Compensatory Carotid Artery Dilatation in Early Atherosclerosis

W. Steinke, MD; T. Els, MD; M. Hennerici, MD

Background From pathological studies of coronary arteries, it has been recognized that progressive plaque development may be compensated for by an increase of the arterial diameter. However, the dynamics of this process have not been investigated, and it is not known whether compensatory dilatation is a general pathomechanism in human arteries.

Methods and Results Using a high-resolution duplex scanner and subsequent three-dimensional plaque reconstruction, we prospectively studied the effect of carotid plaque development on the vascular geometry in 32 patients at 6- to 12-month intervals. Plaque progression in 41% (n=26) of studies was associated with an increase of the vessel diameter between 0.4 and 1.2 mm in 76% (n=20). Among 36 unchanged plaque developments, enlargement of the arterial diameter was assessed in only 28% (n=10) (P<.001).

Conclusions Our data suggest that increasing plaque volume is significantly associated with enlargement of carotid artery segments, which compensates for arterial narrowing in early stages of the disease. (Circulation. 1994;89:2578-2581.)

Key Words • atherosclerosis • ultrasonics • carotid arteries

From pathoanatomic studies, it has been recognized that coronary artery enlargement occurs in response to the formation of atherosclerotic plaques. On the basis of a study of 125 human left main coronary arteries, Zarin et al suggested that increase of the arterial diameter is a compensatory mechanism that may prevent significant luminal narrowing. These results were in contrast to previous studies attributing enlargement of atherosclerotic coronary arteries primarily to coincidental vessel dilatation with age.

The natural history of carotid atherosclerosis has been investigated in several prospective ultrasound studies. Contrary to the general opinion that atherosclerosis represents a progressive or at best unchanging disease for years, plaque regression occurred in 7% of the nonstenotic lesions in our study of the development of small carotid atheroma. In this study, distinct echomorphological features and hemodynamic patterns were associated with different plaque development. However, to the best of our knowledge, no data exist on the effect of plaque progression on the vascular geometry of carotid arteries. We have therefore reevaluated our prospectively collected material to analyze whether compensatory enlargement similar to that seen in coronary artery specimens occurs in carotid atherogenesis as well.

Methods

Thirty-two patients (14 men, 18 women; mean age, 65 years; range, 48 to 79 years) with nonstenotic (diameter reduction <30%) carotid artery plaques were consecutively examined as part of a larger prospective study of carotid atherosclerosis with regard to plaque development and associated changes of the arterial diameter. Patients were selected if the extent and morphology of the small plaques could be displayed adequately by high-resolution B-mode scanning. Each patient had a baseline study and two follow-up examinations at 6- to 12-month intervals (mean interval, 7.6 months). Thus, the total number of follow-up studies was 64 with a mean follow-up time of 15.2 months (range, 12 to 22 months). Plaques were located at the bifurcation (n=17), in the distal common carotid artery (CCA) (n=8), and in the internal carotid artery (ICA) (n=7).

A duplex scanner (Picker Microwav) with a high-resolution B-mode imaging system (10-MHz insonation frequency) and a specially designed three-dimensional reconstruction device was used for the assessment of the plaque configuration and the lesion volume. Sequential perpendicular cross sections along the axis of the vessel or parallel longitudinal sections from the medial to the lateral vascular wall were recorded on videotape continuously throughout the cardiac cycle for subsequent three-dimensional reconstruction (Fig 1). Technical details of the procedure have been reported elsewhere. Classification of progressive or regressive plaque developments was based on the volume calculation. With regard to the intraobserver and interobserver variability in previous calibration experiments, plaque progression and regression were accepted with increasing and decreasing volumes of >30%.

Since the media-adventitia boundary can be determined with a high reproducibility, we measured the maximal systolic “interadventitial” diameter at the central level of the plaque (Fig 1). The distance from the tip of the flow divider to the level of measurement was reproduced in follow-up studies. The mean of six measurements (three each in transverse and longitudinal sections) was used to assess changes of the arterial diameter. We did not use the digitized pixel size of the gray-scale image to measure the intimal-medial thickness but considered only an increase of the diameter above the axial resolution of the duplex system (0.35 mm) as a significant enlargement. χ² test and linear regression with Pearson product moment correlation were used for statistical evaluation.

