Transesophageal Echocardiographic Findings in Stroke Subtypes

G.W. Albers, MD; K.A. Comess, MD; F.A. DeRook, MD; P. Bracci, MSc; J.E. Atwood, MD; A. Bolger, MD; J. Hotson, MD

Background and Purpose Transesophageal echocardiography has a high yield for detecting potential cardiac sources of embolism in patients with clinical risk factors for cardioembolism or unexplained stroke. The yield in other stroke subtypes is unknown.

Methods We classified 145 consecutively admitted patients into stroke subtypes based on clinical findings, brain imaging, and carotid ultrasound. Both transesophageal and transthoracic echocardiography were performed to detect left atrial thrombi, spontaneous echo contrast, atrial septal aneurysm, interatrial shunts, ventricular thrombus or aneurysm, and myxomatous mitral valve.

Results Transesophageal echocardiography documented at least one of these findings in 46% of the patients compared with an 8% yield on the transthoracic study (P=.002). The yield of transesophageal echocardiography was substantial in all stroke subgroups. Patients with clinical risk factors for cardiac embolism had the highest frequency of spontaneous echo contrast (P=.001). Atrial septal aneurysms were most frequent in patients with lacunar syndromes (P=.012), and interatrial shunts were common in all stroke subtypes.

Conclusions Transesophageal echocardiographic findings vary considerably between stroke subgroups. (Stroke. 1994; 25:23-28.)

Key Words • cardioembolic stroke • cerebrovascular disorders • echocardiography

Recent progress in the prevention of cardioembolism with the use of low levels of anticoagulation mandates accurate detection of cardioembolic sources of stroke. The diagnosis of cardiac embolism is currently inferred when a presumed high-risk cardiac abnormality is detected in the absence of an alternative explanation for the stroke. Because direct imaging of potential sources of cardiac embolism with transthoracic echocardiography has a low sensitivity, the diagnosis of cardioembolic stroke remains indirect and unsatisfactory.

The introduction of transesophageal echocardiography has improved the visualization of cardiac structures such as the left atrium, left atrial appendage, and interatrial septum. Abnormalities in these regions may predispose to cardioembolic stroke. A number of recent studies have demonstrated that the detection of intracardiac abnormalities in patients who present with stroke or transient brain ischemia is significantly enhanced when transesophageal echocardiography is used in conjunction with transthoracic echocardiography.

However, these studies have not provided a clear indication of which subgroups of patients are most likely to benefit from a transesophageal evaluation. Previous studies have focused on populations selected for having either risk factors for cardioembolism or “unexplained stroke.” The value of transesophageal echocardiography in other stroke subtypes from a general neurology setting remains unknown. For example, no data are available regarding the yield of transesophageal echocardiography in stroke patients with other plausible stroke etiologies such as ipsilateral carotid stenosis or a typical lacunar syndrome.

For these reasons, we examined consecutive stroke admissions with both transthoracic and transesophageal echocardiography to determine whether certain transesophageal echocardiographic findings are associated with established cardioembolic causes of stroke, typical “lacunar” syndromes, stroke ipsilateral to a carotid stenosis, or stroke of unclear cause. Preliminary data from this study have been presented.

Subjects and Methods

The study population consisted of consecutive patients admitted to the Santa Clara Valley Medical Center (the county medical facility affiliated with Stanford University) and the Palo Alto Veterans Administration Medical Center with a diagnosis of stroke or transient ischemic attack (TIA). The diagnosis of stroke or TIA was made by neurology house officers and confirmed by an attending neurologist. Stroke was defined as an acute ischemic neurological deficit that persisted at least 24 hours. TIA was defined as an ischemic neurological deficit that resolved within 24 hours. All patients underwent general medical and neurological examinations, chest radiograph, electrocardiogram, general blood chemistries, brain imaging (head computed tomography or magnetic resonance imaging), carotid duplex (B-mode and Doppler) scanning, and transthoracic and transesophageal echocardiography using a standard protocol. Two neurologists (G.W.A. and J.H.), who were unaware of the echocardiographic findings, classified patients into five stroke groups based on predetermined criteria. All clinical data were collected prospectively, and patients were placed into the following stroke classification.
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groups: group 1, high-risk cardiac embolism; group 2, typical small-vessel "lacunar" infarction; group 3, hemispheric infarction with carotid stenosis; group 4, hemispheric infarction without carotid stenosis; and group 5, other.

