
<td>73.3±13.5</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>24.3±3.3</td>
<td>24.9±3.7</td>
</tr>
<tr>
<td>SBP, mm Hg</td>
<td>125±15</td>
<td>122±15</td>
</tr>
<tr>
<td>DBP, mm Hg</td>
<td>74±8</td>
<td>76±10</td>
</tr>
<tr>
<td>HR, bpm</td>
<td>63±9</td>
<td>61±11</td>
</tr>
<tr>
<td>Never smoked, %</td>
<td>50</td>
<td>29</td>
</tr>
<tr>
<td>Past smoker, %</td>
<td>25</td>
<td>47</td>
</tr>
<tr>
<td>Current smoker, %</td>
<td>25</td>
<td>24</td>
</tr>
<tr>
<td>Total cigarette-years</td>
<td>7986</td>
<td>5910</td>
</tr>
</tbody>
</table>

BMI indicates body mass index; SBP and DBP, systolic and diastolic blood pressure; HR, heart rate; bpm, beats per minute. All values are given as mean±SD except gender and cigarette smoking data.

Results

The results from the measurement of intima-media thickness in the common carotid artery have been presented previously.4 Briefly, the results showed a significantly thicker intima-media complex in the far wall of the common carotid artery in the FH group than in the control group. The mean difference in thickness between the groups was 0.13 mm for mean intima-media thickness ($P<.001$; 95% CI, 0.07 to 0.18 mm) and 0.20 mm for maximum intima-media thickness ($P<.001$; 95% CI, 0.09 to 0.23 mm).

The anthropometric data, blood pressure, and heart rate were very similar in the two groups included in the femoral analysis (Table 2). The proportions of never, past, or current smokers and total cigarette-years did not significantly differ between groups.

Serum Lipid and Lipoprotein Levels

Total cholesterol and LDL-C, apoB, and Lp(a) levels were higher in the hypercholesterolemic group than in the control group (Table 3). For serum triglycerides, HDL-C, apoA-I, and apoE, 95% CIs in the two groups overlapped.

Femoral Intima-Media Thickness and Lumen Diameter

The mean and maximum measurements of the intima-media complex of the far wall of the common femoral artery were significantly thicker in the hypercholesterolemic group than in the control group ($P<.01$; Table 4 and Fig 2). The mean difference in thickness between the groups was 0.33 mm for mean wall thickness (95% CI, 0.11 to 0.54 mm) and 0.42 mm for maximum wall thickness (95% CI, 0.10 to 0.74 mm). Mean near-wall plus lumen diameter was 8.53 mm in the hypercholesterolemic group and 9.49 mm in the control group ($P<.001$; 95% CI for the difference, 0.43 to 1.49 mm). Analysis showed no relation between
TABLE 3. Serum Lipid and Lipoprotein Levels of Femoral Analysis Study Participants

<table>
<thead>
<tr>
<th>Variable</th>
<th>Control Group (n=36)</th>
<th>Familial Hypercholesterolemia Group (n=34)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean±SD</td>
<td>95% CI</td>
</tr>
<tr>
<td>Cholesterol, mmol/L</td>
<td>5.64±1.00</td>
<td>5.30-5.98</td>
</tr>
<tr>
<td>Triglycerides, mmol/L</td>
<td>1.33±0.73</td>
<td>1.08-1.57</td>
</tr>
<tr>
<td>HDL-C, mmol/L</td>
<td>1.43±0.42</td>
<td>1.29-1.57</td>
</tr>
<tr>
<td>LDL-C, mmol/L</td>
<td>3.70±0.90</td>
<td>3.39-4.01</td>
</tr>
<tr>
<td>ApoA-I, g/L</td>
<td>1.54±0.35</td>
<td>1.43-1.66</td>
</tr>
<tr>
<td>ApoE, g/L</td>
<td>0.054±0.013</td>
<td>0.050-0.059</td>
</tr>
<tr>
<td>ApoB, g/L</td>
<td>1.08±0.30</td>
<td>0.98-1.18</td>
</tr>
<tr>
<td>Lp(a), mg/L*</td>
<td>62 (7-1040)</td>
<td>73-206</td>
</tr>
</tbody>
</table>

Cl indicates confidence interval; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; apo, apolipoprotein; Lp(a), lipoprotein(a).

*For Lp(a) values are median and (in parentheses) range.

Femoral Intima-Media Thickness and Serum Lipid and Lipoprotein Levels

In the analysis of the relation between intima-media thickness and serum lipid or lipoprotein levels, the two groups were analyzed together (n=70). Mean wall thickness was significantly correlated to total serum cholesterol ($r=0.41, P<0.001$; Fig 3), to LDL-C ($r=0.39, P<0.001$), and to apoB ($r=0.33, P<0.01$).

