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Atherosclerotic Disease of the Aortic Arch and the Risk of Ischemic Stroke

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ABSTRACT

Background Atherosclerotic disease of the aortic arch has been suspected to be a potential source of cerebral emboli. We conducted a study to quantify the risk of ischemic stroke associated with atherosclerotic disease of the aortic arch.

Methods Using transesophageal echocardiography, we performed a prospective case-control study of the frequency and thickness of atherosclerotic plaques in the ascending aorta and proximal arch in 250 consecutive patients admitted to the hospital with ischemic stroke and 250 consecutive controls, all over the age of 60 years.

Results Atherosclerotic plaques ≥ 4 mm in thickness were found in 14.4 percent of the patients but in only 2 percent of the controls. After adjustment for atherosclerotic risk factors, the odds ratio for ischemic stroke among patients with such plaques was 9.1 (95 percent confidence interval, 3.3 to 25.2; P<0.001). Among the 78 patients who had brain infarcts with no obvious cause, 28.2 percent had plaques ≥ 4 mm in thickness, as compared with 8.1 percent of the 172 patients who had infarcts whose possible or likely causes were known (odds ratio, 4.7; 95 percent confidence interval, 2.2 to 10.1; P<0.001). Plaques of ≥ 4 mm in the aortic arch were not associated with the presence of atrial fibrillation or stenosis of the extracranial internal carotid artery. In contrast, plaques that were 1 to 3.9 mm thick were frequently associated with carotid stenosis of ≥ 70 percent.

Conclusions These results indicate a strong, independent association between atherosclerotic disease of the aortic arch and the risk of ischemic stroke. The association was particularly strong with thick plaques. Atherosclerotic disease of the aortic arch should be regarded as a risk factor for ischemic stroke and as a possible source of cerebral emboli.

Until recently, atherosclerotic disease of the aortic arch was not regarded as a source of cerebral emboli[1]. We have reported on the basis of autopsy studies that the presence of ulcerated plaques in the aorta is an independent risk factor for ischemic stroke, particularly in patients with strokes of unknown cause, and that ulcerated plaques are predominantly found in patients who are 60 years of age or older[2]. The advent of transesophageal echocardiography has made it possible to detect protruding atherosclerotic plaques in the aortic arch and descending aorta[3,4]. Although a causal link

between pedunculated and highly mobile plaques and cerebral emboli seems likely,[5] only retrospective studies of this association have been reported[6,7]. One of these studies found a threefold increase in the risk of embolic disease in patients with protruding plaques[7]. However, since these series included selected patients referred for echocardiography to detect the sources of the emboli, they may have been biased. In particular, atherosclerotic disease of the thoracic aorta may simply be a marker for general atherosclerotic disease[8] and for the actual cause of the stroke[9]. The aims of our study were to determine with transesophageal echocardiography the frequency of plaques in the aortic arch in consecutively admitted patients with brain infarcts, as compared with the frequency in controls, and to evaluate the clinical importance of these plaques as possible sources of cerebral emboli.

Methods

This was a prospective case-control study of consecutively admitted patients with ischemic stroke and consecutively admitted controls.

Patients and Controls

All patients over the age of 60 years with brain infarcts who were hospitalized between September 1991 and October 1993 were enrolled in the study. The following risk factors were noted: hypertension, hypercholesterolemia, cigarette smoking, diabetes mellitus, a high body-mass index, a previous myocardial infarction, peripheral vascular disease, and known atrial fibrillation or atrial fibrillation recorded within eight days after the detection of the brain infarct. The patients underwent a diagnostic workup that included cranial computed tomographic (CT) imaging or magnetic resonance imaging (MRI) of the brain (or both), ultrasound examination of the internal carotid and vertebral arteries (according to a standard protocol), transcranial Doppler examination, 12-lead electrocardiographic studies, and transesophageal echocardiographic studies, including an assessment of the thoracic aorta within 15 days after the onset of the stroke.

After these studies had been performed, the patients were divided into four groups according to the presence of other potentially causal lesions. These assignments were made without knowledge of the transesophageal echocardiographic assessment of the aorta. The first group included patients with brain infarcts likely to have been caused by $\geq$ 70 percent stenosis of the ipsilateral internal carotid artery or a definite cardiac source of embolism (acute anterior myocardial infarction, atrial fibrillation with left atrial thrombus or spontaneous echo contrast, mural thrombus in left-heart cavities, mitral stenosis, a prosthetic heart valve, or endocarditis). The second group included patients with infarcts that may have been caused by 31 to 69 percent stenosis of the ipsilateral carotid artery, isolated atrial fibrillation, or atrial fibrillation occurring after the brain infarction. Patients in the third group were presumed to have lacunar infarcts due to lipohyalinosis of small deep intracranial arteries, with one of the four major lacunar syndromes (pure motor hemiplegia, pure sensory loss, hemiparesis and ataxia, or sensori-motor impairment) and with infarcts that were small (<15 mm) and deep or not demonstrable with two CT or MRI scans, in the absence of a cardiac or carotid source of embolism. Patients in the fourth group had no detectable lesions or they had lesions that have not been shown to increase the risk of brain infarction in subjects over the age of 60 years, such as ipsilateral carotid stenosis of $\leq$ 30 percent, patent foramen ovale, atrial septal aneurysm, or mitral-valve prolapse.

