Carotid Artery Diameter Correlates With Risk Factors for Cardiovascular Disease in a Population of 55-Year-Old Subjects

Kerstin Jensen-Urstad, MD, PhD; Mats Jensen-Urstad, MD, PhD; Jan Johansson, MD, PhD

Background and Purpose—We investigated whether, in a randomly selected population of 55-year-old men and women, there is a relationship between common carotid artery (CCA) diameter and intima-media (IM) thickness and conventional risk factors for cardiovascular disease such as gender, smoking, elevated blood lipids, and high blood pressure.

Methods—CCA diameter and IM thickness of the distal right and left CCAs were measured by high-frequency ultrasound methods. Fifty-seven men (73% of the invited men) and 47 women (62% of the invited women) participated.

Results—In the whole group the CCA diameter was correlated with gender (\(P<0.001\)), cholesterol (\(P=0.007\)), triglycerides (\(P<0.001\)), apoB (\(P<0.001\)), apoB/A-1 (\(P<0.001\)), systolic blood pressure (\(P=0.001\)), and glucose (\(P=0.006\)). HDL was inversely correlated with mean CCA diameter (\(P=0.003\)). In men the CCA diameter was correlated with a combined risk factor score (\(P=0.005\)), systolic blood pressure (\(P=0.011\)), platelet count (\(P=0.033\)), apoB (\(P=0.025\)), and occurrence of plaque (\(P=0.003\)). In women the CCA diameter was correlated with a combined risk factor score (\(P=0.010\)), systolic blood pressure (\(P=0.033\)), body mass index (\(P<0.001\)), cholesterol (\(P=0.009\)), triglycerides (\(P=0.14\)), apoB (\(P=0.002\)), and apoB/A1 (\(P=0.003\)). IM thickness was correlated with systolic blood pressure (\(P<0.001\)).

Conclusions—There are correlations between risk factors for cardiovascular disease and carotid artery diameter and IM thickness in both women and men in a population of 55-year-old subjects. The increased vessel diameter in subjects with cardiovascular risk factors may be a sign of attenuated vasoregulation, which could be an important factor during the development of atherosclerosis. (Stroke. 1999;30:1572-1576.)

Key Words: cardiovascular diseases ▪ carotid arteries ▪ epidemiology ▪ ultrasonography

During the development of atherosclerosis the intima-media (IM) of the arterial wall thickens. Increased IM thickness of the carotid artery has been associated with such risk factors for cardiovascular disease as age, blood pressure, diabetes, LDL cholesterol, and smoking.1-7 Asymptomatic subjects with increased IM thickness have an increased risk of acute myocardial infarction or stroke.8

We have previously shown9 that in healthy 35-year-old subjects, brachial artery diameter is correlated with risk factors for cardiovascular disease. Whether there is a relationship between arterial diameters and cardiovascular risk factors in a population at an age at which manifest atherosclerosis is more common has been studied less. In an elderly population (aged 59 to 72 years), luminal enlargement was related to risk factors such as male gender and systolic blood pressure but not to LDL cholesterol.10

Arterial diameters have usually been studied at the site of a vessel stenosis and discussed in terms of compensatory enlargement, whereas vessel diameters in plaque-free areas are studied less frequently. This study characterizes carotid artery IM thickness and diameter in the distal common carotid artery (CCA) with ultrasonography in a 55-year-old population and investigates the possible relationship between these measures and conventional risk factors for cardiovascular disease, such as gender, smoking, elevated blood lipids, and high blood pressure.

Subjects and Methods

Subjects
One hundred fifty-four subjects, 78 men and 76 women, all aged 55 years, were invited by letter to participate in a cardiovascular risk factor study. They constituted a random sample of the inhabitants of the community of Sollentuna, a suburb of Stockholm. If the subjects had not responded to the invitation within 10 days, a second letter of invitation was sent. Finally, if there was no answer, the subjects were contacted by telephone. One woman and 2 men had moved from the community.

