Potential of Carotid Ultrasonography in the Diagnosis of Coronary Artery Disease

A Comparison With Exercise Test and Variance ECG

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Background and Purpose—Carotid artery atherosclerosis has been shown to correlate with coronary artery disease (CAD). This study evaluates the capacity of duplex ultrasonography of the carotid arteries as a tool in the diagnosis of CAD in comparison with exercise stress test and variance ECG.

Methods—Carotid ultrasonography, exercise stress test, and variance ECG were performed in 184 symptomatic patients evaluated with coronary angiography. The diagnostic capacity of the studied noninvasive methods was assessed by use of receiver operating characteristic (ROC) curves constructed by successive consideration of several cut points, such as (1) the presence of unilateral/bilateral plaques and (2) cross-sectional common carotid artery (CCA) intima-media (IM) area from 10 to 30 mm² for ultrasonography; (1) ST depression ≥0.1 mV and ≥0.2 mV with and (2) without chest pain for exercise test; and electrical variability index from 50 to 100 for variance ECG.

Results—Coronary angiography revealed the presence of CAD (≥50% luminal stenosis in 1 or more major epicardial arteries) in 147 patients (80%). Identification of carotid plaques on one or both sides and calculation of the left-sided (but not right-sided) CCA IM area provided a significant discrimination (P<.001 and P<.01, respectively) of patients with CAD. The discriminating capacity of the ultrasound procedures was equal to that of variance ECG and exercise test with ST depression criterion only but somewhat lower than that of exercise test with the combined chest pain and ST depression criterion (P<.05). However, at the chosen cut points, carotid plaque identification offered higher sensitivity than exercise test with either criterion (P<.01 and P<.001, respectively).

Conclusions—Carotid ultrasonography is a useful diagnostic method that is comparable to exercise test and variance ECG for detection of CAD in a high-prevalence population. (Stroke. 1998;29:439-446.)

Key Words: carotid artery disease ■ coronary artery disease ■ duplex scanning ■ electrocardiography

Recent developments in ultrasonographic arterial imaging created a technical basis for a new diagnostic approach to arteriosclerotic disease by offering the possibility of accurate and reproducible quantification of the structural changes in the arterial wall by high-resolution B-mode ultrasonography.1 This, together with the results of autopsy studies that revealed a close correlation between coronary artery atherosclerosis and the extent of atherosclerotic lesions in extracranial carotid arteries,2,3 provided a rationale for ultrasonographic evaluation of carotid atherosclerosis in patients with suspected CAD. Indeed, through use of this approach, a significant association of various B-mode variables with the risk of acute myocardial infarction has been demonstrated.4 In other studies, a similar correlation was noticed between carotid IM thickening and the extent of angiographically defined CAD,5,6 even if the relation between this B-mode parameter and the severity of coronary atherosclerosis appeared to be weak.7 Against this background we decided to evaluate more systematically the value of carotid ultrasonography as a possible tool in the identification of patients with CAD and to compare the diagnostic performance of B-mode parameters with the performance of the traditionally used exercise stress test and that of the recently introduced variance ECG.10-13

Subjects and Methods

The study involved 184 consecutive patients, 125 men aged 36 to 84 years and 59 women aged 28 to 83 years, referred to the Division of Cardiology, Huddinge University Hospital, for coronary angiographic evaluation of symptoms suggestive of CAD. The inclusion criteria were a history of suspected angina pectoris and absence of preexcitation, atrial fibrillation/flutter, or frequent ectopic beats in the resting 12-lead ECG on admission. The study was approved by the Ethics Committee of Huddinge University Hospital, Stockholm, and all subjects gave their informed consent to participate.

