Enhanced Detection of Intracardiac Sources of Cerebral Emboli by Transesophageal Echocardiography

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We performed transesophageal echocardiography in 50 consecutive hospitalized patients with recent transient ischemic attack or stroke of embolic origin to determine whether transesophageal echocardiography is more sensitive than transthoracic echocardiography in detection of possible intracardiac sources of embolism. Twenty-six of 50 patients with a negative transthoracic echocardiogram for potential source of emboli had a transesophageal echocardiography study that demonstrated at least one intracardiac abnormality. Abnormalities noted by transesophageal echocardiography included five of 50 patients with either a left atrial or left atrial appendage clot, four patients with a patent foramen ovale, and nine patients with spontaneous echocardiographic contrast. In 11 of 50 patients with no other source of embolism, we found highly mobile filamentous strands on the mitral valve, which have not been described previously. These mitral valve echo strands may represent a fissured surface or fibrosis that can serve as a nidus for thrombus formation. We detected no unexpected left ventricular thrombus or left atrial myxoma. Factors significantly associated with a greater likelihood of a positive transesophageal echocardiography study included left atrial enlargement, atrial fibrillation, and a calcified or thickened mitral valve. Our study suggests that transesophageal echocardiography is a valuable addition to transthoracic echocardiography in investigating potential intracardiac sources of embolism. (Stroke 1991;22:734-739)

Intracardiac pathology resulting in embolic phenomena is a well-recognized cause of cerebral ischemia and infarction. Previous studies suggest that 6–23% of all cerebral ischemic events have a cardiac origin. Factors predisposing to cardiac embolism include left atrial enlargement, spontaneous left atrial echocontrast, atrial septal aneurysm, interatrial shunts, atrial fibrillation, valvular disease (including rheumatic, endocarditis, mitral valve prolapse, mitral valvular calcification, and prosthetic valves), and abnormal ventricular wall motion (including aneurysm and globally reduced left ventricular function resulting from myocardial infarction or cardiomyopathy). Transthoracic echocardiography is a commonly used technique to detect possible intracardiac sources of emboli. It is estimated that 23–51% of transthoracic echocardiograms demonstrate cardiac abnormalities that may predispose a patient to emboli. However, definitive cardiac lesions associated with embolism such as left atrial clot, left ventricular thrombi, or mitral valve thrombi and vegetation are visualized in only 3–8% of patients presenting with embolic stroke. Explanations for this low yield have included emboli originating from noncardiac sources, cardiac lesions that have completely embolized, and suboptimal transthoracic echocardiogram examinations. Transthoracic echocardiography is sensitive in detecting left ventricular thrombi, left ventricular dysfunction, and valvular disease. Furthermore, transthoracic echocardiography accurately assesses left atrial size and mitral valvular motion. However, it is unreliable in identifying atrial clots, especially left atrial appendage clots, and mitral valve thromboli.

The use of transesophageal echocardiography has gained wide acceptance because of its superior resolution of basal structures such as the left atrium, left atrial appendage, mitral valvular apparatus, and atrial septum. This study was designed to determine whether transesophageal echocardiography is more sensitive than transthoracic echocardiography in detecting possible intracardiac sources of embolism.
Subjects and Methods

Fifty consecutive hospitalized patients with a recent embolic event (transient ischemic attack or stroke), aged 20–82 years (mean, 63±13 years; 31 men, 19 women), from the neurology service of Stanford University Hospital underwent transesophageal echocardiography studies. Inclusion criteria for the study were the following: 1) Clinical diagnosis by the neurology service of an embolic transient ischemic attack or stroke occurring within the previous week. These were patients experiencing the abrupt onset of a focal neurologic deficit in the vascular territory of the anterior or middle cerebral arteries, with no evidence of mass or hemorrhage on head computerized tomographic (CT) scan. Patients with deficits in the territory of the posterior circulation or the diagnosis of lacunar stroke were excluded. 2) A negative transthoracic echocardiogram for potential intracardiac sources of embolism. The transthoracic echocardiogram included contrast echocardiography with a minimum of two injections of agitated saline with and two injections without Valsalva maneuver.

