Multiplane Transesophageal Echocardiography and Stroke

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Transesophageal echocardiography (TEE) is considered a basic tool in the diagnostic and follow-up evaluation of stroke patients, since up to 40% of cerebral ischemic events are *presumed* to have a cardiac origin. TEE offers a superior resolution of the posterior cardiac structures, such as left atrium and appendage and atrial septum, as well as of the aorta. By means of TEE, evidence has accumulated that some cardiovascular abnormalities (left-sided thrombi, tumors and vegetative lesions, complicated plaques of the aortic arch) are associated with ischemic stroke. Nevertheless, some issues remain unresolved. Will exclusion of atrial thrombus by multiplane TEE preclude embolism after cardioversion of atrial fibrillation? If anticoagulation before and after cardioversion is needed to provide adequate protection against embolism, will TEE be indicated in all patients? Moreover, can the detection of spontaneous echo contrast or enlarged and hypokinetic left atrial appendage in atrial fibrillation modify the therapeutic strategy? Is atrial septal aneurysm (ASA) a real embolic source, particularly when a right-to-left shunt is not associated? Considering the high prevalence of patent foramen ovale (PFO) in normal subjects, how can we identify patients at higher risk of embolism? Furthermore, methodologic points have to be taken into account when we analyze data from the literature. First, most studies are retrospective; a sole prospective study demonstrated that atherosclerotic plaques >4 mm thick in the aortic arch are significant predictors of recurrent brain infarction and other cardiovascular events in patients ≥60 years of age. Second, the association between the aforementioned cardiac abnormalities (mainly ASA and PFO) and cardiogenic embolism is biased by the patient-enrollment criteria used in those studies so that their pathogenetic role has not yet been established. Prospective studies with the enrollment of appropriate control groups will be necessary to define what can be considered a *marker* of embolic risk; the diagnosis "cardiogenic embolism" will not be a definitive diagnosis in most cases. ©1998 by Excerpta Medica, Inc.

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Ischemic stroke represents one of the major sources of mortality and morbidity among industrialized countries, with approximately ≥500,000 events/year occurring in the United States, with an equal or greater number of transient ischemic attacks. Stroke registries show that up to 20–40% of ischemic strokes are caused by cardiogenic emboli.

Conventional transthoracic echocardiography is insensitive in detecting intrathoracic sources of embolism, allowing <10% of positive findings in unselected patients with stroke. Transesophageal echocardiography (TEE) has gained a wide acceptance because of its superior resolution of basal structures such as the left atrium, left atrial appendage, interatrial septum, and thoracic aorta.

For many years, left atrial or ventricular thrombi, tumors, or valve vegetations have been recognized as *definite* causes of thromboembolism. Recently, there has been a growing interest in cardiac abnormalities, such as aortic arch atheroma, patent foramen ovale (PFO), and atrial septal aneurysm (ASA) as *probable* sources of emboli.

AORTIC ATHEROMATIC LESIONS

In the past few years, evidence has accumulated that atherosclerotic disease of the aortic arch may be a source of cerebral embolism. A strong association has been found between protruding plaques in the aortic arch detected by TEE and the risk of ischemic stroke, particularly when the plaques were >4 mm in thickness.[1] The study performed by the French Study of Aortic Plaques in Stroke Group has now assessed the prognostic relevance of this finding in a cohort of 331 patients consecutively admitted to the hospital with brain infarction and followed for up to 2.4 years.[2] Multivariate analysis showed that the presence of plaques >4 mm thick in the aortic arch was a predictor of recurrent brain infarction (relative risk, 3.8) and of all vascular events (relative risk, 3.5) independent of the presence of carotid stenosis, atrial fibrillation, and peripheral arterial disease. However TEE has the ability to assess not only the size of the lesion but also its composition and mobility, and studies are lacking that have addressed whether the various morphologies of the lesions and the presence of mobile components can account for a different clinical course and prognosis.

PATENT FORAMEN OVALE AND ATRIAL SEPTAL ANEURYSM

Paradoxical embolization through a PFO or occult atrial septal defect has been identified as a presumptive mechanism for embolic stroke. Previous studies have focused on stroke populations for having an increased prevalence of PFO compared with healthy people (up to 30%). Nevertheless, these data vary considerably among echocardiographic laboratories, principally due to differences in (1) stroke population

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selection, usually without adequate control groups; (2) techniques used; and (3) diagnostic criteria applied. Moreover, most of the reports are retrospective studies conducted on patients with previous cerebral embolism.

The role of intracardiac right-to-left shunt as a probable source of emboli is still a matter of intense debate. In fact, whereas the statistical association between stroke and PFO prevalence is frequently reported, no data are presented on the correlation with the contemporaneous presence of the real source of thrombus (i.e., deep venous thrombosis, transient or primary hematologic state of hypercoagulability). Besides, no mentions are made of the physiologic conditions (i.e., cough, defecation, or physical activity) able to transiently increase the pressure in the right chambers, and hence to make the shunt easier, immediately before the embolic event.

TEE, particularly by using a multiplane approach, represents the method of choice for diagnosing PFO and ASA, also permitting a high resolution imaging of the interatrial septum anatomical findings. Some researchers have tried to identify the morphologic and functional characteristics of those PFO that more frequently allow paradoxical embolization. Hausmann et al[3] identified a more severe right-to-left contrast shunting and a larger opening of the PFO as the main characteristics, in estimating the clinical likelihood of paradoxical embolism in PFO patients. Van Camp et al[4] demonstrated that an early and massive shunting through an abnormal PFO may represent a possible mechanism of cryptogenetic stroke. On the other hand, the separation between the muscular atrial septum and fossa ovalis membrane, and hence the degree of shunting, may be different from cardiac cycle to cardiac cycle, depending on hemodynamic and respiratory changes. In addition, there are no studies on the feasibility and reproducibility of these functional parameters in the same patient at different times, and consequently under different conditions.