A total of 263 patients were enrolled in the study. Patients with impaired consciousness for more than 15 days were excluded, as well as patients with respiratory failure and those in whom introduction of the echocardiographic probe was technically impossible. After these exclusions, there were 250 patients in the study group.

The control group consisted of 250 consecutively enrolled patients over 60 years of age with no history of ischemic stroke who underwent transesophageal echocardiography for assessment of cardiac conditions such as mitral or aortic valvulopathy, possible impairment of a prosthetic valve, myocardial infarction, atrial fibrillation, or suspected endocarditis. Patients with aortic diseases, such as dissection or a saccular aneurysm, were excluded. Risk factors were noted at the time of examination.

Transesophageal Echocardiographic Assessment of the Aorta

Patients and controls underwent transesophageal echocardiography performed by trained cardiologists who were given information about the cause of brain infarction. The examinations were recorded on videotape. Transesophageal echocardiography was performed within two weeks after the onset of the stroke, according to standard techniques[8]. We used commercially available imaging systems with a 5-MHz single-plane probe (in the first 346 patients), biplane probe (in the next 97 patients), or multiplane probe (in the last 57 patients). After examination of the cardiac structures, the transducer was gradually withdrawn to a point above the level of the aortic valve to obtain serial short-axis views of the ascending aorta (with a single-plane probe). With a counterclockwise rotation of the entire probe in the transverse plane, a short-axis image of the descending aorta was then obtained (40 to 45 cm from the incisors). The probe was progressively pulled back to the curve of the distal arch (18 to 20 cm from the incisors). This portion was important to visualize in order to differentiate the distal and proximal segments of the aortic arch. The probe was then rotated clockwise to study the proximal arch and, in some patients, the distal part of the ascending aorta.

Videotapes of the transesophageal examinations of all 500 subjects were reviewed by one of us (a senior echocardiographer) randomly and without knowledge of the status of the patient (case or control) or the classification of the cause of the stroke. In addition, the videotaped examinations of 100 randomly selected patients and controls were reviewed by two of us (also senior echocardiographers) according to the same protocol.

We measured the thickness of the intimal and medial layers of the far wall during systole on a freeze frame, as previously described[10,11,12]. Wall thickness was measured in the descending aorta, distal arch, proximal arch, and ascending aorta, with the largest measured at all levels (Figure 1 and Figure 2). Since the ascending part of the aorta and the proximal arch are both more likely to be sources of cerebral emboli than the other regions, we decided to pool the studies of lesions located in these two parts of the thoracic aorta.

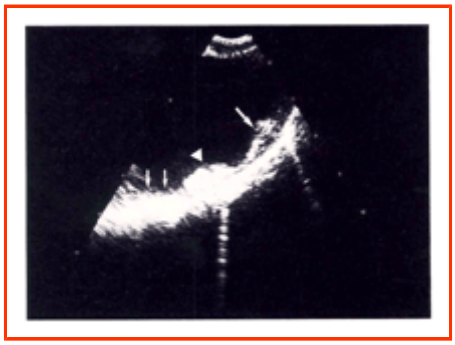

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Figure 1. Transesophageal Echocardiogram of the Aortic Arch Obtained with a Single-Plane Probe (Transverse View).

The plaque thickness, measured perpendicularly to the far wall, is calculated as the distance between the medial-adventitial border and the internal side of the lesion. The thickest portion is 5.9 mm (large arrow) and is located in the distal part of the aortic arch. The second lesion (arrowhead), which is more echogenic, is located in the proximal arch and is 4.5 mm thick. The two small arrows indicate an extensive plaque in the proximal arch and the upper part of the ascending aorta.

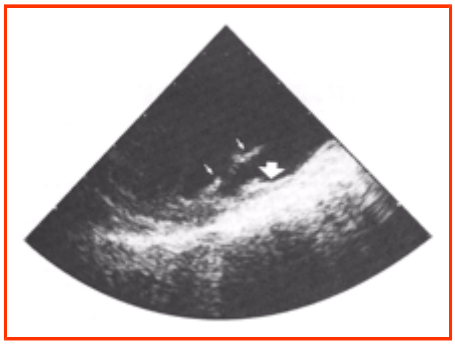

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Figure 2. Transesophageal Echocardiogram of the Aortic Arch Obtained with a Biplane Probe (Transverse View).

A highly mobile component suggesting a thrombus (small arrows) is superimposed on a complex and extensive atherosclerotic plaque (large arrow). This free-floating thrombus is localized in the proximal arch.

Statistical Analysis

We used two-tailed t-tests for comparisons of means and chi-square tests for comparisons of proportions. First, we performed a classic case-control analysis. We compared the patients with brain infarcts (case patients) and the controls with respect to various vascular risk factors and the presence of aortic plaques in the ascending aorta and proximal arch. Then we compared the frequency of high-grade plaques (those most likely to cause infarction) with the frequency of atrial fibrillation and carotid stenosis in the case patients. Finally, we compared the frequency of plaques in the patients who had ischemic strokes with known causes with the frequency in the patients who had infarcts with undetermined causes. Odds ratios were calculated by stepwise unconditional multiple logistic regression, with adjustments for age, sex, hypertension, cigarette smoking, cholesterol levels, diabetes, previous myocardial infarction, and atrial fibrillation. We used the kappa test to determine the degree of interobserver agreement on the assessment of plaques in the thoracic aorta. The data were analyzed with SAS software[13].