Carotid Ultrasonography

Ultrasonographic assessment of carotid arteries was performed the day after the coronary angiography with use of a duplex scanner (Ultrasound 9, HDI, Advanced Technology Laboratories) with a 5- to 10-MHz linear array transducer.
Selected Abbreviations and Acronyms

- CAD = coronary artery disease
- CCA = common carotid artery
- IM = intima-media
- ROC = receiver operating characteristic

All subjects were examined in a supine position, with the head slightly turned from the sonographer. Both the right and left carotid arteries were carefully scanned with regard to vessel wall changes by one experienced sonographer who was unaware of the results obtained with the three other methods. The entire scanning procedure was videotaped (Panasonic NV-FS 90 EB VCR) for subsequent analysis by a computer system (Macintosh II vx, with Quick Image 24-video frame grabber card from MASS Microsystems Inc.) IMAGE software (National Institutes of Health, Research Services Branch, National Institute of Mental Health) was used to trace and measure the distances between the wall echoes within a 10-mm-long section of the CCA in late diastole, defined by a simultaneous ECG recording.

The far wall of the CCA, 5 to 10 mm proximal to the carotid bulb, was used for the measurements of IM thickness and lumen diameter on both sides. The IM thickness was measured as a distance between the leading edge of the lumen-intima echo and the leading edge of the media-adventitia echo in the far wall of the vessel, and the lumen diameter as a distance between the leading edge of the intima-lumen echo of the near wall and the leading edge of the lumen-intima echo of the far wall. The mean values of the IM thickness and lumen diameter over the interrogated 10-mm section of the artery were calculated by use of an application developed with 4th Dimension (ACI). The cross-sectional CCA IM area was calculated using the formula: IM area = ((lumen diameter/2 + IM thickness)² - lumen diameter/2)². When a plaque was observed in the region of CCA measurements, the IM thickness was not measured. Carotid plaque was defined as a localized IM thickening of >1 mm and at least 100% increase in thickness compared with the adjacent wall segment. Plaque occurrence was scored as the absence of plaques, the presence of unilateral plaques, and the presence of bilateral plaques.

The differences between the repeated measurements of IM thickness and lumen diameter (healthy subjects, 1 week apart) were 9% and 2% (coefficient of variation), respectively (range, 0.45 to 0.89 mm for IM thickness and 4.63 to 7.14 mm for lumen diameter).

The obtained ultrasonographic data were evaluated at several diagnostic cut points, such as (1) the presence of either unilateral or bilateral carotid plaques, and (2) the presence of bilateral plaques only; (3) the presence of either unilateral or bilateral carotid plaques and the symptoms of angina, and (4) the presence of bilateral plaques and angina; (5) CCA IM thickness values from 0.5 to 1.2 mm; and (6) calculated cross-sectional CCA IM area values from 10 to 30 mm².

Exercise Test

All patients were subjected to exercise on a bicycle ergometer, with the six standard leads and the chest leads V₁ to V₆ continuously recorded on a Schiller ECG recorder (CS 6/12, Schiller AG) for subsequent computerized averaging of ECG signals in consecutive 10-second periods. The ST amplitude was measured 60 ms after the end of the QRS complex, with the amplitude 15 ms before the beginning of the QRS serving as a reference. The exercise was performed on an electrically braked bicycle ergometer (Siemens Elema) as a continuous ramp, with an increase in workload of 10 W/min. ECG was recorded continuously, whereas sphygmonanometric blood pressure and respiratory frequency were measured at intervals. Patients who did not experience chest pain or a change in their ECG were encouraged to continue the exercise as long as possible. If chest pain or other symptoms appeared, the attending physician decided when to interrupt the exercise unless the patient did so himself. The maximal ST-segment depression in any precordial or standard lead during the test was identified visually by independent blinded interpreters, and the accuracy of this identification was then confirmed from the computer output that presented ST-segment amplitude in millivolts. Four cut points were considered, namely (1) an ST-segment depression ≥0.1 mV, (2) an ST-segment depression ≥0.2 mV, (3) an ST-segment depression ≥0.1 mV in combination with exertional chest pain, and (4) an ST-segment depression ≥0.2 mV in combination with exertional chest pain.