Group 1 included patients with clinical cardiac abnormalities known to be highly correlated with cardiac embolism.13,14 Abnormalities that required classification in this group were atrial fibrillation, prosthetic aortic or mitral valve endocarditis, recent myocardial infarction, dilated cardiomyopathy, sick sinus syndrome, rheumatic mitral stenosis, or previously documented intracardiac thrombus, tumor, or left ventricular aneurysm. Patients with high-risk cardiac features who also had a greater than 50% ipsilateral carotid stenosis or a typical small-vessel infarct were assigned to group 5.

Patients were classified into group 2 if high-risk cardiac abnormalities were absent and they had a typical lacunar stroke syndrome (eg, pure motor hemiparesis, dysarthria/clumsy hand, pure sensory stroke, or pure sensory/motor stroke).15 In addition, if brain imaging revealed a new ischemic lesion it was required to be subcortical and less than 1.5 cm in diameter. Patients who met criteria for this group but also had a greater than 50% ipsilateral carotid stenosis or high-risk cardiac abnormality were assigned to group 5.

Patients with an acute hemispheric stroke or TIA in the carotid territory confirmed by clinical and/or neuroimaging studies were classified in group 3 if they had a greater than 50% diameter stenosis of the ipsilateral common or internal carotid artery confirmed by ultrasound.

Criteria for group 4 were identical to group 3, with the exception that there was not a significant carotid stenosis ipsilateral to the new event.

Group 5 included all patients who did not meet criteria for groups 1 through 4 or who met criteria for more than one group.

A limited number of predetermined echocardiographic findings were evaluated in this study. These findings were (1) left atrial or appendage thrombus, (2) spontaneous echo contrast, (3) atrial septal aneurysm, (4) interatrial shunting from right to left via the foramen ovale or an atrial septal defect, (5) ventricular thrombus, (6) ventricular aneurysm, and (7) myxomatous mitral valve thickening or vegetation. These findings were selected based on presumed association with cerebral embolism.16 After the study had begun, several publications identified protruding aortic plaque as a potentially important transesophageal echocardiographic finding. Therefore, the aorta was systematically examined in the final 51 patients enrolled in the study.

Left atrial and appendage thrombi were defined as discrete echo-dense masses within the body of the atrium or appendage with a different echocardiographic density from the adjacent endocardium. Spontaneous echo contrast, also known as swirling atrial echoes or atrial "smoke," was defined as streams of low-intensity acoustic reflectors, having the appearance of loosely organized or aggregated particles, moving with low velocity in complex helical patterns in the atrial cavity or appendage. Atrial septal aneurysm was defined as a thinwalled segment of the interatrial septum in the region of the fossa ovalis with a base of at least 1.5 cm, protruding into either atrial cavity at least 1.5 cm, or moving between the atria by at least this distance.16 Interalarial shunts were directly imaged or were identified by conventional pulsed-wave Doppler, color-flow Doppler, or agitated saline contrast injection. Saline bubbles appearing in the left atrium within three cardiac cycles or directly observed crossing the atrial septum qualified as a positive study for shunting. Evaluation for shunt was performed in the baseline state and with Valsalva maneuver. A ventricular cavity thrombus was defined as a discrete echo-dense mass in an area of abnormal wall motion that was visualized in at least two views. A ventricular aneurysm was defined as an area of myocardial thinning with an unusual rounded contour of the involved segment maintained through-out the cardiac cycle. Myxomatous mitral valve was defined as diffuse thickening of the mitral valve leaflets.

Transsthoracic echocardiography was performed in all subjects using the standard approach and 2.25-, 3.0-, and 7.5-MHz transducers. Transesophageal echocardiography was performed with a 5.0-MHz single-plane probe, introduced after topical oropharyngeal anesthesia. Both transesophageal and transthoracic echocardiography were performed by an experienced echocardiographer using a standard protocol. Carotid stenosis of 50% or greater was defined as a common or internal carotid lesion associated with a peak velocity of greater than 1.24 m/s on duplex scan. This study was approved by the Investigational Review Boards of both institutions, and patients gave informed consent.

