Transesophageal Two-Dimensional Echocardiography in Young Patients With Cerebral Ischemic Events

Gerald Zenker, MD, Raimund Erbel, MD, Günter Krämer, MD, Susanne Mohr-Kahaly, MD, Michael Drexler, MD, Karl Harnoncourt, MD, and Jürgen Meyer, MD

Using transesophageal echocardiography, cardiac structures can be imaged with high resolution. The aim of our study was to evaluate whether transesophageal echocardiography is superior in detecting mitral valve prolapse and other cardiac abnormalities compared with transthoracic echocardiography in an age-matched control group and in young patients with cerebral ischemic events (patient group). Forty patients with cerebral ischemic events (mean age 35.2 years) and 29 controls (mean age 30.4 years) were examined using both methods. Transthoracic and transesophageal echocardiography showed a significantly higher incidence of mitral valve prolapse in the patient group compared with the control group (p<0.001). By means of transesophageal echocardiography, it was possible to measure highly significant bulging in both the anterior and the posterior mitral leaflet in the patient group compared with the control group (p<0.001), and the thickness of the mitral leaflets was significantly higher in the patient group. In 9 of 20 (45%) patients with normal transthoracic echocardiograms, transesophageal echocardiography showed pathologic findings. We found transesophageal echocardiography to be a sensitive method for detecting mitral valve prolapse as well as valve changes and other cardiac abnormalities not detectable by conventional echocardiography. Our study underlines the role of mitral valve prolapse in young stroke patients as a relevant risk factor and emphasizes the importance of changed mitral valve morphology. (Stroke 1988;19:345–348)

A series of studies has demonstrated an association of mitral valve prolapse (MVP) with cerebral ischemic events in younger patients. In 1980, Barnett and coworkers, by means of M-mode echocardiography, pointed out that the incidence of MVP in stroke patients <45 years of age was significantly higher (40%) than in age-matched controls. An increasing number of reports indicate that it is necessary to differentiate between "normal" MVP and a pathologic form with valve thickening and a high degree of myxomatous tissue change. Some clinical retrospective studies address the possibility that the extent of valve involvement may influence the risk of embolic stroke. Transesophageal echocardiography (TEE) is a recently developed imaging technique with a very high degree of reliability and excellent resolution of the cardiac structures, especially the mitral valve. Until now, it has not been used for the cardiologic examination of younger patients with cerebral ischemic events.

Our investigation examined whether TEE can provide additional diagnostic information in comparison with conventional transthoracic echocardiography (TTE) in patients with cerebral ischemic events and in age-matched controls. In addition, we were also interested in analyzing the incidence of MVP by TEE, in quantifying the bulging of the mitral leaflets over the valve plane in normal and changed valves, and in performing measurements related to valve thickness in both patients and controls.

Subjects and Methods

The patient group consisted of 40 subjects under the age of 45 (17 men and 23 women, mean age 35.2, SD 8.4, range 18–45 years) with cerebral ischemic events hospitalized between January and December of 1984 in the Department of Neurology of the University Hospital of Mainz. All patients underwent TTE and TEE in the cardiologic unit of the University of Mainz, and all had a detailed neurovascular diagnostic workup including cerebral computed tomography. Transcatheter cerebral four-vessel angiography was performed in 36 of the 40 patients and revealed a significant stenosis in only one case with a recent whiplash injury. Thirteen patients had transient ischemic attacks, 4 had reversible ischemic neurologic deficits, 21 had a completed stroke, and 2 had multiple cerebral infarctions. In 15 cases, an angiographic pattern suggestive of embolization to the intracranial cerebral vessels was found, mostly in the distribution of the middle cerebral artery. The neurovascular risk factors are listed in Table 1.

The control group consisted of 29 age-matched healthy subjects (14 men and 15 women, mean age 30.4, SD 5.13, range 20–41 years) who were mostly medical students and staff without any cardiac complaints or history of cerebrovascular disease.
TABLE 1. Distribution of Neurovascular Risk Factors in 40 Patients With Cerebral Ischemic Events

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>MVP (n = 24)</th>
<th>No MVP (n = 16)</th>
<th>$\chi^2$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td>0</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Nicotine abuse</td>
<td>1</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Oral contraceptives</td>
<td>3</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Obesity</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Coronary heart disease</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td>0</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>0</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>No risk factor</td>
<td>20</td>
<td>4</td>
<td>p&lt;0.05</td>
</tr>
</tbody>
</table>

MVP, mitral valve prolapse.

