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AJNR Am J Neuroradiol 1986, 7 (2) 311-315

<http://www.ajnr.org/content/7/2/311>

This information is current as
of May 14, 2024.

Sonographic Characterization of Carotid Plaque: Detection of Hemorrhage

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By careful evaluation of the sonographic characteristics of carotid plaques, two patterns can be identified: (1) a homogeneous pattern containing uniform echoes corresponding to dense fibrous tissue and (2) a heterogeneous pattern containing mixed echoes and anechoic areas that represent intraplaque hemorrhage pathologically. A prospective study was conducted of 50 patients to determine the accuracy of identifying these different forms of plaque. The patients' carotid arteries were examined by a high-resolution duplex scanner before carotid endarterectomy. The plaques were evaluated carefully by vascular surgeons and pathologists for the presence of intraplaque hemorrhage. In this study, the accuracy of identifying the presence or absence of intraplaque hemorrhage with sonography was 90% (48 of 54); sensitivity, 94% (17 of 18); and specificity, 88% (27 of 31). High-resolution sonography appears to be an accurate means of identifying intraplaque hemorrhage and may ultimately be useful in identifying patients at risk for embolic disease.

In the past, the radiologic evaluation of carotid arteries has primarily emphasized the identification of flow-limiting lesions with either arteriography, digital vascular imaging, or duplex sonographic scanning. Recently, however, attention has been directed toward identifying those other patients at risk for stroke who develop symptoms as the result of emboli.

Several vascular surgeons, including Imparato et al. [1, 2] and Lusby et al. [3], have reported finding a significant increased incidence of intraplaque hemorrhage in the surgical specimens of carotid artery plaque in their symptomatic patients as compared with those who were asymptomatic. It is believed that embolization may result when intraplaque hemorrhage leads to intimal tears in the vessel lining, initiation of the clotting cascade, and thrombus formation over the tear. Considering then that intraplaque hemorrhage may be the precursor to embolic phenomenon, it would be of great value to be able noninvasively to diagnose accurately the presence of intraplaque hemorrhage in carotid plaque. Reilly et al. [4] have shown that there are two patterns of plaque that can be sonographically separated, a homogeneous and a heterogeneous pattern. We undertook the present study to determine if we could systematically separate these two forms of plaque and accurately determine which of our patients' carotid arteries contained intraplaque hemorrhage.

Subjects and Methods

A prospective study was begun in April 1984 in which the carotid plaque of all patients who had duplex carotid evaluations was characterized into one of three categories: homogeneous, heterogeneous, or indeterminate. Homogeneous plaque was classified sonographically as a uniform echo pattern most commonly consisting of low-level echoes (fig. 1). The surface margin of the plaque was always smooth. In contrast, the echo pattern of heterogeneous plaque was complex in nature and most notably contained focal anechoic areas (figs. 2-4). The presence of calcifications was ignored and was not used in classifying the plaque

This article appears in the March/April 1986 issue of *AJNR* and the May 1986 issue of *AJR*.

Received May 16, 1985; accepted after revision September 3, 1985.

Presented at the annual meeting of the American Roentgen Ray Society, Boston, April 1985.

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AJNR 7:311-315, March/April 1986
 0195-6108/86/0702-0311

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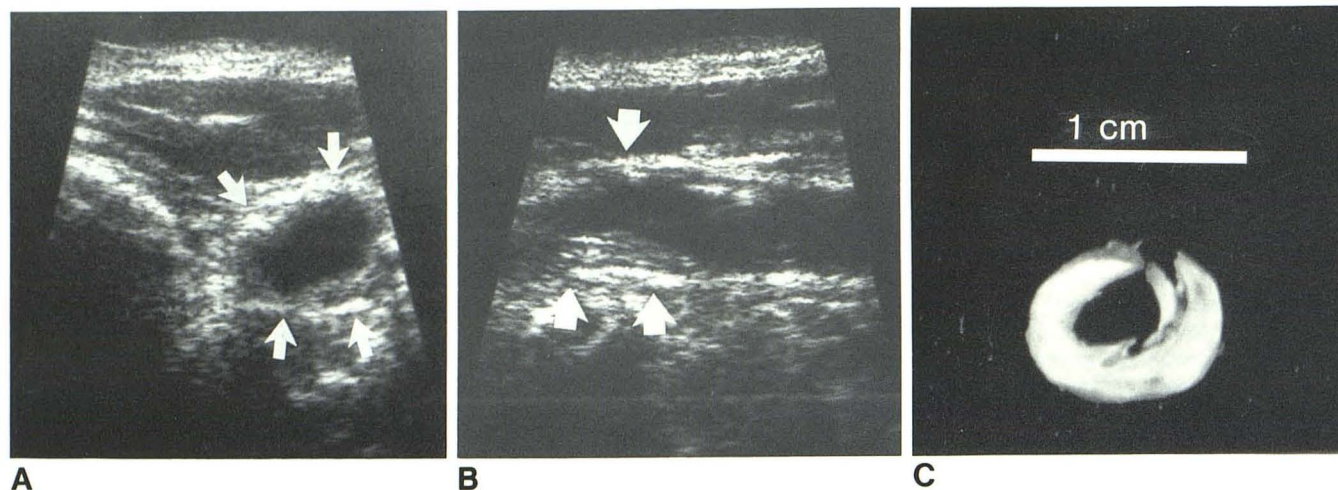