Transesophageal echocardiography and transesophageal echocardiography were performed within 1 week of the onset of symptoms according to standard techniques. M-mode and two-dimensional transthoracic echocardiography were performed with the patient in the left lateral decubitus position using a 77020A imaging system (Hewlett-Packard Co., Palo Alto, Calif.) including a 2.5- or 3.5-MHz transducer. Parasternal long- and short-axis views, apical views, and subxiphoid views were obtained. Transesophageal echocardiography was performed with the patient in the left lateral decubitus position using the Hewlett-Packard 77020A ultrasound imaging system, including the Hewlett-Packard 21362A 5-MHz single-plane transesophageal transducer. Basal short-axis views, four-chamber views, and transgastric short-axis views were obtained. Limb leads were placed on each patient to obtain a simultaneous electrocardiogram rhythm strip.

Evaluation of the echocardiographic findings were performed in a blinded manner by a senior attending cardiologist in the noninvasive laboratory. In addition to the above parameters, left atrial enlargement, defined as greater than 4.4 cm by M-mode, and mitral valvular calcification or thickening were determined from two-dimensional transthoracic echocardiography. Rhythm abnormalities were detected by review of the patients' electrocardiogram and rhythm tracing during the echocardiographic studies. Patients' charts were reviewed for presenting signs and symptoms, for evidence of underlying cardiovascular disease including hypertension, myocardial infarction, cardiomyopathy, and arrhythmias, and for final discharge diagnosis.

Possible sources of embolism were defined as left atrial or left atrial appendage clot, left ventricular thrombus, "swirling" in the left atrium or left ventricle (i.e., spontaneous echocardiographic contrast), left atrial myxoma, valvular masses on the mitral or aortic valve, and interatrial shunt (i.e., patent foramen ovale).

Left atrial and left atrial appendage clots were diagnosed as an echo dense mass with independent motion relative to the chamber wall. Left ventricular thrombus was diagnosed as an echo dense mass adhered to the ventricular wall. "Swirling" was defined as spontaneous echogenic contrast in the left atrium, left atrial appendage, or left ventricle. Contrast settings were optimized to detect spontaneous echogenic contrast.

Valvular masses may represent a vegetation, clot, or fibrin strands. Valvular masses were diagnosed as echo densities on the mitral or aortic valve that had independent motion as compared to the valve.

Interatrial shunts were diagnosed by contrast echocardiography using the four-chamber view and a rapid hand injection of 10 ml agitated saline injected through a peripheral intravenous cannula. At least two saline injections without Valsalva maneuver and two injections during Valsalva maneuver were performed, and images of the interatrial septum and right and left atrium were recorded in each patient. The contrast echocardiogram was considered positive if at least three microcavitations appeared in either the left atrium or left ventricle within two to three cardiac cycles after the appearance of microcavitations in the right atrium.

All patients participating in this study had signed informed consents, and the protocol was approved by the Human Subjects Committee at Stanford University Medical Center.

Data were analyzed for the number of possible intracardiac sources of embolism and possible predictive factors as prior history of cardiovascular disease, arrhythmias, left atrial enlargement, and mitral valvular calcification or thickening. Data were assessed by logistic regression to determine the best predictor for each intracardiac abnormality and $\chi^2$ analysis. Sensitivity, specificity, positive predictive value, and negative predictive value were calculated for each parameter.

Results

Of the 50 patients entered into this study, 29 had transient ischemic attacks and 21 had cerebral infarction. All patients had a negative transthoracic echocardiogram for possible intracardiac sources of embolism, except for 23 patients who had mild diffuse thickening or calcification of the mitral valve but without evidence of definable mass. All patients had a negative contrast study by transthoracic echocardiography, and all had negative head CT scans for a hemorrhagic event. Although not a criteria for study entry, patients over the age of 30 or patients with clinical suspicion of carotid artery disease underwent either carotid arteriogram or Doppler carotid study to exclude significant carotid artery stenosis that could give rise to a thrombotic etiology for the neurologic event. Thirty-eight patients had
either a carotid arteriogram or noninvasive carotid artery study. Three patients had carotid arteriograms that revealed a high-grade stenosis. However, the lesions did not supply circulation to the involved cerebral territory. The remainder of patients undergoing a carotid artery stenosis work up did not have significant carotid artery lesions. Twelve remaining patients were either below 30 years of age or did not have any clinical evidence for carotid artery disease, such as carotid bruits.