Variance ECG

The analysis of ECG signal variance was performed with a variance cardiograph (version 1.5, Vital Heart Systems) that incorporates the modification of previously published algorithm, as described elsewhere. Briefly, the system uses 24 leads, of which 10 are the same as for a standard 12-lead ECG, with additional unipolar leads placed at specific locations on the anterior and left posterior thorax. The signals obtained from the 24 leads are preprocessed by voltage amplification (650X), low-pass filtering (0.05 to 1500 Hz) and digitization (sampling rate, 4 kHz). A total of 220 preprocessed ECG complexes is acquired from the patient in two equal sampling periods at rest.

After rejection of all uncharacteristic beats, an average QRS complex for each lead is established. Subsequent analysis comprises the calculation of a mean squared QRS amplitude difference (variance) at each sampling point between each unrejected complex and the established average QRS complex for each lead. After scaling and normalization procedure, the obtained variance scores are combined into a non-dimensional electrical variability index (CAD index) ranging arbitrarily from an integer value of 0 to 150. Healthy individuals tend to have indices below 70, whereas patients with CAD usually have indices over 90.13

In the present study the data obtained were evaluated at several cut point values from CAD index 50 to 100.

Coronary Angiography

Selective coronary angiography in multiple projections was performed in all patients using the femoral approach and standard Judkins technique. Intracoronary nitroglycerin was injected before filming. The equipment used was a Siemens Bicor angiographic system (Siemens Elema) with Polytron 1000 (Siemens AG) and a 270-mm image intensifier. Cine film with 25 frames/s was used. Angiographic images were interpreted visually by an experienced angiographer who was unaware of the results obtained with the other three methods.

The positive angiographic result was defined as a stenosis ≥50% in one or more major epicardial arteries whereas stenoses <50% were classified as angiographically negative results. In addition, all angiograms were scored according to the severity of luminal narrowing in each analyzed vessel by use of the following graded scale: 1, 0% to 20%; 2, 30% to 40%; 3, 50% to 60%; 4, 70% to 90% stenosis; and 5, 100% occlusion. Five segments of coronary circulation were analyzed, namely, the left main coronary artery, the left anterior descending artery proximal to and including the first septal/diagonal branch, the left anterior descending artery distal to the first septal/diagonal branch, the circumflex artery or a major obtuse marginal branch, and the right coronary artery. If >1 vessel was affected, the individual scores of the respective vessels were summed to give a total coronary score.

Statistical Analysis

All data are presented as mean ± SD. For each test, the relation between a test’s true-positive and false-positive rates was evaluated at several discriminating thresholds by constructing ROC curves based on boundary conditions restricting their theoretical shape. To determine whether a test provided a significant amount of discriminating information, the z statistic based on the test’s ROC curve slope (m) ± SD was compared with m = 1.0, indicative of an uninformative test, with use of standard tables for normal distribution. The difference between two tests’ discriminating abilities was assessed by calculating the area (A) under the respective ROC curves as a percentage of the entire probabilistic area; the area under the identity line between true-positive and false-positive rate equal to 50% of the entire probabilistic area being indicative of totally uninformative test. The z statistic for a difference between the respective areas was then calculated, and the Wilcoxon signed rank test or Student t test for paired samples was performed as appropriate. Comparison of two
The relation between B-mode parameters and coronary scores was analyzed with standard linear regression and correlation techniques for categorical variables. The Student $t$ test for unpaired samples and the Mann-Whitney test were used when suitable.

**Results**

The demographic data on the studied population are presented in Table 1. As can be seen from the table, 169 patients (92% of total) complained of exertional chest pain, and 38% of the patients experienced previous myocardial infarction. Coronary angiography revealed the presence of CAD in 147 patients, thus indicating the overall disease prevalence of 80%. The prevalence of CAD was higher in men (92%) than in women (54%). The presence of single-vessel disease was angiographically verified in 37 patients and multivessel disease in 110 (25% and 75%, respectively, of the patients with CAD).

