Cerebral Ischemic Events in Patients with Mitral Valve Prolapse

BURLON A. SANDOK, M.D.* AND EMILIO R. GIULIANI, M.D.†

SUMMARY All patients 20 years old or older referred for echocardiographic examination and found to have mitral valve prolapse during the period January 1975 through December 1979 were included in the study. Of the 1,138 patients, two-thirds were women and one-third were men. Their average age was 48.4 years. Forty patients (3.5%) had histories of prior focal cerebrovascular ischemic events. In 26 of the 40 patients, no responsible mechanism other than mitral valve prolapse was identified, and in 4, the ischemic event occurred during an episode of bacterial endocarditis, a known complication of mitral valve prolapse. In 10 of the 26 patients, there was clinical information to suggest an embolic mechanism for the ischemia. A conservative estimate of the prevalence rate for cerebral infarction in this group of patients is four times greater than the rate expected in a normal population. This difference is likely due to the contribution of mitral valve prolapse in the pathogenesis of cerebral infarction.

MITRAL VALVE PROLAPSE is a relatively common condition. Based upon the criteria utilized, mitral valve prolapse may occur in approximately 6% of the young female and a lesser percentage of the young male population. Many patients are symptom-free, but most have associated chest pain, palpitations, dyspnea, fatigue, and light-headedness. Although it has generally been regarded as a benign syndrome, four major complications have been recognized: (1) progressive mitral regurgitation, (2) spontaneous rupture of the chorda tendineae, (3) sudden death believed due to ventricular fibrillation (occurring in 1 to 1.6%), and (4) bacterial endocarditis (which occurs in 3% of patients). Generalized, nonfocal neurologic symptoms, such as syncope and giddiness, are common. Focal cerebral ischemic events are a recognized complication of endocarditis. With the exception of one case reported by Barlow and Bosman in 1966, focal neurologic complications in the absence of endocarditis were not reported to be associated with this condition until the group at the University of Western Ontario called attention to this association in a series of reports. Since then, although others have emphasized this relationship, the prevalence of cerebral ischemic events in patients with mitral valve prolapse remains unknown.

Patients and Methods

All patients 20 years old or older who were referred to the Mayo Clinic Echocardiographic Laboratory and found to have mitral valve prolapse during the time interval January 1975 through December 1979 were included in the study. The criteria used for the diagnosis of mitral valve prolapse were: (1) in patients with midsystolic clicks or mitral murmur or both, posterior-superior displacement of the mitral valve leaflets by M-mode or two-dimensional echocardiographic study and (2) in patients with a normal cardiac examination.

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This investigation was supported in part by Research Grant NS-6663 from the National Institutes of Health, Public Health Service.

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Received December 10, 1981; revision accepted February 24, 1982.
TABLE 1 Cerebral Ischemic Events (CIE) in Patients With Mitral Valve Prolapse

<table>
<thead>
<tr>
<th>Age group (yr)</th>
<th>Males</th>
<th>Females</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>20-44</td>
<td>99</td>
<td>341</td>
<td>440</td>
</tr>
<tr>
<td>CIE</td>
<td>2</td>
<td>11</td>
<td>13 (3.0%)</td>
</tr>
<tr>
<td>45-54</td>
<td>92</td>
<td>139</td>
<td>231</td>
</tr>
<tr>
<td>CIE</td>
<td>3</td>
<td>5</td>
<td>8 (3.5%)</td>
</tr>
<tr>
<td>≥ 55</td>
<td>193</td>
<td>274</td>
<td>467</td>
</tr>
<tr>
<td>CIE</td>
<td>10</td>
<td>9</td>
<td>19 (4.1%)</td>
</tr>
</tbody>
</table>

Average age (yr): *31.8, †49.7, ‡63.4.