Results

The case patients were older and had higher frequencies of hypertension, hypercholesterolemia, cigarette smoking, and diabetes than the controls (Table 1). The frequencies of atrial fibrillation and peripheral vascular disease did not differ significantly between the two groups. The frequency of diseases of the coronary arteries or valves was higher in the control group than in the infarct group. Table 2 shows the frequency of plaques in the ascending aorta and proximal arch in patients and controls, according to the thickness of the plaque. We calculated the risk of cerebral infarction for each category of plaque thickness relative to the risk with a reference thickness of <1 mm, which was assigned an odds ratio of 1 (Table 2). Since a univariate analysis showed an abrupt increase in the odds ratio for stroke when plaques were 4 mm or thicker (crude odds ratio, ≤ 4.2 for plaques <4 mm and 13.8 for those ≥ 4 mm), we performed an additional analysis with this cutoff point.

View this table: [in this window] [in a new window] **Table 1.** Base-Line Characteristics of Case Patients and Controls.

View this table: [in this window] [in a new window] **Table 2.** Risk of Cerebral Infarction According to the Thickness of Atherosclerotic Plaques in the Ascending Aorta or Proximal Arch.

Plaques with a Thickness of 1 to 3.9 mm

Patients with aortic plaques that were 1 to 3.9 mm thick differed from those with plaques under 1 mm thick only with respect to the frequency of hypercholesterolemia, which was higher in those with thicker plaques. We found plaques 1 to 3.9 mm thick in the ascending aorta or proximal arch in 46 percent of the patients with brain infarcts and in 22 percent of the controls. The crude odds ratio was 3.9 (Table 3), and the adjusted odds ratio was 4.4 (P<0.001).

View this table: [in this window] [in a new window] **Table 3.** Risk of Cerebral Infarction According to the Thickness of Plaques in the Thoracic Aorta.

Among the case patients, plaques that were 1 to 3.9 mm thick were associated with the presence of carotid stenosis (Table 4). Such plaques were detected in 40 percent of the patients with no carotid stenosis, in 49 percent of those with <70 percent carotid stenosis, and in 61 percent of those with ≥ 70 percent carotid stenosis (P = 0.03).

View this table: [in this window] [in a new window] **Table 4.** Relation between Thickness of Plaques in the Ascending Aorta or Proximal Arch and the Extent of Carotid Stenosis in the 250 Patients with Brain Infarcts.

Plaques with a Thickness of 4 mm or More

Plaques ≥ 4 mm thick were found in the proximal part of the aorta in 41 subjects: in the ascending aorta in 2, in the proximal arch in 38, and in both in 1. As compared with the patients whose plaques were less thick, these patients had a higher frequency of hypercholesterolemia and cigarette smoking and a lower frequency of atrial fibrillation. The mean thickness of protruding lesions was 5.8 mm, with a range of 4 to 13.2 mm. Plaques ≥ 4 mm in thickness were found in the distal arch in 64 patients and in the descending aorta in 113. The kappa index for interobserver agreement on the presence of plaques ≥ 4 mm thick ranged from 0.85 for those in the distal arch to 0.95 for those in the ascending aorta and proximal arch.

We found plaques of ≥ 4 mm in the ascending aorta or proximal arch in 14.4 percent of the patients with brain infarcts and in 2 percent of the controls (P<0.001) (Table 2). After adjustment for atherosclerotic risk factors, the odds ratio for stroke was 9.1 (Table 2). Plaques of ≥ 4 mm were found in the distal arch or the descending aorta more frequently in patients than in controls, but for plaques in the descending aorta, the difference was not statistically significant (Table 3).

Among the case patients, plaques of ≥ 4 mm in the ascending aorta or proximal arch were detected equally frequently in patients with ≥ 70 percent stenosis of the internal carotid artery (15 percent of 33 patients) and in patients with <70 percent carotid stenosis (15 percent of 93 patients) or no stenosis (14 percent of 124 patients; P = 0.9) (Table 4). Aortic plaques were detected less frequently in the patients with atrial fibrillation (7.9 percent of 76 patients) than in those without atrial fibrillation (17.3 percent of 174 patients).

Among the case patients, plaques of ≥ 4 mm in the ascending aorta or proximal arch were found in 5.5 percent of the patients with another likely cause of ischemic stroke, in 9 percent of those with lacunar infarcts, in 11.5 percent of those with another possible cause of stroke, and in 28 percent of those with no other detectable lesions (P<0.001) (Table 5). After adjustment for the covariates, the risk associated with a plaque of ≥ 4 mm was 4.7 (95 percent confidence interval, 2.2 to 10.1) for patients who had no other detectable lesions as possible causes of stroke, as compared with those who had other likely or possible causes or lacunar infarcts.

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Table 5. Frequency of Plaques of greater than or equal to 4 mm in the Ascending Aorta or Proximal Arch in the 250 Patients with Ischemic Stroke, According to the Cause of the Stroke.