One hundred ninety-one consecutive patients admitted between January 1990 and October 1991 with a diagnosis of acute stroke or TIA were screened. Forty-six patients were excluded. The reasons for exclusion were profound neurological deficits or severe medical conditions (30 patients), carotid duplex exam technically inadequate (8 patients), and failure to pass the endoscope (8 patients). Therefore, 145 patients with a mean age of 61±13 years (range, 17 to 85 years) were included in this study. In five patients the transthoracic echocardiogram was of poor quality; therefore, only 140 subjects were used for comparison of the transthoracic and transesophageal techniques.

Statistical Analysis

Data were analyzed with χ2 or Fisher's exact tests. If a significant difference in the distribution of transesophageal echocardiographic findings among stroke subtypes was detected, an analysis of the standardized residuals was performed to determine which subgroups contributed to the difference. A level of P<.05, using a two-tailed analysis, was considered to be statistically significant.

Results

Clinical characteristics and stroke group classification of the patients included in the study are summarized in Table 1. The largest number of patients was classified into groups 4 and 5, in which there was little clinical indication of the cause of stroke. The number of patients in group 1 (high-risk cardioembolism) and group 2 (lacunar syndromes) was similar. The number of patients in group 3 was small, in part because of the design of the study. Four patients who had at least 50% ipsilateral carotid stenosis also had a high risk factor for cardioembolism and therefore were assigned to group 5. Similarly, two patients with ipsilateral carotid stenosis presented with a lacunar syndrome and a subcortical infarct smaller than 1.5 cm and were placed in group 5.

The noncardiac clinical characteristics of the different stroke groups were similar. A history of congestive heart failure was much more frequent in the high-risk cardioembolism group. Myocardial infarction and cardiac disease of any form were frequent in all groups and as a result of the study design were most frequent in group 1 (Table 1).

The number of patients with echocardiographic findings detected by transthoracic compared with transesophageal echocardiography is shown in Table 2. Transesophageal echocardiography was much more sensitive for detecting left atrial or appendage thrombi, spontaneous echo contrast, and interatrial shunting. Ventricular thrombus, ventricular aneurysm, or myxomatous mitral valve were only detected in a small number of patients, and there was no significant difference between transesophageal and transthoracic echo-
cardiography for detection of these findings. Overall, transesophageal echocardiography documented at least one abnormality in 46% of the patients compared with only 8% who had an abnormality documented by the transthoracic approach (P=.002, $\chi^2$). Of the patients with positive transesophageal echocardiographic findings, 39% had two findings and 6% had three findings.

Left atrial thrombus was detected in four patients by transesophageal echocardiography. None of these thrombi were imaged by the transthoracic approach. Three of these patients had associated high-risk factors for cardioembolism (one of these also had a greater than 50% ipsilateral carotid stenosis), while the remaining patient had a hemispheric stroke of unclear cause (group 4). This patient had a history of hypertension, diabetes, hypercholesterolemia, and electrocardiographic evidence of an old inferior wall myocardial infarction. One group 4 patient also had an unsuspected mitral valve vegetation detected only by transesophageal echocardiography.

Left ventricular thrombi were identified in three patients with hemispheric infarction without carotid stenosis. In one patient the left ventricular thrombus was seen only on the transthoracic study, in another it was visualized only by the transesophageal approach, and in the remaining patient it was imaged by both techniques. Therefore, transesophageal echocardiography was superior to transthoracic imaging for detecting atrial thrombi, while the two approaches complemented each other for detecting ventricular thrombi.

The detection of spontaneous echo contrast occurred with a significant variation in frequency across stroke groups ($P=.001, \chi^2$). This was primarily due to the high frequency of this finding in the cardioembolism group ($P<.001$, analysis of standardized residuals) (Figure and Table 3).

