The Clinical Implications of Atherosclerotic Plaques Identified by Carotid Ultrasonography

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Background and Methods To assess the clinical implications of atherosclerotic plaques in the carotid artery and evaluate the usefulness of ultrasonic tissue characterization, we performed carotid ultrasonography using an improved ultrasonic device and magnetic resonance imaging of the head in 297 patients who underwent cerebrovascular disease screening and 139 with essential hypertension.

Results High frequencies of pathological atherosclerotic and cerebral ischemic changes were found in patients who had soft plaques with a low-density lipid core and in patients who had hard plaques.

Conclusions Our results suggest that the presence of plaques in the carotid arteries is an important index of carotid atherosclerotic changes. Soft plaques with a low-density lipid core and hard plaques are often associated with cerebral ischemic changes and are characteristic of pathological atherosclerotic changes.

Key Words : atherosclerosis, carotid artery, ultrasonic tissue characterization

The prevalence of lifestyle related disease associated with atherosclerosis, such as cerebrovascular disease and ischemic heart disease, is steadily increasing and these diseases are now the leading causes of mortality in Japan. Early diagnosis of atherosclerosis and definition of the clinical significance of atherosclerotic changes play a role in preventing cerebrovascular disease and ischemic heart disease. Atherosclerosis is associated with arterial wall thickening and arteroma formation and rupture of atherosclerotic plaques may lead to thrombosis and vascular stenosis or occlusion, which can trigger serious diseases. Pathological atherosclerotic changes, such as luminal expansion, increased carotid artery intima-media thickness, and plaque formation can be evaluated by carotid ultrasonography. Moreover, recently improved techniques for ultrasonography, used in conjunction with conventional diagnostic procedures, have led to the development of methods for the quantitative evaluation of tissues, permitting detailed assessment of atherosclerotic changes in the carotid arteries. We examined the relationship between atherosclerotic plaques in the carotid arteries and cerebral ischemic lesions by quantitative ultrasonic tissue characterization in patients who underwent cerebrovascular disease screening and in patients who had essential hypertension. We also determined the clinical usefulness of this technique.

Methods

We studied 88 men and 70 women with a mean age of 54±6 years who underwent cerebrovascular disease screening at our hospital and 81 men and 58 women with a mean age of 67±11 years with essential hypertension treated at the Hypertension Center of our hospital. The combined study group comprised 169 men and 128 women with a mean age of 61±8 years. Patients with distinct symptoms of cerebrovascular disease were excluded from the study. Magnetic resonance imaging (MRI) of the head was performed with a 1.0-tesla scanner (Magnetom Impact Expert ; Siemens Medical Systems, Erlangen, Germany) on all patients. On the basis of the MRI results, cerebral ischemic changes were considered to be present in patients who had ischemic findings such as silent cerebral infarcts, lacunar infarcts or diffuse white-matter lesions. Carotid ultrasonography was performed with an ultrasound unit (Phillips SONOS 5500 ; Phillips Medical System, CA, USA) and a 4-to 10-MHz broad-band probe. Vascular morphology, the presence or absence of plaque, and the characteristics of the plaque were assessed in the left and right carotid arteries, with the subject in the supine position. To assess vascular morphology, the distal-wall intima-media thickness and diastolic vascular diameter were measured 1 to 2 cm proximal to the bifurcation of the internal and external carotid arteries. The sites were clearly depicted, and no calcification or local thickness was detected on ultrasonography. In addition, carotid artery distensibility was calculated using the following formula:

\[ \text{carotid artery distensibility} = \frac{\text{systolic luminal area of the carotid artery} - \text{diastolic luminal area of the carotid artery}}{\text{diastolic luminal area of the carotid artery} \times \text{pulse pressure}} \]

The results were expressed as the mean value of the left and right carotid arteries.