The ultrasonographic B-mode parameters are presented in Table 2. As can be seen from the table, patients with CAD exhibited a significantly higher incidence of carotid plaques than their unaffected peers ($P<.01$), the difference being mostly accounted by significantly more frequent bilateral plaques ($P<.05$) in the CAD subgroup. When the occurrence of carotid plaques was categorized according to the absence or presence of unilateral or bilateral plaques, the carotid plaque score thus obtained correlated highly with the coronary score (Spearman correlation coefficient, .332; $P<.001$). Not surprisingly, then, patients with multivessel disease presented a significantly higher incidence of bilateral carotid plaques ($P<.001$) than individuals with single-vessel disease (Table 2).

Contrary to carotid plaques, no statistically significant correlation was found between mean CCA IM thickness on either side, or between mean calculated cross-sectional CCA IM area.

**Table 1. Demographic Data**

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>No. of Patients</th>
<th>% of Total</th>
<th>No. of CAD Cases</th>
<th>% of Subgroup</th>
<th>Mean Age, y (Range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td>58</td>
<td>32</td>
<td>47</td>
<td>81</td>
<td>63 (36–84)</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>102</td>
<td>55</td>
<td>81</td>
<td>79</td>
<td>62 (36–84)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>27</td>
<td>15</td>
<td>22</td>
<td>81</td>
<td>63 (36–82)</td>
</tr>
<tr>
<td>Smoking (current)</td>
<td>29</td>
<td>16</td>
<td>23</td>
<td>79</td>
<td>56 (36–74)</td>
</tr>
<tr>
<td>Smoking (previous)</td>
<td>91</td>
<td>49</td>
<td>78</td>
<td>86</td>
<td>62 (40–82)</td>
</tr>
<tr>
<td>Angina</td>
<td>169</td>
<td>92</td>
<td>141</td>
<td>83</td>
<td>63 (36–84)</td>
</tr>
<tr>
<td>Previous infarction</td>
<td>70</td>
<td>38</td>
<td>67</td>
<td>97</td>
<td>63 (36–84)</td>
</tr>
<tr>
<td>Q-wave infarction</td>
<td>35</td>
<td>19</td>
<td>34</td>
<td>97</td>
<td>63 (36–84)</td>
</tr>
<tr>
<td>Heart failure</td>
<td>23</td>
<td>13</td>
<td>19</td>
<td>83</td>
<td>63 (47–79)</td>
</tr>
<tr>
<td>Current treatment</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$\beta$-blockers</td>
<td>145</td>
<td>79</td>
<td>122</td>
<td>84</td>
<td>61 (36–84)</td>
</tr>
<tr>
<td>Calcium blockers</td>
<td>72</td>
<td>39</td>
<td>54</td>
<td>75</td>
<td>63 (40–84)</td>
</tr>
<tr>
<td>Digoxin</td>
<td>5</td>
<td>3</td>
<td>2</td>
<td>40</td>
<td>62 (52–67)</td>
</tr>
<tr>
<td>Long-acting nitrates</td>
<td>102</td>
<td>55</td>
<td>87</td>
<td>85</td>
<td>64 (36–84)</td>
</tr>
<tr>
<td>Men</td>
<td>125</td>
<td>68</td>
<td>115</td>
<td>92</td>
<td>62 (36–84)</td>
</tr>
<tr>
<td>Women</td>
<td>59</td>
<td>32</td>
<td>32</td>
<td>54</td>
<td>63 (28–83)</td>
</tr>
<tr>
<td>Single-vessel</td>
<td>37</td>
<td>20</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Multivessel</td>
<td>110</td>
<td>60</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Table 2. Ultrasonographic B-mode Parameters**

