Morphological But Not Functional Changes of the Carotid Artery Are Associated With the Extent of Coronary Artery Disease in Patients With Preserved Left Ventricular Function

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Background and Purpose—The atherosclerotic process is associated with both morphological and functional changes in the carotid artery. We evaluated the relationship between these parameters of the carotid artery and the extent of coronary artery disease (CAD) in patients with preserved left ventricular function.

Methods—The study population consisted of 104 stable patients with CAD who had preserved left ventricular function (left ventricular ejection fraction $\geq$45%). All patients underwent carotid ultrasonography for evaluation of carotid artery plaque score defined by the sum of plaque thickness, maximum percent area stenosis, and carotid arterial stiffness index by a combination of changes in carotid arterial diameter and blood pressure.

Results—Plaque score and percent area stenosis correlated with the extent of CAD defined as the number of diseased coronary vessels ($P<0.001$ and 0.002, respectively), but arterial stiffness did not ($P=0.39$). Using logistic regression analyses adjusting for confounding coronary risk factors and arterial stiffness, plaque score and percent area stenosis were independently correlated with multivessel CAD ($P=0.001$ and 0.004, respectively).

Conclusions—Carotid artery plaque burden, but not arterial stiffness, is associated with the extent of CAD, suggesting morphological rather than functional changes in the carotid artery may be a more accurate predictor of the extent of CAD and multivessel CAD independent of left ventricular function. (Stroke. 2008;39:1597-1599.)

Key Words: atherosclerosis ▪ carotid arteries ▪ coronary artery disease ▪ ultrasonography

The relationship between carotid and coronary atherosclerosis has been demonstrated using carotid ultrasound. However, previous studies have focused on either morphological changes such as carotid artery plaque burden or functional changes such as carotid arterial stiffness. Furthermore, it has been reported that atherosclerotic changes in the carotid artery relate to left ventricular (LV) function in patients with hypertension and coronary artery disease (CAD). In patients with CAD with preserved LV function, the precise relationship of both morphological and functional carotid properties to the severity of CAD remains unclear. Therefore, the purpose of this study was to determine the relationship between morphological and functional parameters of the carotid artery and the angiographic extent of CAD in patients with preserved LV function.

Materials and Methods
We examined 104 consecutive Japanese patients (73 men; mean age 66±9 years) who had significant coronary artery stenosis confirmed by coronary angiography with preserved LV function on echocardiographic examination (LV ejection fraction $\geq$45%). Patients were excluded from the study if they had atrial fibrillation or flutter, significant valvular heart disease, acute coronary syndrome, a history of coronary bypass grafting, or carotid surgery. Quantitative coronary angiography was performed using the CMSQCA system (CMS-MEDIS, Medical Imaging System). The extent of CAD was coded as 1, 2, or 3 according to the number of major coronary vessels with luminal stenosis $\geq$50% or with a history of percutaneous coronary intervention. Left main stenosis $\geq$50% was scored as 2-vessel disease.

Carotid Ultrasound
Carotid scans were acquired using high-resolution ultrasound (SSA-700A Aplio; Toshiba Medical System) with a 7.5-MHz or 12-MHz liner array transducer. Plaque was defined as any focal structure that protruded in the lumen of the vessel for at least intima media thickness $>1.1$ mm. Plaque score (PS) was defined as the sum of the maximal thickness of all plaques in the bilateral carotid arteries in the scanning area. Maximum percent area stenosis (%AS) was measured as: $1-[(\text{area of residual lumen}/\text{area of the normal vessels})] \times 100$ using serial cross-sectional images on B-mode ultrasonography.

