Protruding Atheromas in the Thoracic Aorta and Systemic Embolization

Paul A. Tunick, MD; John L. Perez, BA; and Itzhak Kronzon, MD

■ *Objective:* To determine whether protruding atheromas in the thoracic aorta are a risk factor for systemic embolization.

■ *Design:* Case-control study.

■ *Setting:* A referral hospital.

■ *Patients:* A total of 122 patients with a history of stroke, transient ischemic attack, or peripheral emboli and an equal number of age- and sex-matched control patients.

■ *Measurements:* Evaluation using transesophageal echocardiography was done in case patients to detect protruding atheromas in the thoracic aorta and in control patients for cardiac indications other than emboli.

■ *Main Results:* Matched logistic regression showed that the presence of protruding atheromas was strongly related to the occurrence of embolic symptoms (odds ratio, 3.2; 95% CI, 1.6 to 6.5; $P < 0.001$). Furthermore, atheromas with mobile components were present only in case patients. When known risk factors for stroke (hypertension and diabetes) were added to the model, the presence of protruding atheromas remained an independent risk factor for embolic symptoms (odds ratio, 3.8). Hypertension was also independently associated with embolic symptoms (odds ratio, 2.7), but diabetes was not (odds ratio, 1.0).

■ *Conclusion:* Protruding atheromas in the thoracic aorta can be detected by transesophageal echocardiography and should be considered as a cause of strokes, transient ischemic attacks, and peripheral emboli.

Annals of Internal Medicine. 1991;115:423-427.

From New York University Medical Center, New York, New York. For current author addresses, see end of text.

Patients with unexplained strokes, transient ischemic attacks, or peripheral emboli are often referred for an echocardiographic evaluation to see if a cardiac source of embolization can be found. However, a two-dimensional echocardiogram is often normal in such patients (1). Even in patients with proved carotid artery disease, the presence of a carotid bruit may not predict the location of future cerebral events (2), and many of these patients may have an unsuspected source of embolization.

Transesophageal echocardiography can reveal potential cardiac sources of embolization (3, 4), and abnormalities in the thoracic aorta (5). We have recently reported the cases of three patients whose transesophageal echocardiograms showed the presence of large, protruding atheromas in the aortic arch (6). In a fourth patient, a protruding atheroma in the aortic arch was removed surgically because of multiple systemic emboli (7). These new findings prompted us to examine the transesophageal echocardiograms from a series of patients referred to our laboratory for various indications, including unexplained neurologic symptoms and other embolic phenomena, to see if protruding atheromas were related to embolic symptoms.

Methods

We used a case-control study design (8). All patients (107 outpatients, 137 inpatients) were referred by their attending physicians for evaluation by transesophageal echocardiography, and the procedures were done in the echocardiography laboratory. The referring physicians included cardiologists or cardiac surgeons (137 cases, 56%), neurologists (57 cases, 23%), internists (26 cases, 11%), vascular surgeons (5 cases, 2%), and various other specialists (19 cases, 8%). The patients were well enough to cooperate for the procedure, which was done without premedication except for antibiotic prophylaxis in patients with prosthetic valves. All patients and their matched controls were selected from the same group of patients referred for transesophageal echocardiography at Tisch Hospital, New York University Medical Center..

Case Patients

All patients in our study were referred to the non-invasive cardiology laboratory for evaluation by transesophageal echocardiography from 1988 through 1990. Of the 507 transesophageal echocardiograms done for various indications, 122 (24%) were done to search for a possible cardiac source of embolization in patients with a history of unexplained stroke, transient ischemic attack, or peripheral embolization. Previous transthoracic echocardiographic evaluation had not revealed a source of emboli.

The history of symptoms was obtained from the patients' attending physicians, from the patients themselves, or from the medical records. Neurologic symptoms (acute weakness or paralysis) involving the right side of the body and aphasia were attributed to left-brain events. Neurologic symptoms involving the left side of the body were attributed to right-brain events. In addition, some patients had peripheral emboli that involved the legs (eight patients), the arm (one patient), or the kidney (one patient). All symptoms had occurred a short time before the transesophageal echocardiogram was obtained; this was not a follow-up study, and no symptoms occurring after the echocardiographic evaluation were ascertained.

Controls

One hundred and twenty-two age- and sex-matched controls were randomly chosen from among 385 patients who had a transesophageal echocardiographic evaluation during the same period for cardiac indications other than embolic symptoms. In 109 instances, the control patient matched the case patient in year of age; in the other 13 instances, there was a 1-year difference in age between the case and the control patient.