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>CCA IM Thickness, mm, Mean±SD</th>
<th>CCA IM Area, mm², Mean±SD</th>
<th>Carotid Plaques, %</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Left Side</td>
<td>Right Side</td>
<td>Left Side</td>
</tr>
<tr>
<td>No CAD</td>
<td>(n=36)</td>
<td>(n=37)</td>
<td>(n=36)</td>
</tr>
<tr>
<td></td>
<td>0.78±0.14</td>
<td>0.80±0.21</td>
<td>16.78±4.54</td>
</tr>
<tr>
<td>CAD</td>
<td>(n=144)</td>
<td>(n=141)</td>
<td>(n=141)</td>
</tr>
<tr>
<td></td>
<td>0.85±0.22</td>
<td>0.79±0.18</td>
<td>20.14±6.16</td>
</tr>
<tr>
<td>Single-vessel</td>
<td>(n=37)</td>
<td>(n=36)</td>
<td>(n=37)</td>
</tr>
<tr>
<td></td>
<td>0.82±0.22</td>
<td>0.74±0.17</td>
<td>18.69±5.68</td>
</tr>
<tr>
<td>Multivessel</td>
<td>(n=107)</td>
<td>(n=105)</td>
<td>(n=104)</td>
</tr>
<tr>
<td></td>
<td>0.86±0.21</td>
<td>0.80±0.18</td>
<td>20.65±6.27</td>
</tr>
</tbody>
</table>

* $P<.05$ vs no CAD; † $P<.01$ vs no CAD; ‡ $P<.001$ vs single-vessel disease. In some cases, measurements of the B-mode parameters listed in the table could not be successfully performed because of a local plaque formation or other technical reasons. These patients were excluded from the analysis, which explains the slightly varying number of B-mode observations (n) not always corresponding to the number of patients in the respective subgroup (compare Table 1).
Table 3. ROC Parameters

<table>
<thead>
<tr>
<th>Method (Diagnostic Criterion)</th>
<th>ROC Slope (m), Mean±SD</th>
<th>P (vs slope=1.0)</th>
<th>ROC Area (A), Mean %±SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carotid ultrasonography</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Presence of plaques</td>
<td>0.330 ±0.130</td>
<td>&lt;0.001</td>
<td>67.9±5.7</td>
</tr>
<tr>
<td>Presence of plaques and angina</td>
<td>0.272±0.112</td>
<td>&lt;0.001</td>
<td>70.7±5.7</td>
</tr>
<tr>
<td>Cross-sectional CCA IM area</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left side</td>
<td>0.345±0.225</td>
<td>&lt;0.01</td>
<td>68.6±9.3</td>
</tr>
<tr>
<td>Right side</td>
<td>0.682±0.416</td>
<td>NS</td>
<td>56.7±9.9</td>
</tr>
<tr>
<td>CCA IM thickness</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left side</td>
<td>0.648±0.403</td>
<td>NS</td>
<td>59.0±8.4</td>
</tr>
<tr>
<td>Right side</td>
<td>1.015±0.520</td>
<td>NS</td>
<td>50.4±8.2</td>
</tr>
<tr>
<td>Exercise stress test</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ST segment depression only</td>
<td>0.414±0.170</td>
<td>&lt;0.001</td>
<td>65.5±6.0</td>
</tr>
<tr>
<td>Chest pain and ST segment depression</td>
<td>0.141±0.086</td>
<td>&lt;0.001</td>
<td>81.0±6.7*</td>
</tr>
<tr>
<td>Variance ECG</td>
<td>0.347±0.185</td>
<td>&lt;0.001</td>
<td>67.8±8.0</td>
</tr>
</tbody>
</table>

* P<.05 vs ST depression, variance ECG, presence of carotid plaques, and CCA IM area, left side.

on the right side, and the coronary score. In accordance with this finding, there appeared no statistically significant differences between mean values for the the above-mentioned parameters in the subgroup of patients with and without CAD (see Table 2). On the other hand, the calculated cross-sectional CCA IM area on left side did correlate significantly with the coronary score (Spearman correlation coefficient,.240; P<.01), and the mean value for this B-mode parameter was significantly higher (P<.01) in patients with CAD (Table 2).