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Fifty-seven of the 78 men (73%) and 47 of the 76 women (62%) were recruited as control subjects. Of these, 55 men and 45 women underwent a vascular ultrasound study. The ultrasound study was not performed in 2 men and 2 women because of sudden illness and the inaccessibility of ultrasound at a later time. The main reasons given for not participating in the study were lack of time (5 men, 6 women) and illness (4 men, 8 women). We were unable to establish contact with 9 subjects (6 men and 3 women).

Height and weight of the men and women were 1.80±0.07 m and 13 kg, respectively. Body mass index (BMI) was 25.1±3.6 kg/m² in the men and 25.8±2.8 kg/m² in the women (P=0.30). None of the subjects had clinical signs or symptoms of infectious disease. They underwent a physical examination and answered standardized questions about medical history, smoking habits, and family history of disease. This was followed by donation of blood for analysis. The ethics committee of Karolinska Institute approved the study.

### Methods

Blood pressure was taken in duplicate after 5 minutes of rest in the sitting position. All measurements were taken between 7:30 AM and 9 AM by the same nurse and with the same equipment.

#### Blood Chemistry

Blood was drawn on one occasion between 8 AM and 10 AM after 15 minutes’ rest from subjects who had been fasting since 9 PM the previous evening. Analysis included leukocyte count, hemoglobin, platelet count, and blood glucose and serum lipoproteins. Lipoproteins were analyzed for serum cholesterol and serum triglycerides by enzymatic techniques. HDL cholesterol was measured in serum after precipitation of the apoB-containing lipoproteins. LDL cholesterol was calculated by the Friedewald formula. Serum was analyzed for the concentration of apoA-I, apoB, and apo(a).

#### Risk Factor Score

We used the following scoring system for conventional risk factors: 1 point for current smoking or ex-smoking; 1 point for heavy smoking, defined as ≥10 years of smoking >10 cigarettes a day; 1 point for cholesterol level of >6 mmol/L; and 1 point for systolic blood pressure of ≥140 or diastolic ≥95 mm Hg.

### Ultrasound Methods

Ultrasound scans were made using a duplex scanner (Acuson 128XP) with a 7.0-MHz ART linear array transducer in a quiet, semidarkened room with the subject supine. Subjects were asked not to drink coffee or tea for at least 2 hours before the study. The left and right CCAs were scanned. Plaques were defined as a local increase in wall thickness of >1 mm.

#### IM Thickness

Left and right CCAs were examined. The subject’s head was tilted to position the CCA just proximal to the bulb horizontally across the screen. Magnified pictures were frozen incidentally with the R wave on the ECG. Only the far walls of the artery were used for calculation. The IM thickness was defined as the distance between the leading edge of the luminal echo to the leading edge of the media/adventitia echo. IM thickness was measured over a length of 1 cm just proximal to the bulb. This was done by using the calipers and the trace function of the ultrasound system and calculating the mean IM thickness over this length.

#### CCA Diameter

The vessel diameter was measured on the same picture of the distal CCA as the IM thickness. Measures were taken from the leading edge of the near-wall echogenic IM line to the leading edge of the luminal echo of the far wall. One measure was taken. All measures were done by the same physician. The intraobserver coefficient of variation for repeated measures of CCA diameter was 2%.

### Statistics

Results are given as mean±SD. Univariate or stepwise multiple linear regression analyses were used. Groups were compared with Student’s 2-tailed unpaired t test. Probability levels of ≥0.05 were considered significant.

### Results

All subjects had adequate ultrasound scans. Systolic blood pressure was 128±18 mm Hg in women and 132±15 mm Hg in men (P=0.28), and diastolic blood pressure was