Among the patients with ischemic strokes and plaques of ≥ 4 mm in the ascending aorta or proximal arch, the brain infarcts involved the right hemisphere (in 15 patients) almost as frequently as the left (in 14); in 7 patients the infarcts were in the posterior circulation. Infarcts were more frequently cortical (in 25 patients) than deep (in 11). A mobile component was present in the aortic plaques in 6 of the 78 patients with no detectable lesions and in 1 (presumably with a lacunar infarct) of the other 172 patients (P<0.001).

Discussion

Atherosclerotic disease of the aortic arch has been considered as a possible but rare cause of embolic events in patients undergoing cardiac surgery, catheterization procedures, or anticoagulant therapy[1,14,15,16,17,18,19,20,21,22,23,24,25,26,27,28,29,30,31,32,33,34]. In a previous autopsy study, we found that ulcerated plaques in the aortic arch may have played a part in causing brain infarction, especially in patients with cerebral infarction of no known cause[2]. The presence of superimposed thrombi could not be assessed in the autopsy study[2]. It was important to confirm these results in live patients, and several studies have shown that transesophageal echocardiography is a reliable method of visualizing the aortic arch, protruding plaques, and thrombi[3,5,35,36].

Our results indicate that the presence of atherosclerotic plaques in the ascending aorta or proximal arch as detected by transesophageal echocardiography is a risk factor for ischemic stroke. The risk appeared to be particularly high for patients with plaques ≥ 4 mm in thickness and for the subgroup of patients who had no other detectable cause of ischemic stroke. However, several methodologic issues should be considered. Since the controls were not referred for assessment of embolic disease, they may have had a lower frequency of plaques in the arch, thus leading to an overestimation of the risk among the case patients. However, the case and control groups were remarkably similar with

respect to the presence of peripheral vascular disease and atrial fibrillation, and the control group had a much higher frequency of coronary artery disease. Since there is a strong link between atherosclerotic disease of the thoracic aorta and diseases of both the coronary and peripheral arteries,[8,37] the high frequency of coronary artery disease in our control group may have accounted for the frequency of atherosclerotic plaques in the arch in this group.

Because of the interposition of the left bronchus, there is a blind region at the upper part of the ascending aorta, regardless of the type of echocardiographic probe used. We may have missed some lesions in this region, but since both patients and controls underwent the same type of examination, it is likely that the underestimation was similar in the two groups. For lesions located in the proximal as well as the distal part of the arch, there was a very high degree of agreement in the detection of plaques ≥4 mm thick (kappa index, 0.95). This distinction between the distal and proximal locations is important, because lesions were located more frequently in the distal part of the arch (distal to the ostium of the left subclavian artery) than in the proximal part of the arch, and the lesions in the distal part of the arch were less likely to give rise to cerebral emboli.

Although we found that plaques in the ascending aorta and proximal arch were associated with an increased risk of stroke, this finding does not establish a causal link. Indeed, plaques that were 1 to 3.9 mm thick were frequently associated with carotid stenosis, which may have been the actual source of the brain emboli. However, with plaques of ≥4 mm, a causal link is quite likely for several reasons. First, one of the striking findings of the present study is that the risk of stroke increased sharply from less than 5 to more than 13 when the thickness of the plaques was ≥4 mm (Table 2). This large increase in risk was observed only for lesions of ≥4 mm in the ascending aorta or proximal arch, not for those in the distal arch or descending aorta. Second, the high increase in the risk of ischemic stroke associated with plaques of ≥4 mm in the proximal arch was independent of the presence of the two major risk factors for stroke in the elderly: carotid stenosis and atrial fibrillation. We found that the frequency of plaques of ≥4 mm in the proximal arch did not differ according to the degree of carotid stenosis and that the frequency of such plaques was lower in patients with atrial fibrillation than in those without fibrillation. Third, plaques of ≥4 mm in the proximal arch were also associated with an abrupt increase in the risk of stroke among patients who had ischemic strokes with no other apparent cause. Furthermore, the presence of a mobile component of the plaque was associated with a risk ratio of 14 among patients with ischemic strokes of unknown cause. This clear-cut difference in the risk of stroke between patients with plaques <4 mm thick and those with plaques ≥4 mm thick may be related to the composition of the larger lesions in the aortic arch. Lesions ≥4 mm thick may contain thrombotic material superimposed on the plaques, as shown during surgery[38]. The presence of a thrombus may also explain the more frequent mobile component.

The substantial increase in the risk of ischemic stroke in association with plaques ≥4 mm in thickness in the aortic arch suggests that such lesions should be investigated as a risk factor for ischemic stroke, particularly in the case of a stroke with no other likely or possible cause. Appropriate treatment of these lesions remains uncertain. Thrombolysis and surgical removal have occasionally been reported to be successful in patients with pedunculated and mobile thrombi in the aortic arch[38,39]. However, prospective studies are needed to determine the natural history of these plaques and to evaluate the efficacy of various treatment regimens.

