Plaque Morphology Correlates With Cerebrovascular Symptoms in Patients With Complex Aortic Arch Plaque

Jesse Weinberger, MD; Nikolais Papamitsakis, MD; Andre Newfield; James Godbold, PhD; Martin Goldman, MD

**Background:** Studies of aortic arch plaques with transesophageal echocardiography have demonstrated that complex aortic arch plaques (CAPs) greater than or equal to 4 mm in thickness are associated with ischemic stroke. Recent studies have demonstrated that the morphological features of plaques may aid in the identification of aortic plaques that are more likely to be associated with embolic stroke.

**Objective:** To identify aortic plaques that are more likely to be associated with embolic stroke by means of their morphological features.

**Methods:** Transcutaneous B-mode ultrasonography was used to image aortic arch plaques in 500 consecutive patients. The criteria used to identify the morphological features of carotid artery plaques that are more likely to be associated with ischemic stroke (heterogeneous rather than homogeneous) were applied to aortic arch plaques. Statistical comparisons were made using the Fisher exact test.

**Results:** Ischemic symptoms (e.g., stroke, transient ischemic attack, and amaurosis fugax) were present in 38% of 104 patients with CAP and in 34% of 391 patients without CAP. Nineteen (51%) of 37 patients with heterogeneous CAP were symptomatic. Twenty-one (31%) of 67 patients with homogeneous CAP were symptomatic ($P = .04$).

**Conclusion:** Transcutaneous B-mode ultrasonography of the aortic arch can help to identify heterogeneous plaques that are more likely to be associated with ischemic stroke using morphological criteria derived from studies of carotid artery plaque.

**Arch Neurol.** 2000;57:81-84

POSTMORTEM examinations$^1$ and transesophageal echocardiographic (TEE) studies$^{2,11}$ have demonstrated an association between ischemic stroke and atherosclerotic aortic arch plaque. Initial studies with TEE defined complex aortic arch plaques (CAPs) in terms of wall thickness. A correlation was found between ischemic stroke and plaques greater than or equal to 4 mm in thickness.$^{5,11}$

Further TEE studies have suggested that the morphological features of plaque are an important factor in determining the relationship between aortic arch plaque and stroke.$^{12,13}$ Similar to the studies of carotid artery atherosclerosis performed with B-mode sonography,$^{14-19}$ in the present study, we used a recently developed technique to image atherosclerotic plaque in the aortic arch with transcutaneous B-mode ultrasonography$^{20}$ (B-scan) to determine if the B-mode criteria that are used to identify carotid artery plaque could be applied to aortic arch plaque to help identify lesions associated with a greater risk of cerebrovascular events.

**RESULTS**

The distal ascending aorta, aortic arch, and proximal descending aorta were well visualized in 468 of the 500 patients. In 27 patients, only the knob of the arch could be visualized, and in 5 patients, the arch could not be visualized.

**CORRELATION OF CEREBROVASCULAR RISK FACTORS WITH PLAQUE THICKNESS**

There was no difference in risk factors for cerebrovascular disease, including hypertension, coronary artery disease, cholesterol levels higher than 5.95 mmol/L ($\geq 230$ mg/dL) or requiring treatment, diabetes, or smoking, between patients with CAP and patients without CAP.
SUBJECTS AND METHODS

SUBJECTS

Transcutaneous B-mode ultrasonography of the aortic arch was performed on 500 consecutive patients referred for clinical neurovascular evaluation, including carotid duplex ultrasonography and transcranial Doppler sonography as well as imaging of the aortic arch. All patients were evaluated by a neurologist (J.W.) at the time of the ultrasound evaluation to define whether the patient had cerebrovascular symptoms. Ischemic stroke was defined as a focal neurological deficit lasting more than 48 hours associated with signs of brain infarction in the appropriate vascular distribution on imaging studies (computed tomographic or magnetic resonance imaging scans). Focal transient ischemic attack was defined as a focal neurological deficit with symptoms directly referable to a cerebral hemisphere or brainstem structure lasting less than 24 hours. Amaurosis fugax was defined as a transient episode of monocular visual loss, usually with a shadow ascending or descending over the affected eye. The data for analysis were acquired from the official clinical reports of the neurovascular testing by investigators who had not participated in performing the testing (N.P. and A.N.). Since all the clinical evaluations were performed prior to the inception of the study, the potential for bias was limited.

Signs of cerebrovascular symptoms were present in 171 patients. The remaining patients were referred because they had a carotid artery bruit or nonspecific symptoms such as dizziness and did not have a history or clinical findings of a focal neurological deficit. These patients were included in the asymptomatic group. Other risk factors for ischemic stroke, including hypertension, coronary artery disease, cholesterol levels higher than 5.95 mmol/L (≥230 mg/dL) or that required treatment, diabetes, smoking, carotid artery atherosclerosis, and atrial fibrillation or other cardioembolic source, were ascertained for each patient.