### Table 1. Blood Chemistry and Carotid Artery Ultrasonography Results in the 55-year-old Men and Women

<table>
<thead>
<tr>
<th></th>
<th>Men (n=55)</th>
<th>Mean</th>
<th>SD</th>
<th>Women (n=45)</th>
<th>Mean</th>
<th>SD</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leucocyte count, 10^9/L</td>
<td></td>
<td>5.9</td>
<td>1.4</td>
<td></td>
<td>5.3</td>
<td>1.4</td>
<td>0.06</td>
</tr>
<tr>
<td>Hemoglobin, g/L</td>
<td></td>
<td>151</td>
<td>8</td>
<td></td>
<td>136</td>
<td>7</td>
<td>&lt;0.001</td>
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<tr>
<td>Platelet count, 10^9 g/L</td>
<td></td>
<td>223</td>
<td>50</td>
<td></td>
<td>266</td>
<td>46</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Glucose, mmol/L</td>
<td></td>
<td>5.4</td>
<td>0.9</td>
<td></td>
<td>4.9</td>
<td>0.7</td>
<td>0.00</td>
</tr>
<tr>
<td>Cholesterol, mmol/L</td>
<td></td>
<td>6.2</td>
<td>1.2</td>
<td></td>
<td>6.0</td>
<td>0.9</td>
<td>0.42</td>
</tr>
<tr>
<td>Triglycerides, mmol/L</td>
<td></td>
<td>1.6</td>
<td>1.0</td>
<td></td>
<td>1.2</td>
<td>0.7</td>
<td>0.04</td>
</tr>
<tr>
<td>High density lipoproteins (mmol/l)</td>
<td>1.6</td>
<td>0.3</td>
<td>2.0</td>
<td>0.5</td>
<td>&lt;0.001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low density lipoproteins (mmol/l)</td>
<td>3.9</td>
<td>1.0</td>
<td>3.5</td>
<td>0.8</td>
<td>0.09</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Apolipoproteins, mmol/L</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ApoA1</td>
<td></td>
<td>1.54</td>
<td>0.23</td>
<td></td>
<td>1.66</td>
<td>0.26</td>
<td>0.02</td>
</tr>
<tr>
<td>ApoB</td>
<td></td>
<td>1.66</td>
<td>0.47</td>
<td></td>
<td>1.43</td>
<td>0.34</td>
<td>0.01</td>
</tr>
<tr>
<td>ApoB/apoA1</td>
<td></td>
<td>1.10</td>
<td>0.35</td>
<td></td>
<td>0.88</td>
<td>0.23</td>
<td>&lt;0.001</td>
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<tr>
<td>Apo(a)</td>
<td></td>
<td>0.28</td>
<td>0.31</td>
<td></td>
<td>0.21</td>
<td>0.31</td>
<td>0.30</td>
</tr>
<tr>
<td>Ferritin, μg/L</td>
<td></td>
<td>165</td>
<td>113</td>
<td></td>
<td>72</td>
<td>74</td>
<td>0.00</td>
</tr>
<tr>
<td>CCA diameter, mm</td>
<td></td>
<td>6.3</td>
<td>0.6</td>
<td></td>
<td>5.6</td>
<td>0.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>IM thickness, mm</td>
<td></td>
<td>0.64</td>
<td>0.09</td>
<td></td>
<td>0.61</td>
<td>0.07</td>
<td>0.06</td>
</tr>
</tbody>
</table>

Diameter CCA indicates the diameter of the distal common carotid artery. Values are mean±SD.
TABLE 2. Summary of Stepwise Multiple Regression Analysis for Vessel Diameter at Rest

<table>
<thead>
<tr>
<th></th>
<th>β</th>
<th>SE</th>
<th>B</th>
<th>SE</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td>−0.55</td>
<td>0.08</td>
<td>−0.76</td>
<td>0.12</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ApoB</td>
<td>0.24</td>
<td>0.08</td>
<td>0.39</td>
<td>0.13</td>
<td>0.002</td>
</tr>
<tr>
<td>Systolic blood pressure</td>
<td>0.19</td>
<td>0.08</td>
<td>0.007</td>
<td>0.003</td>
<td>0.02</td>
</tr>
<tr>
<td>Occurrence of plaque</td>
<td>0.21</td>
<td>0.08</td>
<td>0.42</td>
<td>0.14</td>
<td>0.04</td>
</tr>
<tr>
<td>BMI</td>
<td>0.19</td>
<td>0.08</td>
<td>0.04</td>
<td>0.02</td>
<td>0.02</td>
</tr>
<tr>
<td>Platelet count</td>
<td>−0.16</td>
<td>0.09</td>
<td>0.002</td>
<td>0.001</td>
<td>0.04</td>
</tr>
</tbody>
</table>

β is the standardized regression coefficients, B is the raw regression coefficient. The magnitude of β allows comparison of the relative contribution of each variable in the prediction of the dependent variable. SE is the standard error for both β and B. All subjects were aged 55 y. Multiple R=0.73, R²=0.53, P<0.001.

