Morphologic Correlation Between Atherosclerotic Lesions of the Carotid and Coronary Arteries in Patients With Angina Pectoris

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The morphology of atherosclerosis between the carotid and coronary artery systems was studied in 63 patients with ischemic heart disease to determine if there was a correlation with coronary heart disease. The sclerotic lesions of the carotid and coronary artery systems were imaged with ultrasonography and coronary arteriography, respectively, and divided into 4 types. Hemodynamic variables, serum lipid levels, and serum uric acid concentration were not different among the groups, but the serum C-reactive protein (CRP) concentration in patients without significant atheroma in the carotid artery system was lower than the mean concentration of the other 3 groups with carotid atheroma. The morphological stability of carotid arterial plaques correlated well to coronary artery stenosis. Morphologically unstable plaques of the carotid artery predicted unstable forms of coronary obstruction with a sensitivity of 68%, specificity of 85%, predictive power of 72% and a likelihood ratio of 4.5. These results suggest that ultrasonic examination of the carotid artery is useful for predicting the presence or absence of unstable lesions in coronary arteries. (Jpn Circ J 1999; 63: 522–526)

Key Words: Carotid artery; Coronary artery; Ultrasonography; Unstable atheroma

Methods

The study population consisted of 63 patients with angina pectoris who underwent cardiac catheterization to define the status of their coronary atherosclerosis: 56 had angina pectoris without previous myocardial infarction and 7 had angina with previous myocardial infarction. Exclusion criteria included clinically unstable coronary heart disease (patients with myocardial infarction within the past 12 weeks, unstable angina, cardiogenic shock, or other evidence of clinical instability), previous interventional treatment for coronary obstruction such as coronary artery bypass surgery, angioplasty or thrombolysis, or prevalent symptomatic cerebrovascular disease.

The coronary arteriogram (CAG) was done using Judkins' technique, and measurements of the coronary stenosis were performed by 2 independent cardiologists. The coronary stenosis was considered significant when the luminal diameter at the stenotic lesion was less than 50% of the adjacent normal coronary diameter. Coronary stenosis was categorized into one of 4 types (Fig 1) based on the morphology of the obstruction according to Ambrose et al.9,10 that is, (i) no significant stenosis [type N(CAG)], (ii) concentric stenosis [type C(CAG)], (iii) eccentric stenosis [type E(CAG)] and (iv) multiple stenoses [type M(CAG)]. Type E was further divided into 2 subtypes with (type E-2) or without (type E-1) a narrow neck due to one or more overhanging edges or an irregular or scalloped border, or other evidence of clinical instability.
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their precise location and the number of plaques. Images more arterial plaques were found at this site regardless of was considered present in the carotid artery when one or Plaque vessel lumen with a distinct area 50% or greater than the cation and along the internal carotid artery. Arterial plaque and the transducer was moved cephalad through the bifur-

270A) equipped with a 7.5-MHz transducer was used for done within 2 weeks of the cardiac catheterization study. A Toshiba high-resolution ultrasound unit (Sonolayer SSA-
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Because progression of coronary disease occurs much more frequently in eccentric stenosis type E-2 (group E-2) or with multiple lesions (group M) than in other forms of stenosis (groups C and E-1), the results of the ultrasound examination were also divided into 2 groups (stable and unstable).

Table 2 Relationship of the Form of Plaques Between Coronary and Carotid Arteries

Table 3 Relationship of the Stability of Plaques Between Coronary and Carotid Arteries

both. Participants all provided informed consent.

Ultrasonic examination (UTS) of the carotid arteries was done within 2 weeks of the cardiac catheterization study. A Toshiba high-resolution ultrasound unit (Sonolayer SSA-270A) equipped with a 7.5-MHz transducer was used for scanning the carotid artery. Patients were examined in the supine position, and each carotid segment was interrogated independently from continuous angles to identify the plaque or the thickest intima-media site. Each scan of the common carotid artery was begun just above the clavicle, and the transducer was moved cephalad through the bifurcation and along the internal carotid artery. Arterial plaque was defined as an echogenic structure encroaching into the vessel lumen with a distinct area 50% or greater than the intimal plus medial thickness of neighboring sites. Plaque was considered present in the carotid artery when one or more arterial plaques were found at this site regardless of their precise location and the number of plaques. Images were transcribed onto a hard copy with a digitized pad interfaced to a PC running custom-designed ultrasound-analysis software. Measurements were made from the hard copy, and the lesions were categorized into one of 4 types: type N (UTS), C (UTS), E (UTS) and M (UTS), as in the coronary arterial bed (Fig 1). The type E was also divided into 2 subtypes: type E-1 and E-2. The internal diameter of the carotid artery at the plaque site was measured for calculating the percent stenosis of the vessel. The classification and calculation were based on the most severely affected site on either the right or left side. When no significant plaque was detected in either of the carotid arteries, the patient was categorized type N regardless of the intima-media thickness.