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Source Information

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References

1. Caplan LR. Brain embolism, revisited. Neurology 1993;43:1281-1287.[Abstract]
2. Amarenco P, Duyckaerts C, Tzourio C, Henin D, Bousser M-G, Hauw J-J. The prevalence of ulcerated plaques in the aortic arch in patients with stroke. N Engl J Med 1992;326:221-225.[Abstract]
3. Tunick PA, Kronzon I. Protruding atherosclerotic plaque in the aortic arch of patients with systemic embolization: a new finding seen by transesophageal echocardiography. Am Heart J 1990;120:658-660. [Medline]
4. Amarenco P, Cohen A, Baudrimont M, Bousser M-G. Transesophageal echocardiographic detection of aortic arch disease in patients with cerebral infarction. Stroke 1992;23:1005-1009.[Abstract]
5. Tunick PA, Lackner H, Katz ES, Culliford AT, Giangola G, Kronzon I. Multiple emboli from a large aortic arch thrombus in a patient with thrombotic diathesis. Am Heart J 1992;124:239-241.[Medline]
6. Karalis DG, Chandrasekaran K, Victor MF, Ross JJ Jr, Mintz GS. Recognition and embolic potential of intraaortic atherosclerotic debris. J Am Coll Cardiol 1991;17:73-78.[Medline]
7. Tunick PA, Perez JL, Kronzon I. Protruding atheromas in the thoracic aorta and systemic embolization. Ann Intern Med 1991;115:423-427.[Medline]
8. Fazio GP, Redberg RF, Winslow T, Schiller NB. Transesophageal echocardiographically detected atherosclerotic aortic plaque is a marker for coronary artery disease. J Am Coll Cardiol 1993;21:144-150. [Medline]
9. Chesebro JH, Fuster V, Halperin JL. Atrial fibrillation -- risk marker for stroke. N Engl J Med 1990;323:1556-1558.[Medline]
10. Touboul P-J, Prati P, Scarabin P-Y, Adrai V, Thibout E, Ducimetiere P. Use of monitoring software to improve the measurement of carotid wall thickness by B-mode imaging. J Hypertens 1992;10:Suppl 5:S37-S41.
11. Pignoli P, Tremoli E, Poli A, Oreste P, Paoletti R. Intimal plus medial thickness of the arterial wall: a direct measurement with ultrasound imaging. Circulation 1986;74:1399-1406.[Abstract]
12. Mohr-Kahaly S, Erbel R, Scharf N, Meyer J. Age related normal values for the descending thoracic aorta analyzed by biplane TEE echocardiography. Eur Heart J 1992;13:Abstract Suppl:17-17.abstract
13. SAS user's guide: version 6 ed. Vol. 1. Cary, N.C.: SAS Institute, 1990.
14. Russell RWR. Less common varieties of cerebral arterial disease: cerebral atheroembolism. In: Russell RWR, ed. Vascular disease of the central nervous system. 2nd ed. Edinburgh, Scotland: Churchill Livingstone, 1983:394-5.
15. Winter WJ Jr. Atheromatous emboli; a cause of cerebral infarction: report of two cases. Arch Pathol 1957;64:137-142.
16. Gore I, Collins DP. Spontaneous atheromatous embolization: review of the literature and a report of 16 additional cases. Am J Clin Pathol 1960;33:416-426.
17. Sturgill BC, Netsky MG. Cerebral infarction by atheromatous emboli: report of case and review of literature. Arch Pathol 1963;76:189-196.
18. Soloway HB, Aronson SM. Atheromatous emboli to central nervous system: report of 16 cases. Arch Neurol 1964;11:657-667.
19. Pfaffenbach DD, Hollenhorst RW. Morbidity and survivorship of patients with embolic cholesterol crystals in the ocular fundus. Am J Ophthalmol 1973;75:66-72.[Medline]
20. Hollenhorst RW. Vascular status of patients who have cholesterol emboli in the retina. Am J Ophthalmol 1966;61:1159-1165.[Medline]
21. Case Records of the Massachusetts General Hospital (Case 25-1967). N Engl J Med 1967;276:1368-1377. [Medline]
22. Case Records of the Massachusetts General Hospital (Case 21-1972). N Engl J Med 1972;286:1146-1153. [Medline]
23. Beal MF, Williams RS, Richardson EP Jr, Fisher CM. Cholesterol embolism as a cause of transient ischemic attacks and cerebral infarction. Neurology 1981;31:860-865.[Abstract]
24. Price DL, Harris J. Cholesterol emboli in cerebral arteries as a complication of retrograde aortic perfusion during cardiac surgery. Neurology 1970;20:1209-1214.[Medline]
25. McKibbin DW, Gott VL, Hutchins GM. Fatal cerebral atheromatous embolization after cardiopulmonary bypass. J Thorac Cardiovasc Surg 1976;71:741-745.[Abstract]
26. Gardner TJ, Horneffer PJ, Manolio TA, et al. Stroke following coronary artery bypass grafting: a ten-year study. Ann Thorac Surg 1985;40:574-581.[Abstract]
27. Katz ES, Tunick PA, Rusinek H, Ribakove G, Spencer FC, Kronzon I. Protruding aortic atheromas predict stroke in elderly patients undergoing cardiopulmonary bypass: experience with intraoperative transesophageal echocardiography. J Am Coll Cardiol 1992;20:70-77.[Medline]
28. Cogan DG, Kuwabara T, Moser H. Fat emboli in the retina following angiography. Arch Ophthalmol 1964;71:308-313.
29. David NJ, Klintworth GK, Friedberg SJ, Dillon M. Fatal atheromatous cerebral embolism associated with bright plaques in the retinal arterioles: report of a case. Neurology 1963;13:708-713.
30. Ramirez G, O'Neill WM Jr, Lambert R, Bloomer HA. Cholesterol embolization: a complication of angiography. Arch Intern Med 1978;138:1430-1432.[Abstract]
31. Feder W, Auerbach R. "Purple toes": an uncommon sequela of oral coumarin drug therapy. Ann Intern Med