All patients exercised up to at least 75% of their age-predicted maximal heart rate. Physical performance during exercise testing was limited by exertional chest pain (28.8%) or disabling leg fatigue (28.8%), followed by dyspnea (22.8%) and exhaustion (13.1%). In 6.5% of cases the exercise ended because of other causes, of which increasing ST-segment depression was predominant. The degree of ST-segment depression during exercise correlated highly with the coronary score (Spearman correlation coefficient,.289; P<.001), and the overall frequency of ST-segment depression was significantly higher in patients with single-vessel disease (46%); P<.05) than in the subgroup of patients with single-vessel disease (68%) and diminished the ROC slope (Fig 1, lower panel), but this improvement did not attain the level of statistical significance (see Table 3).

The calculation of cross-sectional CCA IM area on left side also provided diagnostically significant identification of patients with CAD (Fig 2, upper panel, and Tables 2 and 3). In contrast, the calculation of right-sided cross-sectional CCA IM area or measurements of CCA IM thickness on either side lacked any diagnostic value, as evidenced by the respective ROC slopes and the areas under the respective ROC curves (Fig 2, lower panel, and Table 3).

Both variance ECG and exercise stress test provided a significant diagnostic discrimination of patients with CAD. The diagnostic capacity of variance ECG was equal to that of exercise test when ST-segment depression alone was used as a diagnostic criterion (Table 3 and Fig 3). When the combination of ST-segment depression and exertional chest pain was used in diagnostic decision making, the diagnostic ability of exercise stress test improved, being significantly better (P<.05) than that of ST-segment depression alone or variance ECG (Table 3 and Fig 3).

The diagnostic capacity of both carotid plaque identification and calculation of left-sided cross-sectional CCA IM area was equal to that of variance ECG and exercise test with ST-segment depression criterion only, but somewhat lower (P<.05) than that of exercise test with the combined ST depression and exertional chest pain diagnostic thresholds. However, carotid plaque identification gained the discrimination ability matching that of exercise test with the combined diagnostic criteria when the combination of angina symptoms and the presence of carotid plaques was applied as a discriminating factor (Table 3).

The sensitivity and specificity values for the tested methods are given in Table 4. Because the CAD index value of 70 for
variance ECG indicates the lower limit of the overlap between the diseased and nonaffected population, it may be considered to correspond to the softer diagnostic criterion of the ST-segment depression $0.1 \text{ mV}$ (alone or with the exertional chest pain) or the presence of unilateral or bilateral carotid plaques (alone or with the symptoms of angina). Similarly, a cut point at the CAD index value of 90, indicating the upper limit of this overlap, may be considered to correspond to a stiffer threshold of the ST-segment depression $0.2 \text{ mV}$ (alone or in combination with the exertional chest pain) or the presence of bilateral carotid plaques only (alone or in combination with the symptoms of angina). When the diagnostic performance of ultrasonographic plaque detection, exercise stress test and variance ECG were compared at these two corresponding diagnostic cut points, exercise test provided the highest specificity but the lowest sensitivity, whereas variance ECG showed high sensitivity at the softer diagnostic threshold of a CAD index of 70. However, the ultrasonographic detection of carotid plaques, alone or in combination with the symptoms of angina, provided the best combination of sensitivity and specificity values, the sensitivity of the method being significantly higher than that of exercise test with the combined diagnostic criteria (all cut points) or with ST-segment depression as the only diagnostic criterion at the cut point of ST $0.1 \text{ mV}$ (see Table 4).
The best combination of sensitivity and specificity values for the left-sided cross-sectional CCA IM area was found in the interval between 15 and 20 mm² (see Fig 2), and the diagnostic performance of area calculation at various cut points within this interval did not differ from that of variance ECG in the interval between CAD index 70 and 90 (compare, Figs 2 and 3). When the cut points of CCA area $15 \text{ mm}^2$ and $20 \text{ mm}^2$ were assigned to correspond to the softer cut point of ST depression $0.1 \text{ mV}$ and the stiffer cut point of ST depression $0.2 \text{ mV}$, respectively, the calculation of the left-sided CCA IM area provided significantly higher sensitivity (82.3 ± 6.3%; $P < .001$) but lower specificity (33.3 ± 7.9%; $P < .001$) than exercise test with ST depression $0.1 \text{ mV}$ alone or in combination with chest pain (compare, Table 4). With the stiffer criteria employed (area $20 \text{ mm}^2$ and ST $0.2 \text{ mV}$, respectively) the calculation of the left-sided CCA IM area performed equally well in terms of sensitivity (43.3 ± 4.2%), whereas exercise test provided higher specificity but only when a combination of ST depression and exertional chest pain was applied as a diagnostic threshold (97.3 ± 2.7% versus 83.3 ± 6.2%; $P < .001$).