Fig. 1.—Homogeneous plaque. Transverse (A) and longitudinal (B) sonograms through internal carotid artery using 7.5 MHz transducer show typical homogeneous plaque. Outer vessel wall (arrows). Echoes are uniform, and

there is no evidence of anechoic areas. C, Corresponding transverse pathologic specimen. Dense laminated fibrous connective tissue with no evidence of hemorrhage.

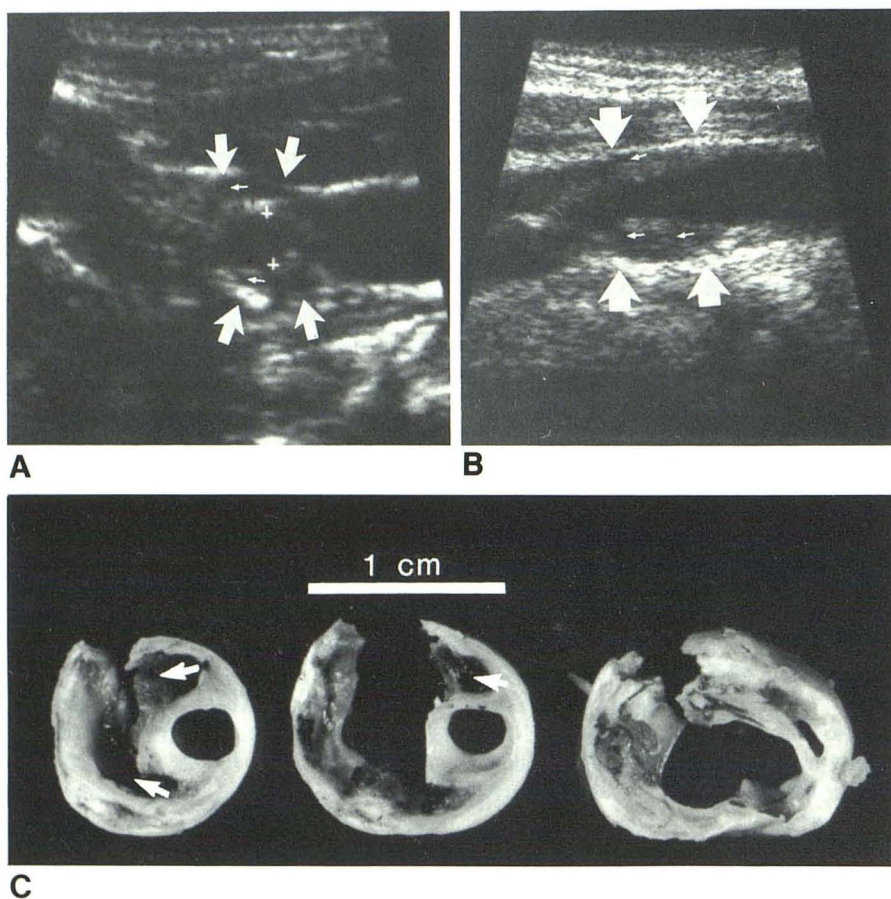


Fig. 2.—Heterogeneous plaque. Transverse (A) and longitudinal (B) 10 MHz high-resolution sonograms show heterogeneous plaque. Outer vessel wall (large arrows). Markers denote inner vessel wall. Anechoic areas are intermixed within echogenic plaque (small arrows). Presence of calcifications is ignored in this classification and does not place plaque in heterogeneous pattern. C, Corresponding pathologic specimens show subintimal hemorrhage (arrows).