Figure 1 shows the distribution of potential intracardiac sources of embolism found using transesophageal echocardiography in our 50 patients. No patients had left ventricular thrombi, left atrial myxoma, or aortic valve mass. Three patients had more than one cardiac abnormality. Figures 2–5 demonstrate each of these intracardiac abnormalities.

We examined various factors to determine whether any of them might help select which patients would have a positive transesophageal echocardiogram for a potential intracardiac source of embolism. Logistic regression demonstrated that mitral valve thickening or calcification is the best factor for predicting a positive transesophageal echocardiogram for mitral valve echo strands, whereas left atrial enlargement is the best predictor for either left atrial appendage clot or spontaneous echo contrast.

The contribution of atrial rhythm in identifying patients with a greater likelihood of having a positive...
incidence of left atrial or left atrial appendage clot or echocardiogram were 0.81 and 0.64, respectively.

In identifying patients with positive transesophageal valve by transesophageal echocardiogram had any were 0.73 and 0.31, respectively.

Mitral valve echo strands (Mv str) prolapsing into the left atrium. Lv, left ventricle.

FIGURE 5. Transesophageal echocardiogram focusing on the mitral valve (Mv) demonstrating mitral valvular echo strands (Mv str) prolapsing into the left atrium. Lv, left ventricle.

study revealed that four of 38 patients with sinus rhythm had either left atrial spontaneous echo contrast or left atrial appendage clot, and eight of 12 patients with paroxysmal or persistent atrial fibrillation had a left atrial appendage clot or left atrial spontaneous echo contrast. These results are significant as analyzed by \( \chi^2 \) analysis (\( p < 0.01 \)). The sensitivity and specificity of atrial fibrillation in predicting which patients would have a positive transesophageal echocardiography study were 0.67 and 0.89, respectively.

Comparing patients with and without a cardiac history of arrhythmias, myocardial infarctions, cardiomyopathies, or hypertension, we found seven of 21 patients with no prior cardiac history who had a potential intracardiac source of embolism (three patients with an interatrial shunt, and four with mitral valvular strands). Nineteen of 29 patients with a prior cardiac history had a positive transesophageal echocardiogram for a potential intracardiac source of embolism. These results are not significantly different. The sensitivity and specificity of cardiac history for identifying which patients would have a positive transesophageal echocardiography study were 0.73 and 0.31, respectively.

Mitra lvalve thickening or calcification was found to be associated with mitral valve echo strands. Only two of 27 patients with a normal-appearing mitral valve by transthoracic echocardiogram had any mitral valve echo strands. Nine of 23 patients with a calcified or thickened mitral valve by transthoracic echocardiogram had mitral valve echo strands (\( p < 0.01 \)). The sensitivity and specificity of this factor in identifying patients with positive transesophageal echocardiogram were 0.81 and 0.64, respectively.

Left atrial enlargement is associated with a greater incidence of left atrial or left atrial appendage clot or spontaneous echo contrast. Two of 36 patients with a normal left atrial size had a left atrial appendage clot and nine of 14 patients with left atrial enlargement had either a clot, spontaneous echo contrast, or both a clot and spontaneous echo contrast. These results were highly significant (\( p < 0.001 \)). The sensitivity and specificity of this factor in identifying patients with a positive transesophageal echocardiography study were 0.82 and 0.87, respectively.

Analysis by \( \chi^2 \) revealed that left atrial enlargement and atrial fibrillation were independent variables as risk factors for intracardiac sources of embolism. Only one of 32 patients with neither left atrial enlargement nor atrial fibrillation had a left atrial appendage clot, and 12 of 18 patients with either atrial fibrillation or left atrial enlargement had left atrial echo contrast or left atrial appendage clot. These results are highly significant by \( \chi^2 \) analysis (\( p < 0.001 \)). The sensitivity and specificity for the combination of left atrial enlargement and atrial fibrillation were 0.92 and 0.97, respectively.

Discussion

This study demonstrates that transesophageal echocardiography is substantially more sensitive than transthoracic echocardiography in detecting potential intracardiac sources of embolism in a group of patients clinically diagnosed as having embolic transient ischemic attacks or strokes. We believe that this group of patients is representative of patients referred by neurologists for echocardiographic evaluation of a possible intracardiac source of embolism.