77±10 mm Hg in women and 81±8 mm Hg in men (P=0.062).

Blood Chemistry
Men had higher levels of triglycerides than women (P=0.039). Women had higher levels of HDL cholesterol (P<0.001), apoA-I (P=0.017), and apoB/A-I (P<0.001).

Risk Factors
Smoking
Twelve men were smokers; 6 of these were heavy smokers (defined above). Seven women were smokers; 3 of the 7 were heavy smokers.

Cholesterol
Twenty-two men and 22 women had cholesterol >6 mmol/L.

Blood Pressure
Twenty men and 13 women had systolic blood pressure of ≥140 mm Hg and/or diastolic blood pressure of ≥90 mm Hg.

Carotid Ultrasound Investigation
Plaque
Seven women and 8 men had plaques; all of them were small, just >1 mm.

IM Thickness
IM thicknesses in left and right CCAs were similar in men and women.

CCA Diameter
The CCA diameter was larger in men than in women, with a mean diameter of 6.3±0.6 mm in men versus 5.6±0.5 mm in women (P<0.001). The men and women with plaques had larger carotid artery diameter than those without plaques, 6.4±0.84 mm versus 5.89±0.64 mm (P=0.008). They also had thicker IM, 0.70±0.10 mm versus 0.62±0.07 mm (P<0.001). There was no difference in blood lipids between those with and without plaques.

Correlations With Risk Factors

Vessel Diameters
In a univariate analysis, the CCA diameters (both left and right, presented as mean; Table 2) were correlated with cholesterol (r=0.27, P=0.007), triglycerides (r=0.33, P<0.001), apoB (r=0.43, P<0.001), apoB/A-I (r=0.37, P<0.001), glucose (r=0.27, P=0.006), and systolic blood pressure (r=0.42, P<0.001). HDL cholesterol was inversely correlated with mean CCA diameter (r=−0.29, P=0.003).

Gender, smoking, systolic blood pressure, BMI, platelet count, triglycerides, apoA-I, apoB, glucose, and occurrence of plaque was entered in a multiple regression analysis against CCA diameter. Gender, systolic blood pressure, BMI, apoB and occurrence of plaque had independent contributions to the equation.

Analyses were also made separately in men and women (because there was a difference in vessel size between men and women).

Men
The CCA diameter was correlated with a combined risk factor score (r=0.40, P=0.005), systolic blood pressure (r=0.34, P=0.011), platelet count (r=0.287, P=0.033), apoB (r=0.30, P=0.025), and occurrence of plaque (P=0.003). When systolic blood pressure, platelet count, apoB, occurrence of plaque, smoking, glucose, and BMI were entered in a multiple regression analysis against CCA diameter, occurrence of plaque was the only factor with an independent contribution to the equation; other factors contributing to the equation were apoB, systolic blood pressure, and platelet count.

Women
In women the CCA diameter was correlated with a combined risk factor score (r=0.41, P=0.010), systolic blood pressure (r=0.32, P=0.033), BMI (r=0.56, P<0.001), cholesterol (r=0.38, P=0.009), triglycerides (r=0.36, P=0.14), apoB (r=0.45, P=0.002), and apoB/A-I (r=0.43, P=0.003). When systolic blood pressure, BMI, apoA-I, apoB, triglycerides, occurrence of plaque, smoking, and glucose were entered into a multiple regression analysis against CCA diameter, BMI and apoB had independent contributions to the equation.

IM Thickness
IM thickness (Table 3) was correlated with systolic blood pressure (r=0.40, P<0.001). In men IM thickness was correlated with a combined risk factor score (r=0.29, P=0.047), systolic blood pressure (r=0.50, P<0.001), diastolic blood pressure (r=0.40, P<0.001), and occurrence of plaque (P=0.002). In women IM thickness was correlated with cholesterol (r=0.34, P=0.009), triglycerides (r=0.33, P<0.001), apoB (r=0.43, P<0.001), apoB/A-I (r=0.37, P<0.001), glucose (r=0.27, P=0.006), and systolic blood pressure (r=0.42, P<0.001). HDL cholesterol was inversely correlated with mean CCA diameter (r=−0.29, P=0.003).