Atrial septal aneurysms were detected with the greatest frequency in the lacunar syndrome group, occurring in 46% of patients ($P<.001$, analysis of standardized residuals), which accounted for the uneven distribution of this finding across stroke groups ($P=.01, \chi^2$). There was no association between the occurrence of atrial septal aneurysm and hypertension, diabetes, or age. Atrial septal aneurysms were frequently detected in association with interatrial shunts. Twenty (61%) of the 31 patients with atrial septal aneurysms also had interatrial shunts ($P<.001, \chi^2$). Interatrial shunts occurred frequently and relatively equally in all stroke groups (Figure and Table 3). No clustering of interatrial shunts was found in groups 4 or 5 (stroke of unclear cause). In the 51 subjects who had a systematic examination of the aorta, 5 ascending aortic plaques (2 protruding) and 1 transverse plaque were detected.

**Discussion**

The decision to obtain echocardiography in a stroke or TIA patient is based on the likelihood that the test will yield findings that could alter patient management. Previous studies in consecutive stroke patients indicate that the yield of transthoracic echocardiography is low, except in young patients or individuals with known cardiac disease. Recent studies have suggested that transesophageal echocardiography has a substantial yield in selected stroke groups.

**Table 2. Comparison Between Transesophageal and Transthoracic Echocardiography**

<table>
<thead>
<tr>
<th></th>
<th>No. of Patients With Specific Echocardiographic Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Left Atrial Thrombus</td>
<td>4</td>
</tr>
<tr>
<td>Swirling Atrial Echoes</td>
<td>23</td>
</tr>
<tr>
<td>Atrial Septal Aneurysm</td>
<td>27</td>
</tr>
<tr>
<td>Interatrial Shunt</td>
<td>28</td>
</tr>
<tr>
<td>Ventricular Thrombus</td>
<td>1</td>
</tr>
<tr>
<td>Ventricular Aneurysm</td>
<td>0</td>
</tr>
<tr>
<td>Moyaomatous Mitral Valve</td>
<td>1</td>
</tr>
</tbody>
</table>

**Table 1. Clinical Characteristics and Classification by Stroke Groups**

<table>
<thead>
<tr>
<th>Stroke Group</th>
<th>Mean Age, y</th>
<th>Male, %</th>
<th>Hypertension, %</th>
<th>Smoking, %</th>
<th>Diabetes, %</th>
<th>History of CHF, %</th>
<th>Previous MI, %</th>
<th>Any Cardiac Disease, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>1: High-risk cardiac embolism (n=20)</td>
<td>61</td>
<td>60</td>
<td>50</td>
<td>55</td>
<td>20</td>
<td>45</td>
<td>30</td>
<td>100</td>
</tr>
<tr>
<td>2: Typical small-vessel (lacunar) infarction (n=26)</td>
<td>63</td>
<td>65</td>
<td>73</td>
<td>42</td>
<td>46</td>
<td>4</td>
<td>15</td>
<td>50</td>
</tr>
<tr>
<td>3: Hemispheric infarction with carotid stenosis (n=12)</td>
<td>58</td>
<td>42</td>
<td>83</td>
<td>58</td>
<td>50</td>
<td>17</td>
<td>17</td>
<td>58</td>
</tr>
<tr>
<td>4: Hemispheric infarction without carotid stenosis (n=25)</td>
<td>55</td>
<td>60</td>
<td>48</td>
<td>64</td>
<td>36</td>
<td>0</td>
<td>8</td>
<td>56</td>
</tr>
<tr>
<td>5: Other (n=62)</td>
<td>63</td>
<td>60</td>
<td>71</td>
<td>60</td>
<td>31</td>
<td>6</td>
<td>23</td>
<td>63</td>
</tr>
<tr>
<td>Total (n=145)</td>
<td>61</td>
<td>59</td>
<td>66</td>
<td>57</td>
<td>34</td>
<td>11</td>
<td>19</td>
<td>64</td>
</tr>
</tbody>
</table>

CHF indicates congestive heart failure; MI, myocardial infarction.
patients; however, the yield in consecutively admitted stroke patients has not been reported.