Plaque was considered present if a local protrusion of 1.1 mm or more was detected in the region extending from the common carotid artery to the carotid sinus and immediately after the bifurcation of the inter-

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Received February 27, 2005 ; Accepted March 10, 2005
nal and external carotid arteries. Plaques were absent in 169 patients the plaque-negative group and present in 128 the plaque-positive group. The plaque-positive group was divided into 2 groups according to the presence or absence of an acoustic shadow: 97 who had plaques without an acoustic shadow the soft-plaque group, and 31 who had plaques with an acoustic shadow the hard-plaque group (Fig. 1). The patients with soft plaques were then divided into 2 groups according to the results of ultrasonic tissue characterization by acoustic densitometry :29 who had plaques with a low-density lipid core (LDC) and 68 who had plaques without an LDC. LDC was considered present if the integrated backscatter (IBS) value inside the plaque was lower than the IBS value of the intima and media of the normal carotid artery7(Fig. 2). The morphology of the carotid artery including intima-media thickness, diastolic luminal diameter, and vascular distensibility and the presence or absence of ischemic changes on MRI scans of the head were compared among the 4 groups. The results are expressed as mean±SD. Statistical analysis was performed with the SPSS statistical package for Windows (ver. 11.0J) where differences among the groups were compared by analysis of variance with the use of Fisher's test. A difference was considered statistically significant if the p-value was less than 0.05.

Results

The demographic characteristics of the patients in each group are shown in Table 1. The mean ages were higher in patients who had soft plaques with LDC and patients who had hard plaques than in patients without plaques and those who had soft plaques without LDC. The systolic blood pressure was higher in patients who had soft plaques with LDC than in patients without plaques and those who had soft plaques without LDC. The diastolic blood pressure was also higher in those with hard plaques than in patients without plaques. The diastolic blood pressure was higher in patients who had soft plaques without LDC and those who had soft plaques with LDC than in patients without plaques. Finally the pulse pressure was significantly higher in the patients with plaques than in patients without plaques and was also significantly higher in patients who had soft plaques with LDC and those with hard plaques than in patients who had soft plaques without LDC.

The results of MRI scanning of the head are shown in Fig. 3. Overall, 34.3% of the patients had cerebral ischemic changes. The incidence of ischemic changes was higher in patients who had soft plaques with LDC (71.9%) and those with hard plaques (61.3%) than in those without plaques (24.2%) and patients who had soft plaques without LDC (30.4%).

The morphologic features of the carotid artery are shown in Fig. 4. The diastolic luminal diameter was significantly greater in the patients with plaques than in those without and was also significantly greater in patients who had soft plaques with LDC and those with hard plaques than in patients who had soft plaques without LDC. The intima-media thickness was significantly greater in the patients with plaques than in those without and was also significantly greater in patients who had soft plaques with LDC and patients with hard plaques than in those who had soft plaques without LDC. Finally the vascular distensibility was significantly lower in patients who had soft plaques with LDC and patients who had hard plaques than in those without plaques and patients who had soft plaques without LDC.

Discussion

The carotid arteries are particularly prone to atherosclerosis and atherosclerotic changes of these arteries are an index of systemic atherosclerosis and the risk of cerebrovascular disease. Atherosclerotic lesions in the carotid artery, as well as signs of pathologic changes in vascular morphology and function are thus thought to precede cardiovascular events, but are difficult to evaluate by conventional health screening programs. Recent increases in cerebrovascular disease screening programs coupled with the development of improved ultrasonic devices and techniques have per-

![Fig. 1. Carotid ultrasonography. A. soft-plaque: the absence of an acoustic shadow, B. hard-plaque: the presence of acoustic shadow.](image-url)
Fig. 2. Soft-plaque with a low-density lipid core (LDC) by acoustic densitometry. LDC was considered present if the integrated backscatter (IBS) value inside the plaque was lower than IBS value of the intima and media of the normal carotid artery.

Table 1. Characteristics of each groups of patients

<table>
<thead>
<tr>
<th></th>
<th>plaque negative group</th>
<th>soft plaque group Without LDC</th>
<th>soft plaque group With LDC</th>
<th>hard plaque group</th>
</tr>
</thead>
<tbody>
<tr>
<td>n (F/M)</td>
<td>169 (83/86)</td>
<td>68 (24/44)</td>
<td>29 (9/20)</td>
<td>31 (14/17)</td>
</tr>
<tr>
<td>age (yrs)</td>
<td>56.6±9.2</td>
<td>58.4±9.6</td>
<td>68.6±9.6*†</td>
<td>69.2±11.6*†</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>124±19</td>
<td>131±21</td>
<td>141±19*</td>
<td>138±17*</td>
</tr>
<tr>
<td>DBP (mmHg)</td>
<td>74±12</td>
<td>78±13*</td>
<td>78±11*</td>
<td>77±11</td>
</tr>
<tr>
<td>Pulse pressure (mmHg)</td>
<td>50±12</td>
<td>53±12*</td>
<td>63±15*</td>
<td>61±14*†</td>
</tr>
</tbody>
</table>