**Discussion**

The aim of this study was to evaluate the diagnostic value of carotid ultrasonography in the first-line clinical screening for CAD in symptomatic patients. The obtained results confirm the previous reports of a significant correlation between angiographically documented coronary atherosclerosis and similar lesions in carotid arteries as assessed by B-mode measurements.4–9 Furthermore, our results clearly demonstrate...
that this relation can be advantageous for the noninvasive
diagnosis of CAD.

Since the interest of this study was focused on clinically
significant CAD, coronary angiography was used as a reference
method. Coronary angiography relies on lumen reduction to
identify the atherosclerotic disease, and the strength of the
method lies in the detection of more advanced, obstructive
vascular wall changes rather than the identification of early and
mild vascular affection. It could then be expected that the
angiographic results would preferably correlate to a B-mode
finding that reflects rather advanced vascular lesions, such as
presence of carotid plaques. In this study, we applied a
definition of carotid plaque that, in our opinion, provided a
clear division between this more severe vascular lesion and IM
thickening, and, indeed, the occurrence of carotid plaques
correlated highly with the extent and severity of CAD re-
lected by coronary score.

Contrary to carotid plaque identification, the B-mode
measures of IM thickness reflect limited and early atheroscle-
rotic changes. Accordingly, the measurement and character-
ization of carotid IM complex has been shown to be of
significance in studies of early atherosclerosis and various
vascular risk factors. However, it can be anticipated that
these measures correlate more weakly with advanced coronary
atherosclerosis. This view is supported by the results of a recent
study by Adams et al,9 which show that although carotid IM
thickness is significantly correlated with the extent and severity
of coronary atherosclerosis, the relationship is weak and the
B-mode variable lacks any diagnostic value in detecting clini-
cally significant CAD. The present results are in accord with
the above-mentioned findings and clearly demonstrate that
measurement of IM thickness does not provide any statistically
significant discrimination of patients with angiographically
documented CAD. Consistent with this observation, in our
study the thickness of the IM complex did not correlate to
coronary score either. The difference in this respect between
our results and those of Adams and colleagues is not entirely
unexpected. Despite the large number of observations, the
correlation between the B-mode and angiographic variable
was weak in the above-mentioned study. Furthermore, the
cutting line between IM thickness and plaque was less clear
than in our study. This may have led to a number of lesions
that would be classified as plaques in our present study being
taken as IM thickness in the study of Adams et al, a difference
that would certainly increase the degree of correlation.