Before deciding to obtain echocardiography in a stroke patient, considerable clinical information from the patient's history, examination, brain imaging, and carotidduplex is generally available. Based on this information, the etiology of the event can usually be classified into one of four tentative diagnoses: cardioembolic, small-vessel infarction, related to carotid stenosis, or uncertain. This study demonstrates the yield of echocardiography in these subgroups. The major finding of this study is that the distribution of specific transesophageal echocardiographic findings varies substantially between stroke subgroups.

The highest yield of transesophageal echocardiography occurred in group 1, where 65% of the patients had at least one abnormality detected. Both left atrial thrombi and spontaneous echo contrast were most commonly visualized in this group; atrial septal aneurysms and interatrial shunts were also detected frequently, but these findings were also common in other subgroups (Figure).

Spontaneous echo contrast was the most common finding in group 1 patients. This finding may reflect the aggregation of red blood cells secondary to low flow velocity and represent a risk factor for thrombus formation. Spontaneous echo contrast has been shown to be associated with previous stroke as well as atrial fibrillation, mitral valve prostheses, and enlarged left atrial size. Current evidence, including our study, suggests that spontaneous echo contrast is associated with cardiac disorders known to increase the risk for cardiac embolization. It is unclear, however, if spontaneous echo contrast is independently associated with cardiac embolization.

The most surprising finding in this study was that 46% of group 2 (lacunar infarction) patients had atrial septal aneurysms. Twenty-three percent of patients with typical lacunar strokes had interatrial shunts; however, virtually no other abnormalities were detected in this

TABLE 3. Percentage of Patients With Transesophageal Echocardiographic Findings According to Stroke Group

<table>
<thead>
<tr>
<th>Stroke Group</th>
<th>Left Atrial Thrombus</th>
<th>Spontaneous Echo Contrast</th>
<th>Atrial Septal Aneurysm</th>
<th>Interatrial Shunt</th>
<th>Ventricular Thrombus</th>
<th>Ventricular Aneurysm</th>
<th>Myxomatous Mitral Valve</th>
<th>Any Finding</th>
</tr>
</thead>
<tbody>
<tr>
<td>1: High-risk cardiac embolism (n=20)</td>
<td>10</td>
<td>45*</td>
<td>20</td>
<td>30</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>65</td>
</tr>
<tr>
<td>2: Typical small-vessel (lacunar) infarction (n=26)</td>
<td>0</td>
<td>0</td>
<td>46*</td>
<td>23</td>
<td>0</td>
<td>0</td>
<td>4</td>
<td>50</td>
</tr>
<tr>
<td>3: Hemispheric infarction with carotid stenosis (n=12)</td>
<td>0</td>
<td>17</td>
<td>0</td>
<td>8</td>
<td>0</td>
<td>0</td>
<td>8</td>
<td>33</td>
</tr>
<tr>
<td>4: Hemispheric infarction without carotid stenosis (n=25)</td>
<td>4</td>
<td>16</td>
<td>15</td>
<td>12</td>
<td>8</td>
<td>4</td>
<td>4</td>
<td>36</td>
</tr>
<tr>
<td>5: Other (n=62)</td>
<td>2</td>
<td>13</td>
<td>18</td>
<td>27</td>
<td>0</td>
<td>2</td>
<td>0</td>
<td>42</td>
</tr>
<tr>
<td>Total (n=145)</td>
<td>3</td>
<td>16</td>
<td>21</td>
<td>23</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>45</td>
</tr>
</tbody>
</table>

All values are percentages. *P<.001, analysis of standardized residuals.
subgroup. In particular, no patient with a typical lacunar infarction had an intracardiac thrombus or spontaneous echo contrast visualized.

Before the advent of transesophageal echocardiography, atrial septal aneurysm was rarely diagnosed in stroke patients. However, recent transesophageal echocardiographic studies document a prevalence of approximately 15% to 20% in selected stroke populations. The prevalence in age-matched control subjects is unknown. Multiple recent reports have suggested that patients with atrial septal aneurysms are at increased risk for embolic events.22-26 The strong association between atrial septal aneurysm and interatrial shunts that was seen in this study has also been noted by others.25,27