Results

Follow-up measurements of the plaque volume revealed progression in 41% of the studies (Fig 1), regressive developments in 3%, and no significant
change in 56% (Figs 2 and 3). Progressive lesions were associated with arterial enlargement in 76%, whereas increased vessel diameters were assessed in 28% of the unchanged plaques (P<.001) (Table). None of the duplex follow-up analyses demonstrated a decreasing carotid artery diameter. In addition, the degree of plaque progression as determined from the volume calculation was significantly correlated (r=.7, P<.001) with the degree of arterial enlargement at the lesion site (Fig 4).

Separate analysis of the plaque development and luminal diameter changes for different lesion locations
Carotid Plaque Development of 32 Nonstenotic Plaques and Associated Changes of the Arterial Diameter: Results of 64 Follow-up Duplex Studies

<table>
<thead>
<tr>
<th>Plaque Development, n (%)</th>
<th>Change of Vascular Diameter, * n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unchanged 36 (56)</td>
<td>Unchanged 26 (72) Increased 10 (28)</td>
</tr>
<tr>
<td>Progressive 26 (40)</td>
<td>6 (24)</td>
</tr>
<tr>
<td>Regressive 2 (4)</td>
<td>2 (100)</td>
</tr>
</tbody>
</table>

No instance of decrease in arterial diameter has been observed.

* χ² P<.001.

revealed that plaque progression occurred more frequently in the ICA (67%) than at the bifurcation (49%) or in the CCA (23%). In addition, among progressive plaque developments, arterial enlargement was assessed in lesions of the ICA and the bifurcation in 83% and 72%, respectively, but in only 25% of the progressive plaques in the CCA.

Discussion

The present study demonstrates a strong correlation between progression of small carotid atheroma and arterial enlargement. Similar results have been reported from pathoanatomic and angiographic studies of coronary arteries; however, this is the first report of carotid artery dilation in vivo in response to progressive early atherosclerosis.

Glagov et al. and Zarins et al. found a highly significant association of artery size and plaque area in left human coronary arteries, which delayed the decrease in vascular lumen until the lesion occupied about 40% of the internal elastic lamina. Stiel et al. confirmed the results in a detailed morphometric and angiographic investigation of atherosclerosis in coronary arteries. In contrast to these studies, Hort et al. found no compensatory enlargement in early stages of coronary atherosclerosis, since the mean difference in intimal thickness of anatomic specimens corresponded exactly to the mean difference of the lumen diameters between healthy and sclerotic coronary arteries in postmortem angiograms in their study.

Based on observations that flow separation and plaque formation are most frequently assessed at expansions of an artery such as the carotid bulb, Lo Gerfo et al. suggested in the discussion following the article by Zarins et al. that plaque formation occurs in large segments of the artery at the area of boundary layer separation rather than that plaque progression leads to dilatation. He criticized the fact that follow-up data could not be obtained from anatomic coronary artery specimens, which, hence, produced a "single snapshot in the history of atherogenesis."

Although high-resolution duplex sonography has been available for more than a decade, changes of the arterial geometry in relation to carotid plaque development have not been analyzed systematically to date. Methodological difficulties in the assessment of progression or regression of small nonstenotic carotid atheroma may have contributed to this restraint. To overcome this limitation, we used a three-dimensional reconstruction system with integrated volume calculation for a correct analysis of the plaque development. Since the assessment of the intimal-medial thickness and the media-advetitia boundary is highly reproducible by means of high-resolution B-mode scanning, we used the maximal "interadventitial" diameter as a parameter of arterial enlargement. Our results confirm the observation from coronary arteries that plaque progression is correlated with increasing arterial diameter. Since the age of the patients and the follow-up intervals were not significantly different in progressive, unchanged, or regressive lesions, enlargement of carotid arteries with age, which has been demonstrated in previous ultrasound studies, could not account for the effect.

The mechanism of compensatory dilatation is unknown. Zarins et al. suggested two explanations: (1) Since most plaques are eccentric at the early stage of the disease, local increase in wall stress at the uninvolved vessel wall may stimulate endothelium-dependent arterial dilatation, which represents a normal response to shear stress stimuli. (2) Atheroma formation may lead to degradation of the underlying media and adventitia, with outward bulging of the plaque. Other potential causes of remodeling are outmigration of medial smooth muscle cells and ischemic medial atrophy. The different vessel wall structure of the elastic CCA with a thick media and the muscular ICA may contribute to less frequent compensatory enlargement in the CCA compared with the ICA.

The delay of more severe carotid obstructions represents the major clinical impact of arterial enlargement at the site of early atherosclerotic lesions. Because of the relatively small number of progressive plaques that did not produce significant luminal narrowing during follow-up studies, we cannot determine the maximal compensatory enlargement in the carotid system from our data. Future studies will probably shed some light on this unanswered question.

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References

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