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1597
Table 1. Patient Characteristics (n=104)

<table>
<thead>
<tr>
<th></th>
<th>1VD</th>
<th>2VD</th>
<th>3VD</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(n=42)</td>
<td>(n=34)</td>
<td>(n=28)</td>
</tr>
<tr>
<td>Age, years</td>
<td>65±10</td>
<td>66±9</td>
<td>66±9</td>
</tr>
<tr>
<td>Males</td>
<td>31 (74%)</td>
<td>25 (74%)</td>
<td>17 (61%)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>23 (55%)</td>
<td>25 (74%)</td>
<td>25 (89%)*</td>
</tr>
<tr>
<td>Smokers</td>
<td>24 (57%)</td>
<td>21 (62%)</td>
<td>13 (46%)</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>30 (71%)</td>
<td>21 (62%)</td>
<td>18 (64%)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>26 (62%)</td>
<td>12 (35%)*</td>
<td>16 (57%)</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>24±4</td>
<td>24±2</td>
<td>24±3</td>
</tr>
<tr>
<td>SBP, mm Hg</td>
<td>127±18</td>
<td>133±21</td>
<td>138±18*</td>
</tr>
<tr>
<td>DBP, mm Hg</td>
<td>73±13</td>
<td>74±13</td>
<td>72±12</td>
</tr>
<tr>
<td>LVEF, %</td>
<td>59±6</td>
<td>57±7</td>
<td>55±7*</td>
</tr>
</tbody>
</table>

Values are mean±SD.  
*P<0.05 versus 1VD.

1VD indicates one-vessel disease; 2VD, 2-vessel disease; 3VD, 3-vessel disease; SBP, systolic blood pressure; DBP, diastolic blood pressure; LVEF, left ventricular ejection fraction.

Statistical Analysis

Group differences in continuous variables were assessed with the unpaired Student t test or one-way analysis of variance as appropriate. Subgroup differences were analyzed post hoc using the Bonferroni correction for multiple comparisons. Correlations between continuous and categorical variables were assessed with Pearson or Spearman methods as appropriate. Multiple linear regression analyses, including all univariate correlates of PS, with %AS as an independent variable, were performed. For the presence of multivessel coronary artery disease such as 2- or 3-vessel disease, logistic regression analyses were performed. Values of P<0.05 were considered statistically significant.

Results

Clinical characteristics of the study patients are described in Table 1 for 3 groups of patients: patients with one-vessel disease (n=42), 2-vessel disease (n=34), and 3-vessel disease (n=28).

Both PS and %AS correlated with the extent of CAD (r=0.33, P<0.001 and r=0.32, P=0.002, respectively) and there was a stepwise increase in both PS and %AS with the extent of CAD (one-vessel disease versus 2-vessel disease versus 3-vessel disease: 3.2±3.2 versus 5.6±5.0 versus 6.6±4.0 mm, P=0.002 and 15±21 versus 26±18 versus 31±20%, P=0.006, respectively; Figure). PS was significantly associated with body mass index (r=0.21, P=0.035) and hypercholesterolemia (r=0.27, P=0.005) and %AS with body mass index (r=0.31, P=0.002). On multiple regression analysis, the relations of PS and %AS to the extent of CAD remained significant (P<0.001 in both cases).

There was no significant correlation between carotid arterial stiffness β and the extent of CAD (P=0.39), and stiffness β was similar among the 3 groups described (one-vessel disease versus 2-vessel disease versus 3-vessel disease: 11.9±3.9 versus 12.0±6.2 versus 13.0±6.3, P=0.63). Stiffness β was significantly associated with age (r=0.31, P=0.001) and smoking (r=0.22, P=0.024).

On logistic regression analyses after adjusting for age, body mass index, hypertension, hypercholesterolemia, smoking, diabetes mellitus, and stiffness β, PS (odds ratio, 1.28; 95% CI, 1.10 to 1.48; P=0.001) and %AS (odds ratio, 1.55; 95% CI, 1.15 to 2.09; P=0.004) correlated independently with the presence of multivessel CAD (Table 2).