(unless the calcifications obscured adequate evaluation). The indeterminate classification was used to describe plaque in those patients we could not satisfactorily evaluate. These studies were performed in the sonography section of the Department of Radiology using

either a 7.5 or 10 MHz transducer as part of a complete duplex carotid sonographic evaluation. To evaluate the plaque, patients were scanned in the transverse, longitudinal, and oblique planes. Those patients who after having sonographic evaluations went on to have

Fig. 3.—Minimal heterogeneous plaque. Transverse (A) and longitudinal (B) 7.5 MHz sonograms through internal carotid artery show minimal heterogeneous plaque (*small arrows*). On pathologic evaluation, plaque was found to represent slitlike foci of hemorrhage. Outer vessel wall (*large arrows*). Plaque has irregular margin.

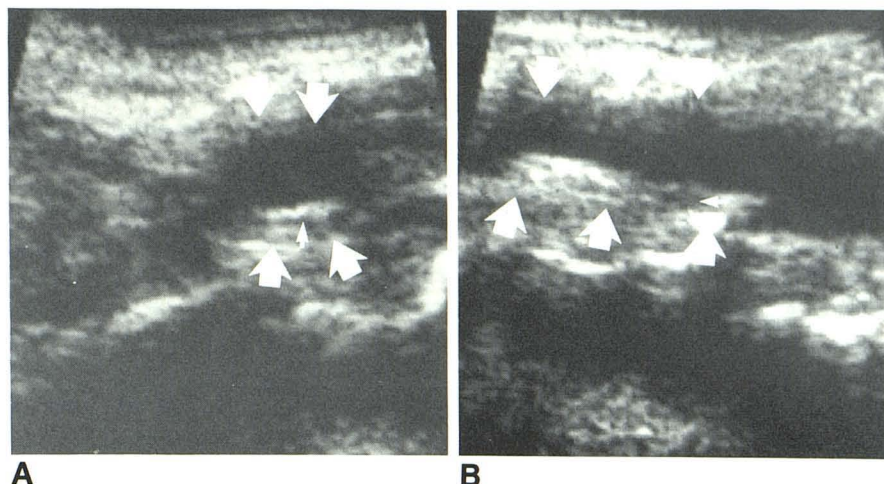
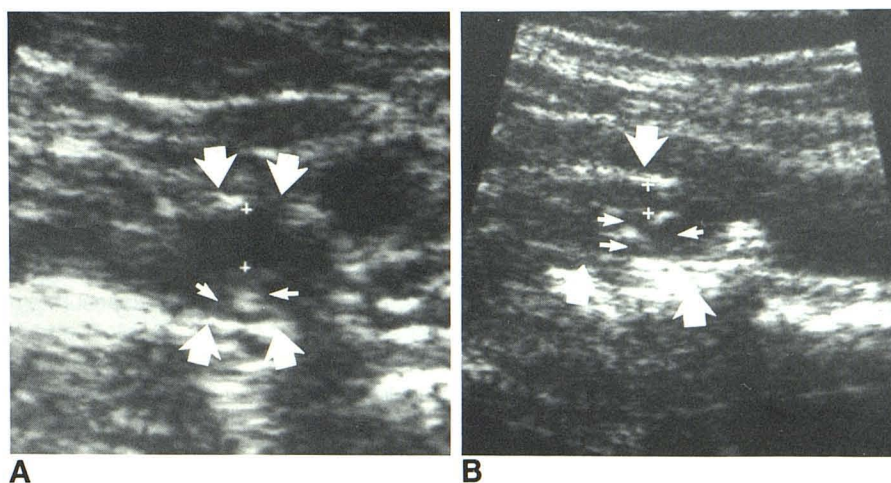


Fig. 4.—Large intraplaque hemorrhage. Transverse (A) and longitudinal (B) sonograms of internal carotid artery show large anechoic areas (*small arrows*) indicative of intraplaque hemorrhage. A 7.5 MHz transducer was used. Plaque has irregular surface. Outer vessel wall (*large arrows*).