Assessment of Atheromas

To determine whether the presence of protruding atheromas in the thoracic aorta conferred an increased risk for embolic

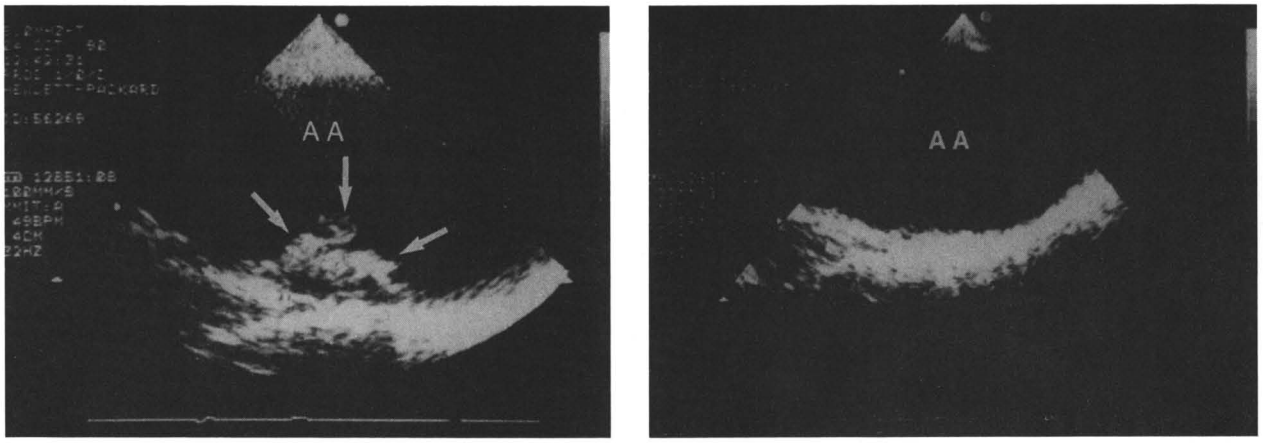

Figure 1. Protruding atheroma as shown by transesophageal echocardiography. Left. A protruding atheroma (*arrows*) located in the aortic arch of a 75-year-old man who had had a stroke. **Right.** For comparison, a transesophageal echocardiogram showing the aortic arch with no protruding atheroma. (AA = aortic arch.)

symptoms, we assessed the number of case patients and controls who had such atheromas. For the purposes of our study, atheromas that protruded 0.5 cm or more into the aortic lumen were considered to be significant. Intimal thickening was not considered to be significant. In addition, we recorded whether or not atheromas had mobile components that moved freely in the blood.

Transesophageal echocardiography was done while patients were awake using a Hewlett-Packard (Andover, Massachusetts) Sonos 500 system and a 5.0-MHz 21362-A transesophageal transducer. The oropharynx was anesthetized with topical lidocaine spray, but no other premedications were given (no sedatives or drying agents). The procedure was done after a fast of at least 4 hours. No patient experienced complications. The thoracic aorta was evaluated from the level of the stomach (approximately 45 cm from the teeth) up to and including the aortic arch and ascending aorta, and images were recorded on videotape for later analysis. The presence or absence of protruding atheromas was noted (Figure 1), as were any mobile components of the atheromas.

Possible Confounding Variables

To control for other major risk factors and to determine whether protruding atheromas were an independent cause of embolic symptoms, we assessed the case-control pairs for diabetes and hypertension using information available from the patients themselves, their physicians, or the medical records. Such information was available in 95 of the 122 pairs (78%); the remaining 27 pairs were excluded from this part of the analysis because the appropriate information was unavailable for one or both members of the pair.

Table 1. Frequency of Protruding Atheromas among 122 Case-Control Pairs

		Case: Atheroma Present	Case: Atheroma Absent
Control	Atheroma Present	1	10
	Atheroma Absent	32	79

Odds ratio, 3.2; $P < 0.001$.

Blinding and Observer Variability

Transesophageal echocardiography was done by five cardiologists who read the echocardiograms at the time the studies were done. Therefore, the interpreting cardiologist was not originally blinded to the patient's clinical situation. To assess observer variability, 100 consecutive studies were re-read by a designated cardiologist (one of the authors) who was blinded to the patients' histories. In addition, the upper left corner of the video screen was blacked out to hide the patients' names and identifying numbers. Of these 100 studies, the 36 that had been originally read by this cardiologist were used to assess intraobserver variability. The other 64 studies, which had been originally read by other cardiologists, were used to assess interobserver variability.