B-SCAN

Transcutaneous B-mode ultrasonography of the aortic arch was performed with a colorflow duplex Doppler instrument (model XP 128; Acuson, Mountain View, Calif) using an L7-phased array linear probe at 7.5 MHz. Doppler examination was performed at 5.0 MHz. A lateral supraclavicular approach was used to visualize the distal ascending aorta, aortic arch, and proximal descending aorta. In the aforementioned study, all complex plaques visualized with TEE in the distal ascending aorta and aortic arch proximal to the origin of the left internal carotid artery were also visualized with B-scan. In the present study, a total of 37 patients also underwent TEE. The sensitivity of B-scan compared with TEE was 93.75%, and the specificity was 80.95%. The positive predictive value was 78.93%, and the negative predictive value was 94.40%.

PLAQUE MORPHOLOGY

Plaques were characterized as simple if they were less than 4 mm in thickness and complex if they were greater than or equal to 4 mm in thickness as defined initially in prior TEE studies. They were also described as sessile, crescentic, pedunculated, flat, mobile or immobile, and irregular or regular. The B-mode criteria of heterogeneous lucent plaque and homogeneous echodense plaque as described for the carotid bifurcation14-17 were also applied. In these studies, heterogeneous lucent plaque correlated with intraplaque thrombus, while homogeneity correlated with simple fibrous plaque and calcification14,21 (Figure 1 and Figure 2).

STATISTICAL ANALYSIS

Univariate and multivariate analyses of cerebrovascular risk factors in relation to plaque thickness were performed using linear regression analysis with the SAS statistical package (SAS Inc, Cary, NC). Statistical comparisons of the morphological characteristics of plaque with symptoms were performed using the Fisher exact test.

CORRELATION OF CEREBROVASCULAR SYMPTOMS WITH PLAQUE THICKNESS

Complex aortic arch plaque was identified in 104 of the 500 patients studied with B-scan. Stroke, transient ischemic attack, or amaurosis fugax occurred in 40 patients with CAP (38%). Symptoms occurred in 34% of 391 patients without CAP. The size of the CAP in either area or thickness and the mobility or irregularity of the CAP did not correlate with symptoms when analyzed by multivariate regression analysis. When patients with the coexisting risk factors of atrial fibrillation and carotid artery stenosis greater than 50% were excluded, 22 (43%) of the remaining 55 patients with CAP were symptomatic, whereas 89 (32%) of the remaining 278 patients without CAP were symptomatic (P = .08).

CORRELATION OF SYMPTOMS WITH MORPHOLOGICAL CHARACTERISTICS OF COMPLEX PLAQUE

The CAP was evaluated as to whether it was homogeneous or contained heterogeneous lucency. Patients with simple plaque were not included in this analysis, since almost all simple plaques were homogeneous. Nineteen (51%) of the 37 patients with heterogeneous plaques were symptomatic, while 21 (31%) of the 67 patients with homogeneous plaques were symptomatic (P = .04). Thus, while there was no correlation between plaque thickness and cerebrovascular symptoms, patients with heterogeneous plaques that were equal to or greater than 4 mm in thickness were at significantly greater risk for cerebrovascular events than patients with homogeneous plaques. This finding is analogous to the increased incidence of cerebrovascular symptoms ipsilateral to heterogeneous carotid artery plaque compared with homogeneous carotid artery plaque, regardless of the degree of stenosis. Patients with other possible risk factors for stroke were not excluded from the analysis. Therefore, the correlation of heterogeneous CAP with symptomatic cerebrovascular disease may represent a generalized activation of the atherosclerotic process rather than embolic events from the CAP. Further studies analyzing sequential changes in CAP in relation to symptoms will be necessary to clarify the role of aortic arch plaque as a cause of ischemic stroke.

©2000 American Medical Association. All rights reserved.
Complex aortic plaque in the arch of the aorta can be identified with B-scan with an accuracy that approaches that of TEE. The application of the B-mode criteria that are used for categorizing carotid artery plaques as heterogeneous or homogeneous to CAP demonstrated a significant association between heterogeneous lesions and ischemic cerebrovascular symptoms, while measurement of wall thickness alone did not. A recent study using TEE also determined that while there was a significant association between plaque thickness greater than 4 mm and stroke, hypoechoic and ulcerated aortic arch plaques had a significantly higher correlation with ischemic stroke than homogeneous dense plaques.12 Plaque mobility may also be an important factor,13 but there was no correlation between plaque mobility and ischemic symptoms in the present study.

Morphological examination of postsurgical surgical carotid plaque specimens has demonstrated that hypoechoic plaques are associated with intraplaque thrombus,14,2 which makes them more likely to cause ischemic symptoms through embolization and arterial thrombosis.14-19 The same may be true for aortic arch plaques. However, it cannot be assumed that the presence of a heterogeneous, hypoechoic aortic arch plaque is the cause of a particular stroke, since most strokes in patients with aortic arch plaque also involve other pathogenetic factors.22,23

The present study was retrospective. Prospective studies have demonstrated a greater risk of recurrent ischemic stroke in patients with CAP, but follow-up imaging of changes in plaque morphology was not performed.10,11,12 Further prospective studies are planned using the noninvasive B-scan technique to correlate changes in the morphological characteristics of aortic plaque with occurrence of cerebrovascular symptoms.