a carotid endarterectomy were entered into our study. This report describes the first consecutive 50 patients who had surgery. En bloc endarterectomy was performed when possible. At the time of surgery, our vascular surgeons classified the lesions by gross morphology as to the presence or absence of intraplaque hemorrhage and ulceration. The surgical specimens were then carefully evaluated for gross and microscopic evidence of intraplaque hemorrhage. Soft cylinders of atheromatous plaques and calcified atheromatous plaques, after decalcification, were sectioned horizontally so that the degree of luminal compromise, the character of the intima, and the varying degrees of plaque thickening and distortion could be evaluated. The changes seen were generally combinations of laminated fibrous connective tissue, irregular pale masses of calcified material, and slitlike or massive intraplaque hemorrhages. The larger the hemorrhagic area, the greater appeared its likelihood of elevation and disruption of the intima. Intimal disruption was usually associated with clot formation, roughening, and luminal compromise. Microscopically, intimal thickening caused by fibrosis, histiocytic infiltration, calcification, and hemorrhage constituted the predominant changes. Calcified masses appeared as acellular, roughly circular masses of pale-staining debris. The surgeons and pathologists were unaware of the sonographic classification of the carotid plaque.

Results

The carotid plaques of 50 patients were prospectively evaluated by radiologists, surgeons, and pathologists. Four patients (8%) in our study group were classified as indeterminate because of either lack of patient cooperation (one patient) or the presence of significant calcifications (three patients) that obscured the carotid bifurcation. Seven patients had bilateral carotid endarterectomies. A total of 53 carotid plaques were evaluated and classified into the two categories: 32 plaques were classified as homogeneous and 21 plaques as heterogeneous (table 1). On evaluation by the pathologist, 18 of the plaques contained evidence of intraplaque hemorrhage and 35 plaques did not. Four patients (false positives) were identified as heterogeneous, but neither the pathologist nor the surgeon identified intraplaque hemorrhage. Three (75%) of these four patients had significant nodular calcification in the media. No other unusual unifying pathologic features were evident. No significant lipid deposits were identified. One carotid plaque classified as homogeneous did, on

TABLE 1: Sonographic Characteristics of Carotid Plaques

	No. of Cases	
	Homogeneous	Heterogeneous
Pathologic findings:		
Intraplaque hemorrhage	1	17
No intraplaque hemorrhage	31	4
Total	32	21
Symptoms:		
Transient ischemic attack	10	9
Asymptomatic bruit	11	6
Cardiovascular accident in past	2	1
Screening	3	0
Syncope, dizziness	3	1
Total	29	17
Ulcerations	0	7

evaluation by the pathologist, contain intraplaque hemorrhage (false negative), however, this hemorrhage was not seen grossly and was microscopic in nature. Hemorrhage within the plaque varied from microscopic, slitlike foci of fresh hemorrhage with no appreciable changes in the configuration of the plaque to massive, older hemorrhage with separation of the varying plaque components, elevation and disruption of the intima, and clot formation. Older hemorrhages could be identified easily because of disruption of the red blood cells and formation of cholesterol clefts. Varying degrees of peripheral organization by ingrowth of connective tissue elements assured that these hemorrhages were not perioperative. It must be admitted, however, that any hemorrhage, whether small or large, composed only of fresh red blood cells, with no evidence of organization, could have occurred perioperatively.

Chi-square analysis was used to compare the actual incidence of intraplaque hemorrhage found at surgery in patients classified as having homogeneous or heterogeneous plaques as assessed by sonography. The incidence of hemorrhage in patients with heterogeneous plaque of 17 (81%) of 21 patients was significantly greater than the one (3%) in 33 patients with homogeneous plaque (Chi-square, 1 df = 42.57; $p < 0.005$). The sensitivity of identifying intraplaque hemorrhage was 94% (17 of 18); specificity, 88% (27 of 31); and accuracy, 90% (48 of 53).

There was no difference in the two groups of plaque relative to age. The average age of patients with homogeneous plaque was 66.7 years (range, 46–84); with heterogeneous plaque, 69.4 years (range, 58–84). More men had homogeneous plaque than had heterogeneous plaque (19 and seven patients, respectively), but there was no significant difference in the type of plaque in female patients (10 each). However, it should be emphasized that our numbers in each group are small. In regard to symptoms (table 1), although 56% of the heterogeneous group presented with transient ischemic attacks (TIAs), in actual numbers more patients with homogeneous plaque presented with this complaint. Of interest, nearly twice as many patients with homogeneous plaque presented with asymptomatic bruits than did patients with heterogeneous plaque.