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One experienced cardiologist performed all the scanning, classification and measurement of the carotid lesions. Another 2 well-trained cardiologists, who were unaware of the results of the carotid scanning, measured and classified the coronary lesions after consulting the coronary arteriograms.

Statistical Analysis

Data were expressed as mean ± SD. Comparison of parameters among the groups was made by ANOVA and Bonferroni’s modified student t-test, and univariable comparison in categorical factors were performed with chi-squared tests. A difference was considered significant when the p-value was less than 0.05. To evaluate the probability of predicting the form of coronary atherosclerosis, a test of the sensitivity and specificity of the shape of carotid plaques versus either the stable or unstable form of coronary atheroma was used. The pretest likelihood (PL) was defined as the probability of unstable coronary atheroma in a patient to be tested:

\[
PL = \frac{\text{No. of patients with unstable coronary atheroma}}{\text{total number of patients tested}}
\]

The sensitivity (SE) of the test was the probability of a positive test result in a patient with unstable coronary atheroma.


\[ SE = \frac{\text{No. of patients with unstable coronary atheroma in patients with unstable carotid plaques}}{\text{no. of tested patients with unstable coronary atheroma}} \]

The specificity (SP) of the test was the probability of not having the positive test result (absence or stable coronary atheroma) in a patient without unstable coronary atheroma:

\[ SP = \frac{\text{No. of patients without unstable coronary atheroma in patients not showing unstable carotid plaques}}{\text{no. of patients without unstable coronary atheroma}} \]

The predictive power (PP) was calculated according to Bayes theorem:

\[ PP = \frac{PL \times SE}{PL \times SE + (1-PL)(1-SP)} \]

The likelihood ratio was also calculated as follows:

\[ \text{Likelihood Ratio} = \frac{SE}{1-SP} \]

Results

UTS classified the 63 patients into 21 type N [N (UTS)], 15 type C [C (UTS)], 9 type E-1 [E-1 (UTS)], 11 type E-2 [E-2 (UST)] and 7 type M [M (UTS)], and CAG categorized the patients into 11 type N [N (CAG)], 17 type C [C (CAG)], 13 type E-1 [E-1 (CAG)], 9 type E-2 [E-2 (CAG)] and 13 type M [M (CAG)]. Background data for each group categorized with carotid lesions are presented in Table 1. Mean age and sex distribution were similar among the groups. Heart rate, systolic and diastolic blood pressure, left ventricular end-diastolic pressure (LVEDP), and cardiac index (CI) for each group did not differ. Serum lipid levels and uric acid concentration were not significantly different among the groups, whereas the serum C-reactive protein (CRP) concentration of group N was significantly lower than the mean concentration of the other groups with atheromas in the carotid arteries (p=0.027). Twenty-two patients smoked the equivalent of more than one-pack of cigarettes per day, and the remaining 41 did not smoke. The prevalence rate of smokers was not different among the 4 UTS groups.

The prevalence of severe carotid stenosis (>50%) was low at 11.1%, and moderate stenosis (26–50%) was observed in about one-quarter (25.4%) of the patients. The group with mild carotid stenosis (1–25%) was slightly more than one-quarter (27.0%). Thirty-seven percent of the patients had vessels without plaque deposition in the carotid artery beds. The percent stenosis of the coronary artery was plotted against that of each carotid lesion. Though, as shown in Fig 2, no significant relationship was observed between the 2 measurements, all of the 7 patients with severe carotid stenosis (≥50%) had coronary obstruction greater than 75%.

The relationship of the form of stenosis between the coronary and carotid arterial beds is represented in Table 2, and that of the morphological stability of the atherosclerosis in the coronary and carotid arteries is shown in Table 3. The morphological stability of the carotid artery plaques correlated well to coronary artery narrowing. When predicting the morphological stability of coronary lesions from that of carotid plaques, one could estimate unstable coronary lesions with a sensitivity of 68%, specificity of 85% and a predictive power of 72%. The likelihood ratio was 4.5 for estimating the morphological stability of coronary artery lesions.

Discussion

The present study demonstrated that the morphological stability of carotid plaques correlates with that of the coronary artery: unstable carotid plaques suggest unstable morphology of the coronary arteries, which frequently causes progression of coronary disease.