The association of cerebrovascular symptoms with aortic plaque thickness of greater than 4 mm that has been demonstrated in studies using TEE was not found in this study. This observation probably reflects a difference in population. In the present study, there were more patients with generalized atherosclerotic disease identified primarily by the presence of an asymptomatic carotid bruit; therefore, a greater proportion of patients with large asymptomatic aortic arch atheroma may have been identified than in the TEE studies. The noninvasive B-scan technique for imaging aortic arch plaque may be valuable in quantifying the prevalence of aortic arch atheroma in the asymptomatic population with atherosclerotic vascular disease and in delineating the risk of future stroke in these patients.

Transcutaneous B-mode ultrasonography is a noninvasive method for visualizing aortic arch plaque that can be applied to a large patient population that would not require TEE. B-mode criteria can be used to identify heterogeneous hypoechoic plaques that are more likely to be associated with thromboembolic events. The B-scan technique is a screening procedure that can identify aortic arch plaque in a large percentage of patients, but it cannot replace TEE to evaluate whether an aortic arch plaque is present in patients with stroke. The B-scan technique may be particularly useful in natural history studies that require sequential imaging of aortic arch plaque and may also be valuable in therapeutic trials to assess the effect of treatment on the morphological characteristics of plaque over time.

Accepted for publication April 13, 1999.

Reprints: Jesse Weinberger, MD, Department of Neurology, Box 1052, The Mount Sinai School of Medicine, One Gustave L. Levy Place, New York, NY 10029.

REFERENCES

3. Tunick PA, Kronzon I. Protruding atherosclerotic plaque in the aortic arch of pa-
tients with systemic embolization: a new finding seen by transesophageal echo-
4. Tunick PA, Culliford AT, Lamparello PJ, Kronzon I. Atheromatosis of the aortic
114:391-392.
6. Toyoda K, Yasaka M, Nagata S, Yamaguchi T. Aortogenic embolic stroke: a trans-
7. Horowitz DR, Tuhrim S, Budd J, Goldman ME. Aortic plaque in patients with brain
42:1602-1604.
9. Jones EF, Kalman JM, Calafiore P, Tonkin AM, Donnan GA. Proximal aortic ath-
10. The French Study of Aortic Plaques in Stroke Group. Atherosclerotic disease of
334:1216-1221.
half of the FAPS Investigators. Aortic plaque morphology and vascular events: a
follow-up study in patients with ischemic stroke. Circulation. 1997;96:3838-
3841.
13. Dressler FA, Craig WR, Castello R, Labovitz A. Mobile aortic atheroma and sys-
temic embolii: efficacy of anticoagulation and influence of plaque morphology
histology using real time ultrasonography: clinical and therapeutic implications.
1989;59:529-534.
16. Langsfeld M, Gray-Weale AC, Lusby RJ. The role of plaque morphology and di-
ameter reduction in the development of new symptoms in asymptomatic ca-
17. Johnson JM, Kennelly MM, Deesare D, Morgan S, Sparrow A. Natural history of
18. Weinberger J, Robbins A. Neurologic symptoms associated with nonobstruc-
tive plaque at carotid bifurcation: analysis by real-time B-mode ultrasonogra-
changes of atherosclerotic plaque at the carotid artery bifurcation: sequential imaging by real time B-mode ultrasonography. J Am Coll Cardiol. 1988;12:
1515-1521.
20. Weinberger J, Azhar S, Danisi F, Hayes R, Goldman M. A new noninvasive tech-
nique for imaging atherosclerotic plaque in the aortic arch of stroke patients by
transcutaneous real time B-mode ultrasonography: an initial report. Stroke. 1998;
29:673-676.
21. Weinberger J, Marks SJ, Gaul JJ, et al. Atherosclerotic plaque at the carotid ar-
tery bifurcations: correlation of ultrasonographic imaging with morphology,
stroke: a transesophageal echocardiographic study in an ethnically mixed popu-
23. Di Tullio MR, Sacco RL, Homma S. Atherosclerotic disease of the aortic arch as
1461.
The “cobalaminergic” hypothesis extrapolates hematologic knowledge of B12 and folate metabolism to the nervous system, and predicts the characteristic neurotransmitter and structural changes of the disease.

Andrew McCaddon, MD, MRCPG
Rhoslanerchrugog
Gardden Road Surgery
Wrexham LL14 2 EN, Wales
Gareth Davies, MSc, MRSC
Peter Hudson, MSc, MBCS
Wrexham

The work referred to was supported by a grant from The Welsh Scheme for the Development of Health and Social Research under the aegis of the Wales Office of Research and Development.


Error in Author’s First Name and Affiliation. In the article titled “Plaque Morphology Correlates With Cerebrovascular Symptoms in Patients With Complex Aortic Arch Plaque” by Weinberger et al, which was published in the January issue of the ARCHIVES (2000;57:81-84), Dr Papamitsakis’ first name should have been Nikolaos in the byline, and the last sentence of the affiliation footnote should have been “Dr Papamitsakis is now with the Department of Neurology, Henry Ford Hospital, Detroit, Mich.”