Femoral Intima-Media Thickness and Age

The relation between femoral intima-media thickness and age showed a correlation coefficient of $r=0.41 (P<0.05)$ in the hypercholesterolemic group and $r=0.40 (P<0.05)$ in the control group. When the two groups were combined in the analysis, the correlation coefficient was $r=0.34 (P<0.01)$; Fig 4). The slope of the regression line relating age (in years) to intima-media thickness (in millimeters) was 0.019 mm/y in the hypercholesterolemic group and 0.013 mm/y in the control group (NS) (Fig 4).

Plaque Occurrence

Plaques in the carotid and femoral arteries were recorded more frequently in the hypercholesterolemic patients than in the control subjects ($P<0.01$; Fig 5). Nine (25%) hypercholesterolemic patients had small plaques (Grade 1), and 13 (36%) had moderate to large plaques (Grade 2). Nine (20%) control subjects had

![Fig 2. Bar graphs showing distribution of mean intima-media thickness of the common femoral artery in the two study groups. Dashed lines indicate limits for abnormality. **P<.01.](http://atvb.ahajournals.org/)

![Fig 3. Scatterplot showing relation between total serum cholesterol and mean femoral intima-media thickness in control subjects and familial hypercholesterolemia (FH) patients.](http://atvb.ahajournals.org/)
FIG 4. Scatterplot showing relation between age and mean femoral intima-media thickness in control subjects and familial hypercholesterolemia (FH) patients.

plagues of Grade 1, and four (9%) had plaques of Grade 2. No Grade 3 plaques were noted. Plaques were more prevalent in the femoral artery than in the carotid artery (P<.01; Fig 6). One of the 14 carotid artery plaques in this analysis occurred in the common carotid artery. All of the 31 femoral artery plaques occurred in the common femoral artery.

Intima-Media Thickness in the Common Carotid Artery in Relation to the Occurrence of Plaque

The mean intima-media thickness of the far wall in the common carotid artery was 0.74 mm in patients and subjects without plaques (n=79) and 0.86 mm (P<.01, n=18; Table 5) in those with plaques in the carotid bulb or the internal carotid artery. The mean intima-media thickness of the common carotid artery was 0.73 mm in those without plaques in the femoral artery (n=50) and 0.81 mm in those with plaques (n=31) in the femoral artery (NS). When moderate to large plaques were present in the femoral artery the mean intima-media thickness of the common carotid artery was 0.87 mm (P<.01, n=15; Table 5).

Discussion

The present analysis showed that it was possible to record and evaluate the intima-media complex in the common femoral artery, and the results showed an increase of intima-media thickness in the far wall of the common femoral artery in patients with heterozygous FH compared with a control group. The results showing an increased far-wall intima-media thickness in the common carotid artery have been presented previously.4 Plaques were more common in the femoral artery than in the carotid artery (Fig 6) and more common in FH patients than in control subjects. A further important result was that a significant relation was found between the intima-media thickness of the common carotid artery and the occurrence of plaque in the carotid bulb or the internal carotid artery. The intima-media complex in the common carotid artery was also significantly thicker if a moderate to large plaque was present in the femoral artery compared with no plaque in the femoral artery.

Blood pressure, heart rate, and exposure to smoking did not differ between the hypercholesterolemic and the control groups. The greater extent of atherosclerotic changes recorded in the hypercholesterolemic patients may therefore be explained by a background of FH and elevated levels of either total cholesterol, LDL-C, apoB, or Lp(a), which were the only observed differences between the two groups. Like the thickness of the intima-media complex in the common carotid artery,4 the intima-media thickness of the common femoral artery increased with age in both groups, emphasizing the need for including age-matched control subjects in studies on ultrasound evaluation of these variables.

In the past few years there has been an increasing use of B-mode ultrasound in the assessment of atherosclerotic changes by measuring the intima-media thickness in the carotid artery.19-22 However, this is the first study to also measure intima-media thickness in the far wall of the common femoral artery. For technical and anatomic reasons more images were missing from the femoral artery than from the carotid artery (Table 1). From our experience more practice is required for the recording of images and analysis of intima-media thickness of the common femoral artery than for the common carotid artery. With more experience, in our laboratory at present the percentage of images missing from the

FIG 5. Bar graphs showing distribution of plaque occurrence in carotid and femoral arteries in the two study groups. See "Methods" for a discussion of plaque grading. FH indicates familial hypercholesterolemia.

FIG 6. Diagram showing the distribution of plaques in the carotid artery and the femoral artery. Plaques were more prevalent in the femoral artery than in the carotid artery (P<.01).
common femoral artery is substantially less than initially. The wall changes in the common femoral artery are eccentric, and the transverse scan helps to determine the transducer position for recording optimal longitudinal images of the thickest part of the vessel wall. Wall irregularities and acoustic shadowing, created by calcification within the wall, may sometimes cause analyzing difficulties. However, despite the difficulties, the intraobserver variability study showed a satisfactory reproducibility.