B-mode ultrasound examination has proved to be a useful noninvasive method of quantitatively assessing the amount of atherosclerosis in the carotid arterial system. Several reports show that coronary disease and cerebrovascular disease have many common risk factors including age, hypertension, hyperlipidemia, diabetes and smoking. However, in the limited number of patients in the present study, neither hypertension, hyperlipidemia, diabetes nor smoking showed a significant correlation to the the morphology, or the presence or absence, of atheromatous plaque in the carotid artery beds. Only a lower serum CRP concentration identified the patients without carotid plaques from those with atherosclerotic lesions. CRP is the classic acute phase plasma protein, serum levels
of which are extensively used in routine clinical practice to monitor the acute phase response to inflammatory processes. Inflammation is an important feature of atheromas and the concentration of CRP is directly correlated with the presence and severity of coronary, cerebral, and peripheral arterial atherosclerosis. Substantial increases in the serum concentration of CRP have been observed in patients with severe unstable angina compared with stable angina. However, all the patients involved in our study had stable ischemic heart disease, with appropriate medication, but most of them had atherosclerotic plaques in both the coronary and carotid arteries. Though the reason is uncertain for the increased CRP concentration in patients with atherosclerotic plaques in stable ischemic heart disease, the extent of the atherosclerosis the instability of the plaques may play a role in the increased CRP.

The presence of any structural changes in the common carotid arteries or the carotid bulbus is frequently associated with coronary events. As coronary atherosclerosis develops, on average, earlier in life than carotid atherosclerosis, the relationship between carotid atherosclerosis and the risk of coronary heart disease has been considered critically important. According to the cross-sectional study of O’Leary et al., maximum stenosis of the carotid arterial system was highly associated with coronary disease: the prevalence of coronary disease increased from 17.8% in those with 0% stenosis to 45.8% in those with ≥75% stenosis. A follow-up study also demonstrated that large plaques that caused more than 20% stenosis of the carotid arteries showed a greater hazard in coronary events than small plaques. The present study in patients with angina pectoris demonstrated that all patients with a carotid diameter reduced more than 50% showed severe coronary obstruction (≥75%), although in the patients with carotid stenosis less than 50%, there was no significant relationship between the carotid and the coronary arteries of the extent of stenosis. This indicates that severe carotid stenosis strongly suggest the presence of severe coronary narrowing.

Although quantitative anatomic variables are similar, progression of the coronary arterial lesions differs between unstable and stable angina. Ambrose et al demonstrated a characteristic coronary lesion in the majority of patients with acute presentation of unstable angina. An eccentric stenosis in the form of a convex intraluminal obstruction with a narrow neck due to one or more overhanging edges or irregular or scalloped borders, or both, is present in approximately 70% of patients with unstable angina, but in only 16% of patients with stable angina. In addition, they also found from repeated cardiac catheterizations that this type of stenosis appears to be a major cause of unstable angina. A lesion similar in appearance was also reported by Singh in patients with rapidly progressive coronary lesions at the time of recatheterization. Therefore, the morphology of coronary lesions is important for predicting the stability and prognosis of patients with angina pectoris. The studies are based on samples of patients undergoing coronary angiography because there is not an accurate noninvasive means for measuring the disease of the coronary arteries, and because the relation of symptoms to atherosclerosis in this arterial bed is notoriously poor. Noninvasive and easily repeatable methods for predicting the stability of coronary lesions are important for clinical use. For this purpose, we tried to estimate the morphological stability of coronary atheromas from the form of plaques in the carotid artery beds in the patients with angina pectoris. The results suggest that the morphology of carotid plaques can predict the stability of coronary narrowing with a high predictive value. Because none of our patients has had clinical symptoms of disturbed carotid circulation before or at the time of study, we could not comment on the stability of carotid plaques. However, patients with carotid artery disease more often die from acute coronary events than from complications of carotid atherosclerosis.

Study Limitation
Ultrasound examination demonstrates carotid obstruction from the origin of the common to the internal carotid artery 5–10 mm distal to the bifurcation. Lesions more than 5–10 mm distal to the carotid bifurcation are usually unable to be revealed by this method, and, therefore, the distal lesions in the internal carotid artery could modify the present results.

In the present study we used Ambrose et al’s classification of the arteriographic morphology of coronary obstruction for ultrasonographic lesions of the carotid artery. The obstruction on the coronary arteriography consists of the sum of whole dimension of the vessel, whereas the carotid scanning by ultrasonography, along with the longitudinal axis of the vessel, allows observation of the lesion from a limited direction. The observation from the limited direction may categorize the lesion into an inappropriate type, or may cause either under- or overestimation of the obstruction, which may create some difficulties with comparing directly the morphology obtained by carotid ultrasonography with that obtained from coronary arteriography. Although we scanned the carotid vessels in as many directions as possible, including the transverse axis view, to reduce the possibility of incorrect classification, the risk still remained completely unresolved.

References