TABLE 2: Findings in Patients Who Had Both Sonography and Bilateral Endarterectomy

Sonographic Finding: Surgical-Pathologic Finding	No. of Cases
Both sides heterogeneous:	
Intraplaque hemorrhage on both sides	3
Intraplaque hemorrhage on one side only	1
Both sides homogeneous:	
No evidence of intraplaque hemorrhage on either side	2
One side heterogeneous, one side homogeneous:	
No evidence of intraplaque hemorrhage on either side	1
Total	7

Of the seven patients who had bilateral endarterectomies, six (86%) were found to have similar plaque on both sides: three patients had heterogeneous plaque on each side and three had bilateral homogeneous plaque (table 2).

Seven patients were found at surgery to have ulceration. All seven of these patients have been classified sonographically as having heterogeneous plaque (table 1). On evaluation by the pathologist, all seven had evidence of intraplaque hemorrhage. No distinct sonographic characteristics were found in this group that could distinguish this subset of patients from other patients with heterogeneous plaque and no ulceration.

Discussion

Duplex sonography of the carotid arteries has been found to be an accurate means of evaluating the carotid bifurcations [5, 6]. Most attention has previously been directed at identifying flow-limiting stenoses. Recently, however, considerable study has been directed at evaluating other causes of stroke, such as embolic disease. Imparato et al. [2] have shown in a prospective study of the gross morphology of 376 carotid plaques that "hemorrhage is the only gross characteristic that can be identified as significantly more frequent in all symptomatic as compared to all asymptomatic plaques." Intraplaque hemorrhage is implicated as playing a major role in the production of an embolic phenomenon. The atheromatous plaque may be the site of thrombus formation with subsequent embolization of a part of the thrombus through mechanical disruption. Bleeding into an atheromatous plaque can result in disruption of the smooth intimal surface with the initiation of the clotting cascade. The resulting thrombus material can either be lost as an embolus or organized into the wall of the artery, further compromising the lumen and probably setting the stage for subsequent plaque hemorrhage. Reilly et al. [4] found that sonography could be used as a means of detecting intraplaque hemorrhage in carotid vessels with an accuracy of 82%, sensitivity of 91%, and specificity of 65%. In their patients, symptoms also appeared to be related to the identification of heterogeneous plaque.

In our study, we have been able to identify the presence or absence of intraplaque hemorrhage with a 90% accuracy, 94% sensitivity, and 88% specificity. Our favorable results as compared with Reilly et al. may relate to greater physician involvement in the sonographic characterization of the plaque or, more likely, improvements in instrumentation. On many

occasions, it was difficult to characterize the plaque merely by looking at the hard copy. A definitive evaluation was made after directly scanning the patient.

It is interesting to note that in our study the heterogeneous group had only a slightly greater incidence of symptoms (65%) than did the homogeneous group (52%). In fact, there was nearly an equal number of patients with TIAs in both groups. This may be related to the fact that in our study only 40% of the patients had heterogeneous plaque, in comparison with Reilly et al. in which 72% of the plaque was classified as heterogeneous. More important, this is probably related to the fact that all of the patients in our study were sent to surgery because of flow-restricting lesions, as assessed by sonography and confirmed by either digital vascular imaging or arteriography. To really determine if patients with heterogeneous plaque or intraplaque hemorrhage had a greater risk for emboli resulting in symptoms, a study must be conducted on patients with heterogeneous plaque who did not have hemodynamically significant lesions. We are currently involved in such a prospective study. It is interesting to note that nearly twice the number of patients with asymptomatic bruits had homogeneous plaque as compared with the heterogeneous form.

All our cases of ulcerated plaque were found to occur in those with a heterogeneous pattern, although no specific findings could distinguish these groups. Another interesting observation was that in our small group of patients who had bilateral endarterectomies, 86% had the same type of plaque on both sides. This would suggest that very careful evaluation should be made of those carotid plaques with dissimilar patterns.

In summary, it appears that at the present time we can begin to sonographically characterize carotid plaque with a high degree of accuracy. We can separate a homogeneous pattern corresponding to dense fibrous connective tissue from a heterogeneous pattern associated with the pathologic presence of intraplaque hemorrhage. Since it appears that the presence of intraplaque hemorrhage has an etiologic role in the production of an embolic phenomenon, high-resolution sonography may in time play a major role in the identification of patients with increased risk of developing embolic disease.

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