1961;55:911-917.
32. Oster P, Rieben FW, Waldherr R, Schettler G. Blood clotting and cholesterol crystal embolization. JAMA 1979;242:2070-2071.[CrossRef][Medline]
33. Moldveen-Geronimus M, Merriam JC Jr. Cholesterol embolization: from pathological curiosity to clinical entity. Circulation 1967;35:946-953.[Medline]
34. Bruns FJ, Segel DP, Adler S. Control of cholesterol embolization by discontinuation of anticoagulant therapy. Am J Med Sci 1978;275:105-108.[Medline]
35. Horowitz DR, Tuhrim S, Budd J, Goldman ME. Aortic plaque in patients with brain ischemia: diagnosis by transesophageal echocardiography. Neurology 1992;42:1602-1604.[Abstract]
36. Toyoda K, Yasaka M, Nagata S, Yamaguchi T. Aortogenic embolic stroke: a transesophageal echocardiographic approach. Stroke 1992;23:1056-1061.[Abstract]
37. Nihoyannopoulos P, Joshi J, Athanasopoulos G, Oakley CM. Detection of atherosclerotic lesions in the aorta by transesophageal echocardiography. Am J Cardiol 1993;71:1208-1212.[Medline]
38. Culliford AT, Tunick PA, Katz ES, et al. Initial experience with removal of protruding atheroma from the aortic arch: diagnosis by transesophageal echo, operative technique, and follow-up. J Am Coll Cardiol 1993;21:Suppl A:342A-342A.abstract
39. Hausmann D, Gulba D, Bargheer K, Niedermeyer J, Comess KA, Daniel WG. Successful thrombolysis of an aortic-arch thrombus in a patient after mesenteric embolism. N Engl J Med 1992;327:500-501.[Medline]

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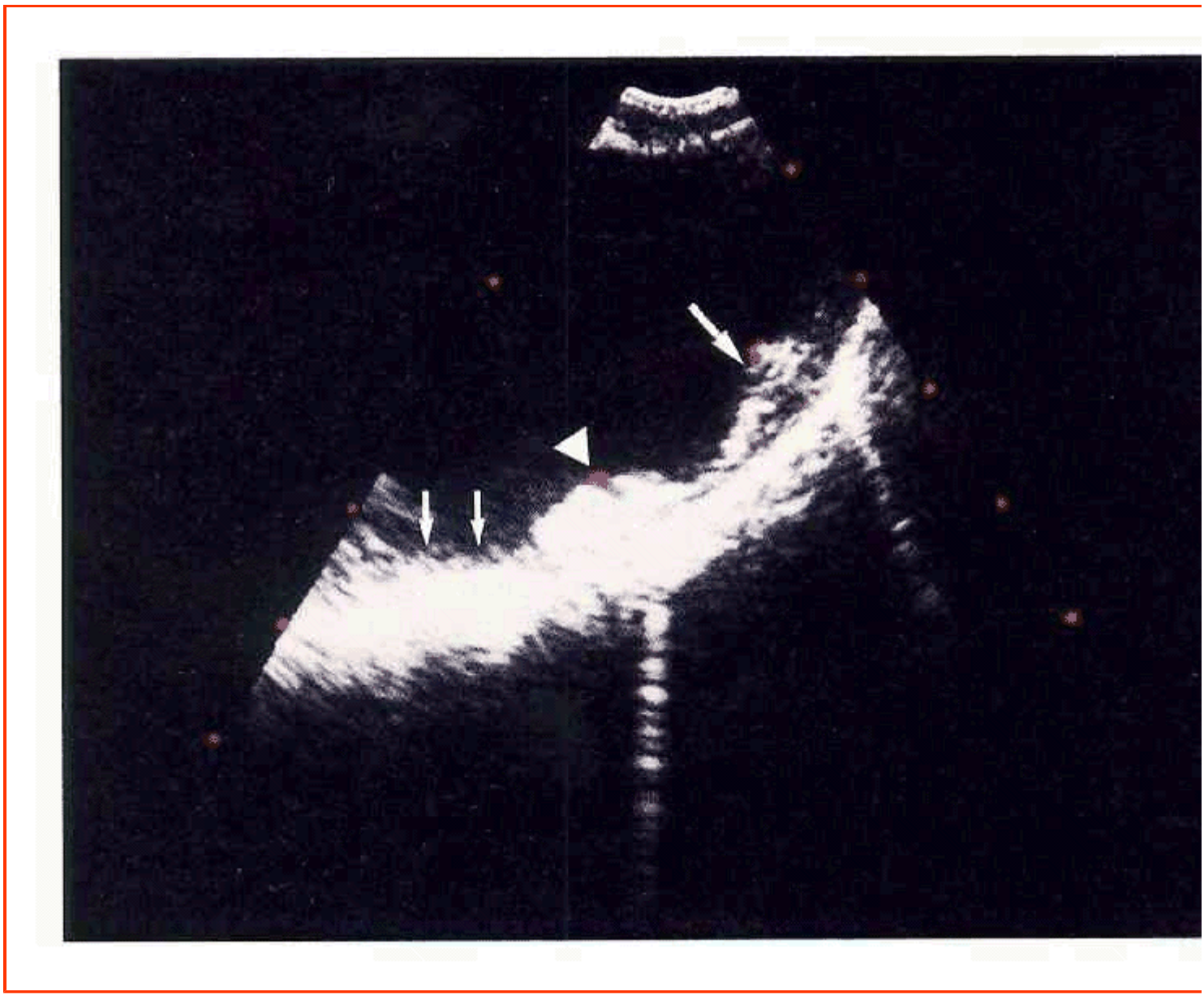

Figure 1. Transesophageal Echocardiogram of the Aortic Arch Obtained with a Single-Plane Probe (Transverse View).