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with diastolic blood pressure \((r=0.34, \ P=0.023)\) and hemoglobin \((r=-0.35, \ P=0.019)\).

All Subjects

IM thickness was entered into a multiple regression analysis against gender, BMI, smoking, triglycerides, apoA-1, apoB, systolic blood pressure, occurrence of plaque, glucose, and hemoglobin. Systolic blood pressure, plaque, gender, and hemoglobin had independent contributions to the equation \((\text{Table 2})\).

Correlations Between Variables

The mean IM thickness was correlated with carotid artery diameter \((r=0.32, \ P=0.001)\).

Discussion

The present data show that there are correlations between carotid artery diameter, IM thickness, and risk factors for cardiovascular disease in a population of 55-year-old men and women. The correlation between risk factors and IM thickness has been shown before,\(^1\) but in the present study the vessel diameter itself was correlated with cardiovascular risk factors such as systolic blood pressure, body mass index, and blood lipids.

Vessel diameters generally increase with age. However, independent of age, there is a greater increase in coronary artery diameters in subjects with atherosclerosis than in subjects without atherosclerosis.\(^1\)\(^3\) Labropoulos and coworkers\(^1\)\(^4\) studied vessel diameters throughout the vascular system in 67±12-year-old subjects with and without atherosclerosis and found that all arteries dilate in the stage of early atherosclerotic plaque formation. They concluded that dilation of the artery occurs to preserve luminal area.

In the EVA study\(^1\) the carotid artery was examined in 1272 subjects aged 59 to 71 years. Increased IM thickness and plaque were accompanied by an increase in lumen diameter, and systolic blood pressure was related to lumen diameter. These results are similar to our findings in a somewhat younger population with a much lower prevalence of plaque.

The increase in arterial diameter in subjects with atherosclerosis is usually discussed in terms of compensatory enlargement, ie, compensatory in relation to stenoses, an increase in vessel diameter to preserve luminal area.\(^1\)\(^4\) However, none of the subjects in the present study had carotid stenosis, and the few subjects in whom a plaque was diagnosed had very small plaques (just over 1 mm). Furthermore, the relationship between vessel diameter and risk factors remained when the few subjects with plaque were excluded. This is in line with our previous studies in 35-year-old subjects (at an age long before atherosclerotic lesions usually appear), in which the brachial artery vessel diameter was correlated with risk factors for cardiovascular disease.\(^9\)

Our findings suggest that the mechanism behind the increased carotid artery vessel diameter in the subjects with risk factors in the present study may be related to regulatory mechanisms present before compensatory enlargement to preserve lumen area and that vessel diameter may be used as a risk factor indicator.

There was a correlation between vessel diameter and IM thickness, but the CCA diameter correlated to more cardiovascular risk factors than IM thickness. The lack of correlation between IM thickness and some risk factors in our study could be due to the fact that relatively few subjects were studied, compared with previous risk factor studies which have included large number of patients. We have, however, excluded 1 main confounding factor, as the study population is of the same age.

It is possible that the vessel diameter in itself is a measure of vascular regulatory function. The regulation of flow and blood pressure is complex, and how it affects arterial diameters is only partly understood. A malfunction of any factor involved in vasoregulation, including baroreceptor function, could result in an increased vessel diameter. A possible reason for increased vessel diameter could be an increased flow. In the microcirculation there is evidence of an increased flow in hyperglycemia,\(^1\)\(^7\)\(^–\)\(^9\) and in the present study there was a correlation between carotid artery diameter and blood glucose levels.

The large vessel diameter may in itself lead to disturbed blood flow regulation, because a larger vessel will have a lesser ability to respond to increased blood flow by both endothelium-dependent and non–endothelium-dependent mechanisms\(^9\)\(^,\)\(^20\) and thereby possibly be a factor in promoting the development of atherosclerosis.

Acknowledgments

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References

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