*P<0.01 : vs. plaque negative group, # P<0.01 : vs. soft plaque without LDC group. SBP : systolic blood pressure, DBP : diastolic blood pressure, LDC : low density lipid core.

mitted the earlier, more detailed evaluation of atherosclerotic changes in the carotid arteries. We previously performed carotid ultrasonography to screen for cerebrovascular disease and found that pathologic changes in vascular structure and function, such as silent cerebrovascular lesions and plaque formation in the carotid arteries, are present before the onset of cardiovascular events. We also reported that a person’s age and blood pressure have an important impact on such changes. Other studies have shown that indices such as the intima-media thickness and plaque score are related to cerebral infarcts and ischemic heart disease.

Unstable plaques may be involved in the development of atherosclerotic infarcts. Also acute coronary syndromes have been attributed to plaque rupture caused by inflammatory changes in the fibrous cap surrounding the lipid-rich core of plaques. Clinically, unstable plaques most vulnerable to rupture are characterized by a thin fibrous cap overlying a lipid-rich core. The early detection of atherosclerotic changes and unstable plaques most likely to rupture thus has a clinically important role in the prevention of cardiovascular events. However, plaque morphology alone, assessed on the basis of conventional ultrasonographic in-
Fig. 3. The incidence of ischemic changes in the brain assessed by MRI scanning in the 4 groups of patients. *p<0.01 : vs. plaque negative group, #p<0.01 : vs. soft plaque without low-density lipid core (LDC) group. MRI: magnetic resonance imaging.

dices such as intima-media thickness and plaque scores, provides inadequate information for the assessment of plaque stability. Conventional untrasoundography is often of limited value for the functional and qualitative evaluation of plaques because ultrasound is attenuated by fibrous tissue and calcification.

Recently developed techniques for acoustic densitometry have been used for ultrasonic tissue characterization of the myocardium\textsuperscript{14,15}. These techniques are based on IBS analysis and are used to generate and analyze IBS values directly derived from tissue signals without the need for postprocessing or nonlinear processing\textsuperscript{16}. Previous studies have shown that the use of intravascular IBS values corrected by blood IBS values improves the diagnostic accuracy. High corrected IBS values indicate fibrous components, whereas low corrected IBS values indicate lipid components. Untrasoundography can thus be used to evaluate the properties of vascular tissue\textsuperscript{17}. Our study showed that the properties of soft plaques, which are difficult to assess by conventional imaging techniques, can be clinically classified by acoustic densitometry. The presence of plaques in the carotid arteries may be an important indicator of carotid atherosclerotic changes in normotensive and hypertensive patients. Soft plaques with LDC and hard plaques are characteristic of pathological atherosclerotic changes in hypertensive patients and such changes are associated with severe atherosclerosis as well as a high risk of cerebral ischemic findings. To some extent, conventional ultrasonography can be used to predict the likelihood of ischemic cerebrovascular events on the basis of localized intimal thickening, plaque ulceration, and apparent stenosis and occlusion. However, ultrasonic tissue characterization permits the quantitative and qualitative assessment of plaques on the basis of the presence or absence of LDC and calcification and therefore may be more useful than conventional techniques for determining the stage of atherosclerosis.

Ultrasonic tissue characterization has several limita-

Fig. 4. The morphologic features of the carotid artery in the 4 groups of patients. *p<0.01 : vs. plaque negative group, #p<0.01 : vs. soft plaque without low-density lipid core (LDC) group.

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we calculated corrected IBS values. Clinically, we believe that our methods permit the quantitative evaluation of the properties of plaques, including the fibrous cap and lipid-rich core. However, standardized procedures, including gain settings and measurement techniques, should be developed to consistently produce objective results.

Ultrasonic tissue characterization may facilitate long-term observation because the procedures involved are non-invasive and can be easily repeated. Future studies should examine the effects of plaque stability and drug treatment as well as the relationship with risk factors for atherosclerosis. Inclusion of histological changes of atherosclerotic lesions and cerebrovascular disease in general screening programs, in addition to morphological changes of atherosclerosis, would likely enable physicians to provide patients with more concrete measures for disease prevention or treatment instead of merely recommending follow-up observation.

References