Moreover, Stone et al[5] noted that patients with large shunting through a PFO are at significantly higher risk for subsequent neurologic events when compared with those with a small degree of shunt. Although this is a prospective study of a pathology with a very low recurrence rate (1–2% per year), it seems interesting to note that 3 patients, of the 5 who suffered a subsequent neurologic event, had a history of prior unexplained stroke. Hence again, the selection of study population may play a role in the interpretation of data.

One of the most discussed *probable* intracardiac sources of emboli is ASA. It has been postulated that it may determine cerebral ischemia by 3 different mechanisms: (1) development of a thrombus within the left side of the aneurysm; (2) association with arrhythmia; and (3) paradoxical embolism via PFO. The association between ASA and PFO is a well-documented abnormality. Mügge et al[6] found that the most common abnormality associated with ASA was PFO. In addition, patients with both anomalies showed a high frequency of previous embolic events, but transesophageal evidence of thrombi attached to ASA was a rare condition. Whereas it seems reasonable to postulate a favorable mechanical influence of ASA in permitting right-to-left shunting in presence of interatrial patency, ASA alone appears unable to determine embolic stroke. Moreover, there is a lack of consensus on anatomical and noninvasive criteria for identification of true interatrial aneurysm. When a cut-off point between redundant membrane and ASA is a definite concept, it should be easier to understand the real impact of this abnormality on cardioembolic stroke.

COST EFFECTIVENESS OF TEE IN CEREBRAL ISCHEMIA

TEE is useful in detecting the potential intrathoracic source of embolism and it is often performed for the evaluation of patients suffering cerebral ischemic episodes or other systemic events. These studies are usually ordered by neurologists as a part of the initial evaluation of patients hospitalized with cerebral ischemic events, as well as to base any therapeutic decisions on the TEE findings. However, it is still controversial whether all such patients should undergo TEE, and there are no strict guidelines as yet for patient selection. The decision to perform TEE after stroke or other embolic events should be based on the likelihood of the findings contributing to patient management; to be cost-effective, a test should provide information leading to therapeutic decisions that could not reliably be made using other, less expensive tests. This is not the case of routine TEE for cerebral ischemia. Although the presence of left atrial thrombus increases the risk of subsequent embolism, and left atrial spontaneous echo contrast may be predictive of future thromboembolic events—both findings indicating the need for a long-term systemic anticoagulation—any other cardiac abnormality found at TEE is often of less clinical and prognostic relevance. Paradoxical embolism through a PFO, atrial septal defect, and aneurysm is a well-recognized mechanism for systemic embolism; unfortunately, this causal relation may be difficult to establish in a given patient. Moreover, there are no studies on which to base therapeutic recommendations for the findings of ASA, PFO, mitral valve prolapse, small atrial septal defect, and aortic atheromas. In this view, an algorithm has recently been proposed for the use of TEE in evaluating patients with cerebral ischemic events.[7] Considering that most patients with atrial fibrillation are candidates for empirical anticoagulation, this approach would limit the use of TEE as a screening test to those patients with clinical evidence of heart disease but without atrial fibrillation and to those whose findings on TTE were suspicious for a significant abnormality, such as vegetation or larger atrial septal defect. Use of this algorithm would decrease the number of TEE examinations by at least two-thirds.

TEE AND ATRIAL FIBRILLATION

Atrial fibrillation is the most common sustained arrhythmia encountered in clinical practice. The rate

of ischemic stroke and transient ischemic attacks among elderly people with atrial fibrillation, even in the absence of valvular disorders, averages about 7% per year.[8] Most ischemic strokes associated with atrial fibrillation are probably due to embolism of stasis-induced thrombi forming in the left atrium and particularly its appendage. TEE is a highly accurate method of detecting atrial thrombi. Moreover, several studies performed by TEE in patients with nonrheumatic atrial fibrillation have demonstrated that the presence of left atrial spontaneous echo contrast is a marker of previous embolism and it is a potent independent risk factor for cerebral ischemic events with a 4-fold increase in risk. Based on these observations, spontaneous echo contrast, as with left atrial thrombus, is felt by many clinicians to be an indication for warfarin sodium therapy.

Cardioversion from atrial fibrillation is commonly used both to prevent thromboembolism and to improve left ventricular function. However, up to 7% of patients undergoing cardioversion without anticoagulation experience clinical thromboembolism. Prophylactic anticoagulation (3 weeks before and 4 weeks after cardioversion) has been shown to decrease the incidence of this complication to 0–1.6% but it carries its own risk, mainly of hemorrhage. Recently, Manning[9] reported no thromboembolic event among 186 patients, with atrial fibrillation lasting >2 days in duration, who underwent successful cardioversion without several weeks of anticoagulation and in whom TEE showed no atrial thrombi. This is by far the largest prospective and consecutive study evaluating the safety of TEE for determining stroke risk in patients undergoing cardioversion. Early studies have reported 17 cases of thromboembolic events after cardioversion despite exclusion of atrial thrombi by TEE.[10] However, these patients were not adequately anticoagulated at the time of embolism, 5 of them had left atrial spontaneous echo contrast and, finally, all patients but one were investigated by means of monoplane or biplane TEE, perhaps yelding an overall lower diagnostic sensitivity of the procedure. At present, the sensitivity or specificity of different transesophageal echocardiographic imaging planes for the detection of atrial thrombi has not been assessed and the additional value of multiplane TEE in this setting remains to be defined.

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