As far as the validity of B-mode measurements of carotid IM
thickness are concerned, it should be kept in mind that the
thickness of the IM layer may vary depending on varying
diameter of the arterial lumen. For example, an increase in the
artery width during systole results in a significant decrease (by
5% to 7%) in the measured far-wall IM thickness. Similarly,
an age–dependent increase of the arterial lumen diameter22,23 or
a widening of the artery caused by compensatory mechanisms
in the course of the lumen-restricting atherosclerotic process24
will lead to stretching of the arterial wall, and this can be
expected to result in narrowing of the IM layer. When this
occurs, the B-mode measurement of the far wall IM thickness
will become inaccurate and result in an underestimation of the
actual IM volume. To circumvent this problem, we calculated
the cross-sectional IM area. Recently, this B-mode procedure
has been shown to compensate for blood pressure–induced
changes in IM thickness,21 and there is reason to believe that
it may also eliminate the effect of varying arterial width due to
compensatory mechanisms or structural changes of the arterial
wall. The present results clearly demonstrate that the cross-
sectional IM area, indeed, is a better predictor of coronary
atherosclerosis than IM thickness. Interestingly, only the left-
sided IM area correlated significantly to the coronary score and
provided significant diagnostic information. The reason for this
side difference is not known at present, but the finding is not
entirely surprising. In fact, in the autopsy study of Solberg and
Eggen25 a mean percentage of intimal areas with raised athero-
sclerotic lesions was higher in the left CCA, and another
recently conducted clinical study15 produced results suggesting
that atherosclerotic lesions develop earlier in the left carotid
artery. The present finding fits in with these results and seems
to indicate that the development of atherosclerosis in the left
carotid artery proceeds faster and parallels the corresponding
process in the coronary arteries. Shear stress is a major
determinant of structural vascular changes, the regions of low
shear stress being favored sites for the development of athero-
sclerosis. The anatomy of the left carotid artery differs from
that of the right, and the distribution of flow and shear stress in
the left carotid may also differ, perhaps being similar to that
prevailing in the major coronary arteries. This would possibly
explain the current finding.

The present study was performed in a symptomatic, high-
prevalence population undergoing elective coronary angiog-
raphy. Since all participating patients were preselected with
clinical indications for coronary angiography, a selection bias
could thus not be avoided. This fact imposes some limitations
on the validity of the obtained results. First, our results cannot
be automatically extrapolated to an intermediate or low-risk
population. Further studies are required to evaluate the per-
fomance of carotid B-mode imaging in screening for CAD in
this group of individuals. Second, a selection bias is known to
influence true-positive and false-positive rates, causing a sys-
tematic overestimation of diagnostic sensitivity and underesti-
ation of diagnostic specificity. However, the evaluation of
the diagnostic ability of the methods in the present study was
performed with use of the hyperbolic ROC curve based on
boundary conditions, which is statistically insensitive to selec-
tion bias; consequently, the data based on this ROC curve are
not significantly distorted.

The present results clearly demonstrate that the B-mode
imaging of carotid plaques and the measurement of cross-
sectional CCA IM area on left side provide a statistically
significant discrimination of patients with CAD. The diagno-
sic ability of the B-mode parameters equaled that of exercise
test and variance ECG and was surpassed only by exercise test
when the occurrence of chest pain was added to ST-segment
depression as a discriminating criterion. However, even this
difference was eliminated when a similar clinical variable,
namely, the presence of angina symptoms, was combined with
the occurrence of carotid plaques and used as diagnostic cut
point.

The frequency of bilateral plaques was significantly higher in
multivessel disease, and the calculated cross-sectional CCA IM
area was largest in this subgroup of patients as well. This can be
taken to indicate that, similarly to exercise testing, these
B-mode variables are probably most efficient in detecting
multivessel disease. However, as far as overall diagnostic
performance is concerned, the distribution of the diagnostic
cut points practically available with each of the methods
studied along the respective ROC curves gave the ultrasono-
graphic identification of carotid plaques the best combination
of true-positive and and true-negative values (compare Figs 1
through 3).

In conclusion, the results of our study demonstrate that
ultrasonographic high-resolution B-mode measurement of
structural changes in the carotid arterial wall is an efficient
method for identification of patients with CAD in a high-
prevalence population. The procedure has the advantage of
being noninvasive, safe, and cost-effective, and it can be
performed repetitively in all patients. The ultrasonographic
screening of carotid arteries thus offers a valuable complement
to other noninvasive tests used for the initial identification
of patients with ischemic heart disease.

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