The intima-lumen interface of the near wall is not as well visualized in the femoral artery as in the carotid artery, and a true measurement of lumen diameter could not be performed in the femoral artery. The measurement performed from the periadventitia-adventitia interface of the near wall included lumen diameter as well as the total near wall thickness. This measurement yet gives a good estimation of lumen diameter, when comparing the two study groups, as atherosclerotic changes are rare in the near wall of the common femoral artery. Data indicated that the hypercholesterolemic group had a smaller lumen diameter than the control subjects. However, the decrease in lumen diameter did not seem to be caused by the increase in far-wall intima-media thickness, because no relation was found between intima-media thickness and the estimate of lumen diameter.

Atherosclerotic changes occur more often in curved arteries than in straight arteries. In curved arteries the wall tends to be more thickened in the inner or concave side of the bend than in the convex (outer) side.\textsuperscript{23,24} This may partly explain why measurements in the far wall of the common femoral artery showed more atherosclerotic lesions than the measurements in the straight common carotid artery. Furthermore, the femoral artery region is exposed to a higher hydrostatic pressure and to larger variations in flow than the carotid artery region, which may also help to explain differences in atherosclerosis development between these two arterial regions.

Preventive measures will probably be assessed with the ultrasound technique in many future studies. If both carotid and femoral arteries are examined, it should be possible to prospectively study both the early thickening of the wall in the common carotid artery and the more advanced atherosclerotic changes in the common femoral artery. Furthermore, the assessment of the intima-media complex in both the carotid and femoral arteries in a treatment study may provide valuable information on treatment effects in different arterial regions.

Atherosclerotic lesions are more often found in the internal carotid artery and carotid bulb than in the common carotid artery. Measurements of the intima-media complex, however, are often performed in the common carotid artery because it is easy to image, with few missing values and with good reproducibility. The question arises whether it is possible to study athero-

### TABLE 4. Thickness of the Intima-Media Complex in the Far Wall of the Common Femoral Artery

<table>
<thead>
<tr>
<th>Variable</th>
<th>Control Group (n=36)</th>
<th>Familial Hypercholesterolemia Group (n=34)</th>
<th>Mean Difference Between Groups</th>
<th>95% Cl for Mean Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Femoral wall thickness</td>
<td>0.82±0.38</td>
<td>1.15±0.52*</td>
<td>0.33</td>
<td>0.11-0.54</td>
</tr>
<tr>
<td>Maximum, mm</td>
<td>1.12±0.59</td>
<td>1.54±0.75*</td>
<td>0.42</td>
<td>0.10-0.74</td>
</tr>
</tbody>
</table>

Cl indicates confidence interval. \*P<.01.

### TABLE 5. Plaque Occurrence in Relation to Intima-Media Thickness of the Common Carotid Artery

<table>
<thead>
<tr>
<th>Variable</th>
<th>Control and Hypercholesterolemic Groups' Intima-Media CCA Thickness, mm</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean±SD</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>Carotid artery</td>
<td></td>
</tr>
<tr>
<td>No plaque (n=79)</td>
<td>0.74±0.13</td>
</tr>
<tr>
<td>Plaque (n=18)</td>
<td>0.96±0.17*</td>
</tr>
<tr>
<td>Small plaque (n=14)</td>
<td>0.92±0.15*</td>
</tr>
<tr>
<td>Moderate to large plaque (n=4)$</td>
<td>(1.00±0.20)</td>
</tr>
<tr>
<td>Femoral artery</td>
<td></td>
</tr>
<tr>
<td>No plaque (n=50)</td>
<td>0.73±0.15</td>
</tr>
<tr>
<td>Plaque (n=31)</td>
<td>0.81±0.17</td>
</tr>
<tr>
<td>Small plaque (n=16)</td>
<td>0.76±0.15</td>
</tr>
<tr>
<td>Moderate to large plaque (n=15)</td>
<td>0.87±0.17</td>
</tr>
</tbody>
</table>

CCA indicates common carotid artery; Cl, confidence interval. Subjects with plaque in the CCA were excluded (see "Methods"). \*P<.05; \**P<.01 (compared with no plaque). \$For difference compared with "No plaque." \$Too few numbers to test statistically.
sclerosis by measuring the intima-media complex in the common carotid artery. The present study showed a relation between this measurement and the prevalence of plaque in the carotid and femoral arteries. This may be interpreted as an indication that an increase in intima-media thickness in the common carotid artery expresses a generalized atherosclerotic process.

To study atherosclerotic disease with ultrasound in extracranial and femoral arteries seems to be a valid technique for these arterial regions. However, further studies are needed to verify our results, and the association between the ultrasound variables and coronary atherosclerosis needs additional clarification. Some studies regarding this have been published.\(^{25-28}\) Wofford et al\(^{28}\) used a B-mode scoring system to evaluate the carotid arteries in patients undergoing coronary angiography. They reported that the extent of carotid artery disease was positively related to the extent of coronary artery disease. Similar studies are needed to assess the relation between intima-media thickness in the far wall of the common carotid artery and coronary atherosclerosis because this variable will probably become a surrogate variable for coronary heart disease.\(^3\)

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