Specifically, transesophageal echocardiography detects an additional 52% of potential intracardiac sources of embolism in patients with a negative transthoracic echocardiogram. There are several possible explanations for the high percentage of positive transesophageal echocardiograms. Transesophageal echocardiography has superior resolution of cardiac basal structures such as the left atrium, left atrial appendage, atrial septum, and mitral valvular apparatus as compared to transthoracic echocardiography.13-17 Therefore, one would expect transesophageal echocardiography to be more sensitive in detecting left atrial or left atrial appendage clot, mitral valve thrombi, and interatrial shunts. Furthermore, transthoracic echocardiography rarely detects left atrial spontaneous echogenic contrast.18 Spontaneous echogenic contrast is commonly thought to be secondary to erythrocyte or platelet aggregation, which is greatest with stagnant flow rates.6,19,20 Finally, the higher percentage of positive transesophageal echocardiography is dependent on the definition of intracardiac pathology that results in an embolic event. In this study, one may argue that the only definitive sources of embolism are clots and valvular masses and vegetations; patent foramen ovale and spontaneous echo contrast are only precursors. When just left atrial appendage clots are considered, transesophageal echocardiography increases the sensitivity of detecting an intracardiac
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state or abnormality that may serve continually as a cerebral emboli; however, left atrial spontaneous atrial masses have been closely associated with residual source of emboli (clot, mass) or a cardiac clot or valvular mass, may have disappeared permanently from the embolic event. The source, such as a left atrial valve or atrial fibrillation, left atrial enlargement, and mitral valve abnormalities such as a left atrial prolapse and mitral annular calcification have been implicated as causes of embolic stroke. 8,9,21 This observation raises the possibility that the observed increased incidence of valvular disease and cerebral emboli is related to mitral valve echo strands.

The histology of mitral valve echo strands is presently unknown. Possibilities include thrombi, fibria strands, torn chordae, or redundant mitral leaflet. The observation that mitral valve echo strands were predominantly associated with calcified or thickened mitral valves suggests that the strands may represent a degeneration of leaflet tissue. Valvular thickening with fissured surfaces or fibrosis also can serve as a nidus for thrombus formation. 22 Recently, gross inspection of a mitral valve removed during a mitral valve replacement at our institution and with documented echo strands by transesophageal echocardiography revealed the strands to be consistent with Lambi's excrescences (pathology report). Lambi's excrescences are filiform processes found on both mitral and aortic valves. 23,24 Such processes have been associated with embolic phenomena. 25,26 Preliminary data at our institution of 27 patients studied by transesophageal echocardiography without clinical evidence of cerebral vascular or cardiovascular disease revealed only two of 27 patients with mitral valve echo strands.

Atrial fibrillation, left atrial enlargement, and mitral valvular abnormalities were sensitive indicators for identifying patients who had a positive transesophageal echocardiogram detecting a potential intracardiac source of embolism. The exclusion from the study of all patients without atrial fibrillation, left atrial enlargement, or a thickened or calcified mitral valve by transthoracic echocardiogram would have resulted in the identification of more than 94% of all potential intracardiac lesions while eliminating at least 32% of the thoracic echocardiogram. Therefore, integration of risk factors and use of clinical judgment can be used to determine which patients may benefit from a transesophageal echocardiogram.

There are several limitations to this study. First, the echocardiographic studies were obtained after the embolic event. The source, such as a left atrial clot or valvular mass, may have disappeared permanently. What we were studying was the possibility of residual source of emboli (clot, mass) or a cardiac state or abnormality that may serve continually as a source (patent foramen ovale, spontaneous echo contrast). Second, potential sources of emboli are not proved sources of emboli. Left atrial clots and ventricular masses have been closely associated with cerebral emboli; however, left atrial spontaneous echo contrast is considered more of a "precursor" for clot formation. Patent foramen ovale, although found in a high incidence in younger stroke victims, may not have been the source of emboli in our somewhat older population. Mitral valve echo strands are a new entity described in this study. The etiology is yet unknown, and their role in cerebral embolism is speculative at this point.

This study demonstrates that transesophageal echocardiography increases the diagnostic yield of detecting intracardiac abnormalities. We conclude that transesophageal echocardiography is complementary to transthoracic echocardiography in identifying potential intracardiac sources of embolism.

References


**Key Words**  • echocardiography  • cerebral ischemia, transient  • embolism  • cerebrovascular disorders
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