TABLE 2 Findings on Cardiac Auscultation of Patients With Mitral Valve Prolapse

<table>
<thead>
<tr>
<th>Finding</th>
<th>No. of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Click-murmur</td>
<td>444</td>
</tr>
<tr>
<td>Apical, mid, or late systolic murmur only</td>
<td>274</td>
</tr>
<tr>
<td>Pansystolic murmur</td>
<td>198</td>
</tr>
<tr>
<td>Mid systolic click only</td>
<td>138</td>
</tr>
<tr>
<td>Normal examination</td>
<td>84</td>
</tr>
<tr>
<td>Total</td>
<td>1,138</td>
</tr>
</tbody>
</table>

age and sex group are listed in table 3. Although the presumed mechanism of ischemia remains unknown in many of the patients, not all the events were likely related to mitral valve prolapse (table 4). Other mechanisms of ischemia were identified in 14 patients. However, four of these had their ischemic event during an episode of bacterial endocarditis, a known complication of mitral valve prolapse. In 26 patients, no mechanism other than mitral valve prolapse was noted. In 10 of the 26 patients with mitral valve prolapse as a presumed cause of their neurologic deficit, there was clinical information available to suggest an embolic mechanism. Two patients had embolic occlusions of intracranial vessels seen on angiography; three patients experienced their focal symptoms at the time of a transient cardiac arrhythmia; three patients had multiple ischemic events involving more than one vascular territory; one patient had amaurosis fugax; and one patient experienced a retinal infarction with a platelet fibrin embolus visible in the retinal arteriole. The occurrence of cerebral ischemic events in these 26 patients did not correlate with the severity of the valvular lesion as determined by cardiac examination. Three events occurred in the presence of a normal cardiac examination, 2 with a mid systolic click only, 3 with a click-murmur, 12 with an apical mid systolic or late systolic murmur, and 5 with a pansystolic murmur.

Discussion

The point prevalence rate for cerebral infarction in a normal population is approximately 500 per 100,000, and this includes persons with all responsible mechanisms for their infarction. Our study group is not a normal population but represents a highly selected group of patients referred to a medical center for further evaluation and found to have mitral valve prolapse. Nonetheless, considering only patients with cerebral infarction and eliminating from consideration the eight patients who were found to have mitral valve prolapse while undergoing evaluation within 1 month of their cerebral infarction, and who likely represent an obvious source of bias, there still remain 25 patients with mitral valve prolapse who have had a prior cerebral infarct. This conservative rate of occurrence of 2,212 per 100,000 is still approximately four times greater than expected. This difference is likely due to the contribution of mitral valve prolapse on the pathogenesis of cerebral infarction.

The patients included in this study represent a selected group of patients who were referred and seen at a...
medical center primarily because of symptoms suggestive of cardiac disease; they are not representative of a population sample of individuals with mitral valve prolapse. It is reasonable to assume that in our study group, complications of all types might be higher than in the mitral valve prolapse population at large. The observed stroke prevalence in an unselected population of individuals with mitral valve prolapse is therefore, likely to be somewhat lower.

The mechanism of focal cerebral ischemic events in many patients with mitral valve prolapse is presumed to be embolic. Clinical observations of multiple events occurring in several vascular distributions — angiographic observation of intracranial branch occlusions in the absence of atheromatous or other disease and pathologic observations of the value at surgery or postmortem — support this presumed mechanism. The shortened platelet survival time in some patients further suggests a thromboembolic mechanism. In spite of the increased prevalence of focal cerebral infarction noted in our patients with mitral valve prolapse, the annual incidence of new symptoms in this group of patients is likely to be low, and we have not advocated preventive treatment (other than antibiotic prophylaxis) in patients with mitral valve prolapse who have not had focal ischemic symptoms. In patients with mitral valve prolapse who have experienced focal cerebral ischemic events, caution should be exercised in attributing the cerebral event to the valve prolapse, and evaluation should be undertaken to attempt to define other potentially responsible mechanisms. In patients with other identifiable mechanisms of infarction, treatment is directed toward that mechanism. When no other mechanism is recognized, mitral valve prolapse is presumed to be the cause. In the latter circumstance, we have advocated the use of medical therapy, most often with antiplatelet agents. In patients with recurrent symptoms, oral anticoagulation has been utilized.

References
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Cerebral ischemic events in patients with mitral valve prolapse.
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*Stroke*. 1982;13:448-450
doi: 10.1161/01.STR.13.4.448

*Stroke* is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0039-2499. Online ISSN: 1524-4628

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