All subjects included gave their informed consent, and the study was performed respecting the principles outlined in the declaration of Helsinki.

Echocardiographic Technique

The echocardiographic examination was performed using a Diasonic 6400 phased-array sector scanner (Palo Alto, California). Within 3–4 weeks after the cerebral ischemic event, the patients were submitted to conventional TTE performed by two echocardiographic examiners without knowledge of the patient’s history. TTE examinations used the parasternal and apical acoustic windows. The diagnosis of MVP was made using the criteria proposed by Markiewicz et al in the one-dimensional echocardiogram and by Morganroth et al in the two-dimensional echocardiogram. The echocardiograms were recorded with a Panasonic video recorder and analyzed frame by frame using two independent observers who were not familiar with the patient’s history. Valves were considered abnormal if the prolapsing mitral valve appeared thickened, shaggy, and redundant on more than one examination plane and club-shaped in the long-axis parasternal view triggered in diastole.

Transesophageal echocardiography. All patients and controls underwent a TEE examination using an echoscope developed by Hanrath et al in which a special 3.5-MHz transducer array of 32 elements is fitted to the distal end of a gastroscope with an outer diameter of 9 mm. Patients fasted for approximately 16 hours before undergoing TEE. Local anesthetic was applied to the pharyngeal region before examination. Since a 3.5-MHz transducer had been fixed in place of the fiber optic system of a conventional gastroscopy, patients suspected of having esophageal disease swallowed barium under x-ray control to exclude a diverticulum of the esophagus. Three patients were excluded from this study because they were not able to swallow the echoscope. The examination lasted between 20 and 25 minutes, with no side effects. As with TTE, the whole examination was recorded with a video recorder and analyzed by two independent observers for semiquantitative statements.

The transesophageal measurements of the mitral valve were performed in a standardized transesophageal examination plane at 10 cm scanning depth (Figure 1) and were taken by one independent observer who was blinded to the origin of the videotapes. The prolapse of the mitral leaflets was measured from a line between the leaflet coaptation point and the mitral anulus to the point of maximum prolapse toward the left atrium. MVP was assumed if one or both mitral leaflets prolapsed at a minimum of 3 mm over the valve plane into the left atrium. The leaflet thickness was measured in late systole, triggered by electrocardiography at the end of the T wave.

**Figure 1. Transesophageal echocardiogram of patient with ischemic stroke and markedly thickened mitral valve and prolapse of anterior mitral leaflet (line connects mitral ring with coaptation of mitral leaflets). LA, left atrium; LV, left ventricle; AML, anterior mitral leaflet; PML, posterior mitral leaflet.**
wave, in the middle of a line drawn from the leaflet coaptation point to the mitral annulus (Figure 1).

Statistical Methods

F test and Student’s t test were used to compare ages. Univariate testing of the variables concerning risk factors and incidence of MVP were evaluated with Χ² analysis. To compare the mitral valve prolapse and thickness, the nonparametric Wilcoxon U test was used. The significance level was 0.05.

Results

A comparison of TTE and TEE shows a higher incidence of MVP detected by TEE in the patient group as well as in the control group, but the difference in detection was not significant within groups. Using both methods, a significantly higher incidence of MVP was found in the patient group compared with the control group (p < 0.001). In comparison, M-mode echocardiography showed MVP in only 10 of 40 patients (25%). The bulging of the mitral leaflets over a defined valve plane, the incidence of morphologically changed valves, and the thickness of the valves were greater measured by TEE in the patient group than in the control group (Table 2).

From the 20 patients with normal TTE, 9 (45%) had additional pathologic findings with TEE. Four of the 20 had MVP; 3 of the 4 had valve thickening, 2 of the 4 had additional tricuspid valve prolapse, and 2 of the 4 had aortic valve prolapse. One of the 20 had thickening of the anterior mitral leaflet, 2 of the 20 had an atrial septal defect with bidirectional shunting confirmed by intravenous contrast administration, and 2 of the 20 had an atrial septal aneurysm. From the 26 controls with normal TTE, 2 (8%) with MVP on TEE had additional atrial and tricuspid valve prolapse.