Discussion

Carotid artery morphological changes relate to the risk and presence of CAD in patients with suspected CAD. Additionally, the association of carotid artery morphological changes such as carotid artery plaque formation2-3 or stenosis4-5 with the extent of CAD has been reported. Although our observations are consistent with these studies, the study population was limited to patients with CAD with preserved LV function and did not include patients without CAD. In addition to the previous studies, we have shown that even in this selected population, carotid morphological changes are still useful and independent predictors of the extent of CAD and multivessel CAD.

![Figure](http://stroke.ahajournals.org/lookup/doi/10.1161/01.STR.0000267240.01131.9f)

**Figure.** Relationships between carotid artery morphological parameters (plaque score on the left panel, %AS on the right panel) and CAD. 1VD indicates one-vessel disease; 2VD, 2-vessel disease; 3VD, 3-vessel disease. *P<0.05 vs 1VD.
A direct association between functional changes of artery and coronary atherosclerosis has been reported in previous studies. However, these studies concluded that this association was stronger for aortic stiffness than carotid arterial stiffness, suggesting that in the larger artery, stiffness could be a significant marker of the severity of coronary atherosclerosis. Within a patient group with preserved LV function in the present study, we did not find a significant relationship between carotid arterial stiffness and the extent of CAD. Recently, several studies have demonstrated that carotid arterial stiffness is closely associated with LV systolic and diastolic function in patients with hypertension and CAD. Thus, a possible explanation for our results may be because this study population excluded patients with multivessel CAD with LV dysfunction accompanied by markedly high carotid arterial stiffness. Furthermore, in the previous studies, there was a significant difference in carotid arterial stiffness between patients without CAD and patients with multivessel CAD, but only a modest difference among patients with CAD. Therefore, carotid arterial stiffness might be similar in the limited population comprising only patients with CAD in this study.

As a limitation of this study, we assessed only carotid arterial stiffness as the functional parameter. Although the arterial stiffness β is less affected by arterial pressure changes and more useful than other parameters, other functional parameters need to be confirmed in future investigations.

**Conclusion**

Morphological changes in the carotid artery may be better predictors of the extent of CAD and multivessel CAD, independent of LV function, than functional changes.

**Disclosures**

None.

**References**


**Table 2. Logistic Regression Analyses for the Prediction of Multivessel Coronary Artery Disease**

<table>
<thead>
<tr>
<th>Predictor</th>
<th>OR (95% CI)</th>
<th>P</th>
<th>OR (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age per years</td>
<td>0.99 (0.93–1.04)</td>
<td>0.62</td>
<td>0.99 (0.94–1.04)</td>
<td>0.70</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>1.00 (0.86–1.17)</td>
<td>0.98</td>
<td>0.97 (0.83–1.14)</td>
<td>0.73</td>
</tr>
<tr>
<td>Hypertension</td>
<td>3.52 (1.33–9.35)</td>
<td>0.012*</td>
<td>3.04 (1.09–8.53)</td>
<td>0.03*</td>
</tr>
<tr>
<td>Smokers</td>
<td>0.93 (0.36–2.94)</td>
<td>0.88</td>
<td>0.72 (0.27–1.93)</td>
<td>0.51</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>1.29 (0.47–3.56)</td>
<td>0.62</td>
<td>1.15 (0.42–3.14)</td>
<td>0.78</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>0.59 (0.24–1.47)</td>
<td>0.26</td>
<td>0.69 (0.27–1.76)</td>
<td>0.44</td>
</tr>
<tr>
<td>Stiffness ß per unit</td>
<td>1.00 (0.92–1.09)</td>
<td>0.88</td>
<td>1.01 (0.93–1.11)</td>
<td>0.81</td>
</tr>
<tr>
<td>Plaque score per millimeter</td>
<td>1.28 (1.10–1.46)</td>
<td>0.001*</td>
<td>1.55 (1.15–2.09)</td>
<td>0.004*</td>
</tr>
<tr>
<td>%AS per percent</td>
<td></td>
<td></td>
<td></td>
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</tbody>
</table>

*Values are statistically significant.
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