Statistical Analysis

A matched analysis was done using a conditional logistic regression model (BMDP Statistical Software Package [9]). The computer implementation of the matched design was adapted from that of Le and Lindgren (10). Ninety-five percent confidence intervals (CIs) were calculated for the odds ratios. Chi-square analysis was used when the given question was not amenable to logistic regression. A P value of less than 0.05 was considered to be significant.

Results

Of the 122 patients with emboli, 33 had protruding atheromas (27%) (Table 1). Thirty-two of these 33 patients (97%) were matched with controls who did not have atheromas. Only one of the case patients who had an atheroma was matched with a control who also had an atheroma. Seventy-nine of the 89 case patients (89%) who did not have atheromas were matched with controls who also did not have atheromas. Only 10 case patients who did not have atheromas were matched with controls who had atheromas. The estimated odds ratio for the occurrence of symptoms in the presence of protruding atheromas was 3.2 (95% CI, 1.6 to 6.5; $P < 0.001$). Eleven case patients had mobile components to their protruding atheromas, but no control patient had this finding ($P = 0.002$). Atheromas, in 29 of the 33 case patients (88%) who had them, were located in the aortic arch. Eleven of these 29 patients (33%) also had atheromas in the descending aorta; the 4 remaining patients

(12%) had atheromas in the descending aorta only. Eleven of the 122 control patients had atheromas; 7 of these 11 patients (64%) had atheromas that were located in the aortic arch. Two patients (18%) had atheromas in both the aortic arch and the descending aorta (18%), and four patients (36%) had atheromas in the descending aorta only.

Possible Confounding Variables

Information related to the presence or absence of hypertension and diabetes was available for 95 case-control pairs. Matched-pair analysis of the relation between these variables and systemic embolization is shown in Table 2. Of the 41 case patients who had hypertension, 32 (78%) were matched with controls who did not have hypertension; thus, only 9 case patients (22%) were matched with controls who also had hypertension. Of the 54 case patients who did not have hypertension, 41 (76%) were matched with controls who also did not have hypertension and 13 (24%) were matched with controls who did have hypertension.

Of the 18 case patients with diabetes, 15 (83%) were matched with controls who did not have diabetes and 3 (17%) were matched with controls who did have diabetes. Of the 77 case patients who did not have diabetes, 64 (83%) were matched with controls who also did not have diabetes and 13 (17%) were matched with controls who did have diabetes.

The matched-pair conditional logistic regression analysis was repeated with atheroma, diabetes, and hypertension in the model ($P < 0.001$) (Table 2). The presence of protruding atheromas was shown to be an independent predictor of embolic symptoms (estimated odds ratio, 3.8; 95% CI, 2.4 to 5.8). Hypertension was also predictive of symptoms (odds ratio, 2.7; 95% CI, 1.9 to 3.9). Diabetes was not predictive of embolic symptoms in these matched pairs (odds ratio, 1.0).

Table 2. Frequency of Protruding Atheromas, Hypertension, and Diabetes among 95 Case-Control Pairs

		Case: Atheroma Present	Case: Atheroma Absent
Control	Atheroma Present	1	8
	Atheroma Absent	27	59

Odds ratio, 3.8; $P < 0.001$.

		Case: Hypertension Present	Case: Hypertension Absent
Control	Hypertension Present	9	13
	Hypertension Absent	32	41

Odds ratio, 2.7; $P < 0.001$.

		Case: Diabetes Present	Case: Diabetes Absent
Control	Diabetes Present	3	13
	Diabetes Absent	15	64

Odds ratio, 1.0; $P < 0.001$.

Table 3. Location of Neurologic Symptoms in 33 Patients with Neurologic Events*

Location	Events, *n* (%)
Left brain	21 (49)
Peripheral	10 (23)
Right brain	8 (19)
Diffuse cerebral	3 (7)
Ataxia, vertigo	1 (2)
Total	43 (100)

* $P < 0.005$ when left-brain or peripheral symptoms were compared with right-brain symptoms.

Left-Brain or Peripheral Symptoms

The 33 case patients with atheromas had 43 symptomatic episodes (Table 3). Thirty-three of the episodes were neurologic (21 strokes and 12 transient ischemic attacks), and 10 involved the peripheral circulation (1 involved the kidney; 1, the arm; and 8, the leg). We hypothesized that right-brain emboli would be less likely to occur than left-brain or peripheral emboli because atheromas located in the aortic arch may be distal to the innominate artery (the great vessels are not visualized on single-plane transesophageal echocardiography, and, therefore, precise location of the atheroma in relation to the innominate is not possible). This hypothesis was confirmed by our finding that 31 symptomatic episodes (72%) involved the left brain (21 episodes [49%]) or the periphery (10 episodes [23%]). Only eight symptomatic episodes (18%) involved the right brain ($P < 0.005$). Four brain events could not be lateralized.