The plaque thickness, measured perpendicularly to the far wall, is calculated as the distance between the medial-adventitial border and the internal side of the lesion. The thickest portion is 5.9 mm (large arrow) and is located in the distal part of the aortic arch. The second lesion (arrowhead), which is more echogenic, is located in the proximal arch and is 4.5 mm thick. The two small arrows indicate an extensive plaque in the proximal arch and the upper part of the ascending aorta.

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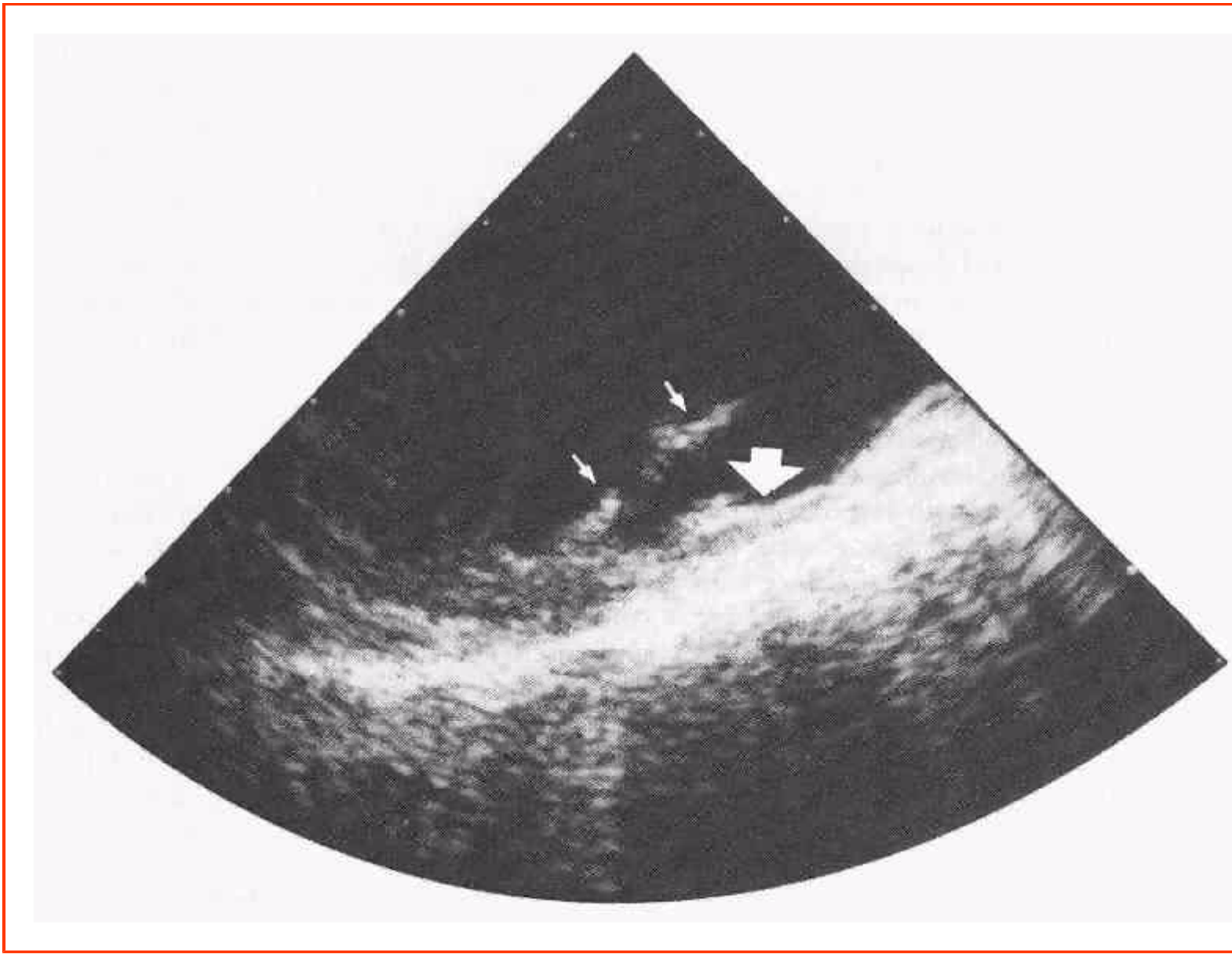

Figure 2. Transesophageal Echocardiogram of the Aortic Arch Obtained with a Biplane Probe (Transverse View).

A highly mobile component suggesting a thrombus (small arrows) is superimposed on a complex and extensive atherosclerotic plaque (large arrow). This free-floating thrombus is localized in the proximal arch.