The association between atrial septal aneurysm and lacunar syndromes is unexpected because traditionally, lacunar strokes have been considered to be caused by occlusion of small perforating arteries by characteristic vascular lesions.28 However, recent reports have emphasized that a variety of etiologies can cause lacunes, and currently approximately 10% of typical lacunes are thought to be caused by cardiac embolism.14,29-33 Therefore, the high frequency of atrial septal aneurysms in lacune patients is of substantial interest. It is possible that some lacunar strokes may be caused by embolism of small thrombi formed on atrial septal aneurysms or paradoxical embolism from related interatrial shunts. Alternatively, the atrial septal aneurysms may be incidental findings unrelated to the actual cause of the lacunar stroke. It is possible that risk factors for lacunar stroke, such as hypertension and diabetes, might also contribute to the development of atrial septal aneurysm. In this study, however, there was no association between atrial septal aneurysm and hypertension, diabetes, or age.

Transesophageal echocardiographic findings were relatively uncommon in patients with a hemispheric stroke and at least 50% ipsilateral carotid stenosis (group 3). Two patients had spontaneous echo contrast, while interatrial shunting and myxomatous mitral valve vegetation were detected only in one patient.

In patients in groups 4 and 5, a variety of transesophageal echocardiographic findings (Table 3). Spontaneous echo contrast, atrial septal aneurysms, and interatrial shunts were each detected in approximately 15% to 20% of these patients. One left atrial thrombus and one mitral valve vegetation were identified in group 4 patients, and these findings significantly altered patient management. Several recent studies have suggested that interatrial shunts (patent foramen ovale or atrial septal defects) are detected more frequently in patients with unexplained stroke than in control groups.34-37 However, up to 20% of control subjects also have interatrial shunts detected by transesophageal echocardiography.38-39 Therefore, in an individual patient with a stroke it is often difficult to determine whether the shunt actually played a role in the pathogenesis of the infarct. This is particularly the case for patients with no evidence for venous thrombosis and have other potential explanations for the event. The results of this study confirm that interatrial shunts are common; however, they did not occur substantially more frequently in patients with "unexplained" stroke (groups 4 and 5) than in individuals with other plausible explanations for their events (groups 1 through 3).

Clinical Relevance

The high yield of transesophageal echocardiography in patients with high-risk cardiac disorders is not unexpected. It can be argued that positive transesophageal echocardiographic findings are unlikely to alter the management of these patients because anticoagulation is likely to be indicated even if the echocardiographic examination is unremarkable. However, documentation of a left atrial thrombus or spontaneous echo contrast may help provide additional evidence to support cardiac embolism as the most likely stroke mechanism and provide additional incentive to anticoagulate a patient who is not an ideal anticoagulation candidate.

In patients with typical small-vessel infarctions, the yield of transesophageal echocardiography is low except for the frequent detection of atrial septal aneurysm, often associated with interatrial shunting. This interesting and unexpected finding merits additional studies aimed at determining the frequency of primary and recurrent stroke in patients with atrial septal aneurysms as well as whether these patients are more likely to experience lacunar strokes than other stroke subtypes. The prevalence of atrial septal aneurysms in control populations also needs to be clarified. In addition, the potential of specific therapies to prevent stroke in patients with atrial septal aneurysms needs to be evaluated. At present there are insufficient data to suggest that the identification of an atrial septal aneurysm in a stroke patient should be considered to be confirmatory evidence for cardiac embolism.

The yield of transesophageal echocardiography also appears to be low in patients with significant ipsilateral carotid stenosis. However, because of the small number of patients in this subgroup, no definitive conclusions can be made.

In patients with little clinical indication of stroke etiology, the yield of transesophageal echocardiography is considerable. Findings that significantly altered clinical management such as left atrial thrombus and a mitral valve vegetation were occasionally detected only by the transesophageal study. In addition, atrial septal aneurysms, interatrial shunts, and spontaneous echo contrast were detected in a substantial percentage of this population. Although these findings are of uncertain clinical significance, their detection may influence management in patients without other plausible explanations for their ischemic events, especially if they have clinical features suggestive of cardiac embolism. Therefore, the high yield of potentially clinically significant findings supports the use of transesophageal echocardiography in this subgroup and highlights the need for prospective studies designed to determine which transesophageal echocardiographic findings are independent and treatable risk factors for stroke.

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