Blinding and Observer Variability

To assess possible variability of interpretation, 100 studies were re-read by a designated cardiologist (one of the authors) who was blinded to the patient's clinical situation. Of the 36 studies originally read by this cardiologist, 4 had been interpreted as showing protruding atheromas and 32 as not showing protruding atheromas. Only 1 of these 36 studies (3%) was interpreted differently on the second reading: An echo density originally thought to show a protruding atheroma was, on rereading, thought to indicate part of the aortic wall.

Of the 64 studies originally read by other cardiologists, 7 had been interpreted as showing protruding atheromas and 57 as not showing protruding atheromas. Only 1 study (2%) was interpreted differently on the

second reading: Originally read as showing "mild atheroma" (negative), the study, on re-reading, was interpreted as showing a protruding atheroma (positive). Thus, both intra-observer variability (97% agreement) and interobserver variability (98% agreement) were minimal.

Discussion

Transesophageal echocardiography has been found to be useful in identifying cardiac abnormalities in young patients with transient ischemic attacks (11). Similarly, Pop and colleagues (12) found transesophageal echocardiography to be superior to routine transthoracic studies in patients who did not have overt heart disease but who had transient ischemic attacks. However, the overall yield of possible embolic sources in these patients was small (10%), and the investigators were not certain the new findings were not just incidental, associated anomalies. The yield of possible embolic sources was higher in patients with clinically overt heart disease, but these findings was thought to be of little clinical relevance. They found that 32 of 72 patients (44%) had aortic atherosclerosis, confirming the previously reported association of atherosclerosis with neurologic events (13). However, they identified diffuse aortic wall irregularities and did not define protruding atheromas or mobility. In addition, their study had no control group of patients without neurologic events, and, therefore, no statement could be made about the causal relation between aortic atherosclerosis and such events. Recently, Karalis and coworkers (14) identified aortic atheromas in 36 of 556 patients (6%) who had transesophageal echocardiography. Eleven of these 36 patients (31%) had embolic symptoms (7 with cerebral symptoms and 4 with peripheral symptoms).

We found protruding atheromas in the thoracic aorta in 33 of 122 case patients (27%). Matched-pair logistic regression showed that the chance of having symptoms is three times greater in the presence of protruding atheromas. Furthermore, only case patients had atheromas with mobile components. Even when the known risk factors, hypertension and diabetes, were added to the model, protruding atheromas were still independently associated with strokes, transient ischemic attacks, and peripheral emboli.

That embolic symptoms were significantly more likely to have involved the left brain or periphery than the right brain is probably evidence that the protruding atheromas caused the patients' symptoms, because lesions in the aortic arch were probably more likely to be distal to the innominate artery. Factors other than the site of the atheroma, such as blood flow distribution, may have also influenced the location of symptoms.

Once atheromas are identified, the problem of clinical management arises. We have reported the case of one patient (7) who had four embolic events. This patient's protruding atheroma was removed under circulatory arrest. Repeat transesophageal study 2 months later showed a clean aortic arch, and the patient continues to do well. In addition, investigators at our institution have reported the removal of protruding atheromas in patients undergoing open heart surgery (15). However, surgical removal may be indicated only in highly selected patients, and there is no evidence that such surgery decreases the risk for embolization in patients with these lesions; on the contrary, surgery might increase the risk for an adverse outcome.

Although the transesophageal echocardiograms were originally interpreted at the time the procedures were done, 100 consecutive studies were re-interpreted at the end of the study by a cardiologist who was blinded to the patient's clinical situation. Intra- and interobserver variability were minimal; however, in a few cases involving patients with other obvious diagnoses, less attention was paid to meticulously exploring the thoracic aorta when the test was done, and some atheromas may have been missed because of this operator-recording bias.