Characteristic	Case Patients (N = 250)	Controls (N = 250)	P Value
Age (yr)	76.4±7.9	72.5±7.9	0.001
Female sex	54.8 (137/250)	43.6 (109/250)	0.012
High blood pressure	66.8 (167/250)	35.4 (87/246)	<0.001
Body-mass index†	25.1±4.5 (160)	24.2±4.3 (209)	0.493
History of diabetes	18.0 (45/250)	11.8 (29/245)	0.055
Cigarette smoking	40.8 (102/250)	32.0 (79/247)	0.041
High serum cholesterol level	31.2 (78/250)	23.5 (57/243)	0.054
Peripheral vascular disease	7.2 (18/250)	8.4 (21/250)	0.738
Previous myocardial infarction	9.6 (24/250)	22.4 (55/246)	<0.001
Atrial fibrillation	30.4 (76/250)	31.4 (77/245)	0.804

*Plus–minus values are means ±SD. All other values are percentages of patients, with numbers of patients given in parentheses.

†Calculated as the weight in kilograms divided by the square of the height in meters.

Table 1. Base-Line Characteristics of Case Patients and Controls.

Plaque Thickness (mm)	Case Patients (N = 250)	Controls (N = 250)	Crude OR (95% CI)	Adjusted OR (95% CI)†	P Value
	% of patients (no.)				
<1‡	39.6 (99)	75.6 (189)	1	1	
1–1.9	11.2 (28)	6.4 (16)	3.3 (1.7–6.5)	4.4 (2.1–8.9)	<0.001
2–2.9	22.4 (56)	10.4 (26)	4.1 (2.4–7.0)	5.0 (2.7–9.0)	<0.001
3–3.9	12.4 (31)	5.6 (14)	4.2 (2.2–8.3)	3.4 (1.5–7.4)	<0.001
≥4	14.4 (36)	2.0 (5)	13.8 (5.2–36.1)	9.1 (3.3–25.2)	<0.001

*The adjusted risk associated with plaques 1 to 3.9 mm thick was 4.4 (95 percent confidence interval [CI], 2.8 to 6.8). OR denotes odds ratio.

†After adjustment for age, sex, hypertension, smoking status, serum cholesterol level, diabetes, previous myocardial infarction, and atrial fibrillation.

‡Reference category.

Table 2. Risk of Cerebral Infarction According to the Thickness of Atherosclerotic Plaques in the Ascending Aorta or Proximal Arch.

Plaque Thickness (mm)	Case Patients (N = 250)	Controls (N = 250)	Crude Odds Ratio (95% CI)*
	no. of patients		
Ascending aorta or proximal arch			
<1†	99	189	1
1–3.9	115	56	3.9 (2.6–5.9)
≥4	36	5	13.8 (5.2–36.1)
Distal arch			
<1†	47	93	1
1–3.9	156	140	2.2 (1.5–3.4)
≥4	47	17	5.5 (2.8–10.6)
Descending aorta			
<1†	7	6	1
1–3.9	171	203	0.7 (0.2–2.2)
≥4	72	41	1.5 (0.5–4.8)

*CI denotes confidence interval.

†Reference category.

Table 3. Risk of Cerebral Infarction According to the Thickness of Plaques in the Thoracic Aorta.

Plaque Thickness (mm)	Carotid Stenosis		
	None (N = 124)	<70% (N = 93)	≥70% (N = 33)
	no. of patients (%)		
<1 (n = 99)	58 (47)	33 (35)	8 (24)
1–3.9 (n = 115)	49 (40)	46 (49)	20 (61)
≥4 (n = 36)	17 (14)	14 (15)	5 (15)

*Percentages may not total 100 because of rounding.

Table 4. Relation between Thickness of Plaques in the Ascending Aorta or Proximal Arch and the Extent of Carotid Stenosis in the 250 Patients with Brain Infarcts.

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Cause of Stroke	No. of Patients	Plaque of ≥4 mm in Ascending Aorta and Proximal Arch	Adjusted Odds Ratio (95% CI)*
		no. of patients (%)	
Another likely cause (≥70% carotid stenosis or definite cardiac source of embolism)	74	4 (5.4)	7.8 (2.5–24.7)
Presumed lacunar infarct	44	4 (9.1)	4.5 (1.4–14.7)
Another possible cause (31 to 69% carotid stenosis and isolated atrial fibrillation)	54	6 (11.1)	3.1 (1.2–8.4)
No other apparent cause†	78	22 (28.2)‡	—

*Odds ratio for the comparison between patients with no detectable lesions and those with likely or possible causes or lacunar infarcts; the covariates that were adjusted for are listed in Table 2. CI denotes confidence interval.

†Patients with no other apparent cause were divided into two groups: 44 with patent foramen ovale, atrial septal aneurysm, or <30 percent carotid stenosis and 34 with no lesions. The frequency of plaques of ≥4 mm was similar in the two groups (27 and 29 percent, respectively).

‡The odds ratio was 4.7 (95 percent confidence interval, 2.2 to 10.1) for the comparison between patients with no other apparent cause and the group of 172 patients with likely or possible causes or lacunar infarcts.

Table 5. Frequency of Plaques of greater than or equal to 4 mm in the Ascending Aorta or Proximal Arch in the 250 Patients with Ischemic Stroke, According to the Cause of the Stroke.