In Table 3 the additional diagnostic capabilities of TEE regarding different cardiac pathology compared with conventional echocardiography are demonstrated.

Discussion

MVP is one of the most common echocardiographic findings. The Framingham Study revealed an incidence of approximately 5–7% in the normal adult population using M-mode criteria. Although many studies seem to prove the causal relation between MVP and ischemic stroke in young patients, the individual risk of stroke in MVP is still an enigma. Follow-up studies indicate that the occurrence of cerebral ischemic events in MVP is a rare event. However, for the examination of the valves, only M-mode echocardiography was used. Assessment of mitral valve motion or thickness by M-mode echocardiography is hampered by failure of the ultrasound beam to provide spatial orientation relative to surrounding structures. Two-dimensional echocardiography would seem to be the ideal technique for defining MVP because of its ability to define spatial relations. However, the sensitivity of the method depends very much on the use of different examination planes and selected combinations of echocardiographic signs. From the point of view of pathology, the primary problem is the infiltration by a myxomatous material that varies greatly according to the extent of valve involvement. Postmortem studies in young patients with myxomatous valve involvement described endocardial friction lesions and platelet-fibrin deposits between the posterior mitral leaflet and the left atrial wall. In addition, these lesions were found in conjunction with ischemic stroke. Valvular fibrosis and thickening are common signs, and fissures of the valve surface are another nidus for thrombus formation. In connection with these pathologic findings, it seems plausible that, with increasing histologic changes of the mitral valve apparatus, the likelihood of endocardial friction lesions and fibrin-platelet deposits in the mitral valve area increases. Retrospective two-dimensional echocardiographic studies have emphasized the necessity to differentiate between thickened valves with prolapse and echocardiographically normal but prolapsing valves. A higher incidence of mitral regurgitation, tricuspid prolapse, and aortic dilatation was shown in the group with valve thickening. However, as a result of poor

| TABLE 3. Incidence of MVP Analyzed by TTE and TEE and Measurements Concerning Bulging of Mitral Leaflets Over Valve Plane and Mitral Valve Thickness Measured by TEE |
|-----------------|-----------------|-----------------|-----------------|
|                  | Controls (n = 29) | Patients (n = 40) |
|                  | TTE  | TEE  | TTE  | TEE  |
| Aortic valve prolapse | 0   | 2    | 0    | 4    |
| Tricuspid valve prolapse | 0   | 2    | 0    | 11   |
| Atrial septal defect | 0   | 0    | 0    | 2    |
| Atrial septal aneurysm | 0   | 0    | 0    | 1    |
| None             | 25   | 22   |      |      |

| Values are mean±SD. MVP, mitral valve prolapse; TTE, transthoracic echocardiography; TEE, transesophageal echocardiography. |
|-------------|-------------|-------------|-------------|
| *Χ² analysis; †Wilcoxon U test. |
resolution and imaging quality, these echocardiographic signs could not be well defined. In our study, we used TEE to evaluate young stroke patients. This method proved to have the highest resolution of the ultrasonic methods because of the close anatomic relation of the esophagus to the heart, the high transducer frequency, and the possibility of obtaining axial examination planes. Several studies demonstrated the superiority of TEE over conventional TTE in the detection of infective endocarditis.

In our study, 65% of the MVP patients had morphologic changes of the valves on TEE and differed significantly from the control group concerning measured valve thickness. Using our criteria for the diagnosis of MVP, by means of TEE we detected MVP in 60% vs. 50% by means of TTE. We also independently measured the extent of valve bulging over the valve plane in a standardized examination plane in TEE. TEE defined the prolapsing leaflets of the mitral valve with a higher degree of accuracy than TTE. In 9 of 20 patients with normal TTE, TEE enabled us to diagnose important findings such as aortic valve prolapse, tricuspid valve prolapse, and atrial septal defect, which might be important for further follow-up.

Although the transesophageal technique causes some discomfort to the patient, the high image quality and the fact that stroke patients can be examined with this method. In agreement with other studies, we were able to point out that, in a selected group of young patients, MVP with morphologic valve changes is a relevant neurovascular risk factor.

Acknowledgments

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