We found 50 protruding atheromas in the 507 patients who had a transesophageal echocardiographic evaluation in our laboratory. This rate of 10% is higher than that found (6%) in the 556 patients studied by Karalis and colleagues (14). This higher incidence does not reflect the incidence of protruding atheromas in the general population because of referral bias; all case patients were referred for evaluation because of symptomatic events. The transesophageal echocardiograms were done after, not before, the events occurred. Therefore, the ability to predict future events has not been determined. A prospective study to evaluate the importance of protruding atheromas in asymptomatic patients cannot be done at present because, despite the lack of complications seen among our patients, transesophageal echocardiography is a somewhat invasive and potentially harmful procedure (16). However, a prospective study of patients referred for evaluation by transesophageal echocardiography should be done to avoid the problems inherent in a retrospective analysis.

Two other issues deserve mention. Because the distal part of the ascending aorta is masked by the trachea and not seen on a single-plane transesophageal echocardiogram, some atheromas in this location may have been missed. Finally, material was removed from one patient (an atheroma with superimposed thrombus), but pathologic information is not available for the group as a whole, and the importance of the composition of this material is not known.

Requests for Reprints: Paul A. Tunick, MD, New York University Medical Center, 560 First Avenue, Suite 2-E, New York, NY 10016.

Current Author Addresses: Dr. Tunick, Mr. Perez, and Dr. Kronzon: Department of Medicine, New York University Medical Center, 550 First Avenue, New York, NY 10016.

References

1. **Good DC, Frank S, Verhulst, S, Sharma B.** Cardiac abnormalities in stroke patients with negative arteriograms. Stroke. 1986;17:6-11.
2. **Wolf PA, Kannel WB, Sorlie P, McNamara P.** Asymptomatic carotid bruit and the risk of stroke. The Framingham study. JAMA. 1981; 245:1442-5.
3. **Daniel WG, Engberding R, Erbel R, Hanrath P, Iliceto S, Kasper W, et al.** Transesophageal echocardiography in arterial embolization and cerebral ischemic events: a European multicenter study in patients with preknown cardiac disease [Abstract]. Eur Heart J. 1989;10:204.
4. **Pearson AC, Labovitz AJ, Tatineni S, Gomez C.** Superiority of transesophageal echocardiography in detecting cardiac source of embolism in patients with cerebral ischemia of uncertain etiology. J Am Coll Cardiol. 1991;17:66-72.

5. **Gussenhoven WJ, Taams MA, de Jong N, Bos E, Sutherland GR, Roelandt J.** Transesophageal echo in the diagnosis of thoracic aorta pathology [Abstract]. Eur Heart J. 1988;9(Suppl I):I-1572.
6. **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: 658-60.
7. **Tunick PA, Culliford AT, Lamparello PJ, Kronzon I.** Atheromatosis of the aortic arch as an occult source of multiple systemic emboli. Ann Intern Med. 1991;114:391-2.
8. **Fletcher RH, Fletcher SW, Wagner EH, eds.** Clinical Epidemiology: The Essentials. 2d edition. Baltimore: Williams & Wilkins, 1988.
9. **Dixon WJ,** editor. BMDP statistical software. Berkeley, California: University of California Press; 1985.
10. **Le CT, Lindgren BL.** Computational implementation of the conditional logistic regression model in the analysis of epidemiologic matched studies. Comput Biomed Res. 1988;21:48-52.
11. **Zenker G, Erbel R, Kramer G, Mohr-Kahaly S, Drexler M, Harnoncourt K, et al.** Transesophageal two-dimensional echocardiography in young patients with cerebral ischemic events. Stroke. 1988;19:345-8.
12. **Pop G, Sutherland GR, Koudstaal PJ, Sit TW, de Jong G, Roelandt JR.** Transesophageal echocardiography in the detection of intracardiac embolic sources in patients with transient ischemic attacks. Stroke. 1990;21:560-5.
13. **Young W, Gafman JW, Tandy R, Malamud N, Waters ES.** The quantitation of atherosclerosis. III. The extent of correlation of degrees of atherosclerosis within and between the coronary and cerebrovascular beds. Am J Cardiol. 1960;6:300-8.
14. **Karalis DG, Chandrasekaran K, Victor MF, Ross JJ, Mintz GS.** The recognition and embolic potential of intraaortic atherosclerotic debris. J Am Coll Cardiol. 1991;17:73-8.
15. **Culliford AT, Colvin SB, Rohrer K, Baumann FG, Spencer FC.** The atherosclerotic ascending aorta and transverse arch: a new technique to prevent cerebral injury during bypass: experience with 13 patients. Ann Thorac Surg. 1986;41:27-35.
16. **Daniel WG, Erbel R, Kasper W, Visser CA, Engberding R, Sutherland GR, et al.** Safety of transesophageal echocardiography. A multicenter survey of 10,419 examinations. Circulation. 1991;83:817-21.