Mitral Valve Prolapse and Cerebral Infarction

ROBERT G. HART AND J. DONALD EASTON

SEVERAL RECENT REPORTS, including the one by Scharf et al.¹ in this issue, have firmly established the association of mitral valve prolapse (MVP) and cerebral infarction, especially in young adults with unexplained stroke (table 1). It is not surprising that this association is more difficult to demonstrate in older stroke patients, in whom atheroembolic mechanisms predominate.²,³ Assuming that the incidence of MVP-associated cerebral ischemia does not vary with patient age, as suggested by Sandok and Giuliani⁴ in this issue, and even if one-third of all cerebral infarctions in young adults are related to MVP, the incidence of MVP-related strokes is only 1/100,000/year. In older adults who have a stroke incidence of 80/100,000/year, the contribution of MVP (estimated to be 1.25%) could easily be overlooked.

MVP is an important cause of cerebral infarction in young patients with otherwise unexplained cerebral ischemia. Nevertheless, MVP-associated ischemia remains a diagnosis of exclusion and other causes of cerebral ischemia must be vigorously excluded before attributing stroke to MVP. Barnett et al.² reported MVP as the only abnormality in 30% of unselected patients under age 45 with cerebral ischemia. In a population-based, retrospective survey of causes of ischemic stroke patients, in whom atheroembolic mechanisms predominate (criteria vary from 2mm to 5mm posterior displacement). Angiocardiographic diagnosis of MVP is also poorly quantifiable with no standardized criteria being used. Recently 2-D echocardiography has been proposed as the diagnostic standard, but it has not been generally confirmed as such due to variations in technical expertise.

It is clear that cerebral ischemia rarely occurs in unselected young adults with MVP. The apparent paradox found in the low risk of stroke in unselected people with MVP and the high prevalence of MVP in young patients with unexplained stroke, as noted by Jones et al.⁶ in this issue, is easily explained. Again assuming that one-third of stroke in young adults is due to MVP (probably an over-estimate), a stroke incidence of 3/100,000/year in patients under age 40,¹¹ and a 6% prevalence of MVP in all young adults, it is quickly calculated that the risk of stroke in all young adults with MVP is only 1/6,000/year. Clearly, no prophylactic treatment to prevent stroke is warranted in asymptomatic people with MVP.

Establishing or excluding the presence of MVP in an individual patient is often difficult, as diagnostic standards are controversial.¹² We have recently evaluated two young adults with unexplained cerebral infarction who illustrate this dilemma: one had definite auscultatory findings of MVP in the opinion of a senior cardiologist but had four M-mode and three 2-D echocardiograms that were normal; the other had no auscultatory findings, a normal 2-D echocardiogram, but MVP on M-mode echocardiography.

Auscultatory findings are absent in about 20% of patients with M-mode echocardiographic evidence of MVP. However, MVP has been reported in 6 to 21% of asymptomatic females using M-mode echocardiographic testing, emphasizing the variation in diagnostic criteria (criteria vary from 2mm to 5mm posterior displacement). Angiocardiographic diagnosis of MVP is also poorly quantifiable with no standardized criteria being used. Recently 2-D echocardiography has been proposed as the diagnostic standard, but it has not been generally confirmed as such due to variations in technical expertise.

Notably, most reports of MVP-related cerebral ischemia do not specify the diagnostic criteria used. At present, the aggregate data from careful auscultation by expert physicians and M-mode and 2-D echocardiography are most useful. The presence of typical auscultatory findings and clear M-mode echocardiographic evidence would seem to make the diagnosis definite. The presence of only auscultatory or echocardiographic evidence should be considered probable MVP. The ultimate role of 2-D echocardiography awaits further data.

Routine echocardiography is not indicated in unselected, older stroke patients, in whom cerebrovascular atherosclerosis is the likely mechanism even in the presence of MVP. Even if one assumes a similar incidence of MVP-associated cerebral ischemia for all age groups, it is calculated that only 1% of cerebral infarctions would be associated with MVP in unselected patients, explaining the low yield of routine echocardiography in such patients. If no etiology for cerebral ischemia is found after a search for common causes, echocardiography seeking MVP may be warranted, although the relationship of MVP to ischemia should still be regarded with some skepticism.

There are currently no reliable clinical, laboratory or echocardiographic indicators to distinguish which people with MVP are prone to stroke.¹³ A relationship

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References


### Table: Prevalence of Mitral Valve Prolapse (MVP) in Cerebral Ischemia

<table>
<thead>
<tr>
<th>Category</th>
<th>N</th>
<th>Mean Age</th>
<th>% MVP (patients)</th>
<th>% MVP (controls)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unselected ischemia</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Barnett et al^2</td>
<td>60</td>
<td>≤45</td>
<td>40%</td>
<td>6.6%</td>
</tr>
<tr>
<td>— age under 45</td>
<td>141</td>
<td>&gt;45</td>
<td>5.7%</td>
<td>7.1%</td>
</tr>
<tr>
<td>Greenland et al^4</td>
<td>117</td>
<td>58</td>
<td>11%</td>
<td>4%</td>
</tr>
<tr>
<td>Bergeron &amp; Shah^2</td>
<td>184</td>
<td>59</td>
<td>1%</td>
<td>—</td>
</tr>
<tr>
<td>Bensaid et al^6</td>
<td>116</td>
<td>&gt;40</td>
<td>5.2%</td>
<td>—</td>
</tr>
<tr>
<td>Unexplained ischemia†</td>
<td>36</td>
<td>≤45</td>
<td>61%</td>
<td>6.6%</td>
</tr>
<tr>
<td>Bensaid et al^6</td>
<td>20</td>
<td>&lt;40</td>
<td>20%</td>
<td>—</td>
</tr>
<tr>
<td>Hart et^7</td>
<td>15</td>
<td>≤40</td>
<td>47%</td>
<td>—</td>
</tr>
<tr>
<td>DeBono &amp; Warlow^3</td>
<td>40</td>
<td>58</td>
<td>15%</td>
<td>4%</td>
</tr>
<tr>
<td>Scharf et al</td>
<td>47</td>
<td>&lt;40</td>
<td>28%</td>
<td>8.4%</td>
</tr>
</tbody>
</table>

*Data on patients over age 40 are classified in the unselected category because of lack of angiographic data, although the authors state there was no obvious etiology for stroke.*

†Patients with other probable causes are excluded, although Barnett et al^2 and Scharf et al include women on oral contraceptives and few of Bensaid et al’s^6 patients had cerebral angiography.

between MVP-associated cerebral ischemia and migraine has been noted in a small number of patients. 14, 15 Platelet abnormalities have been reported in MVP patients with and without cerebral ischemic symptoms, as well as in young stroke patients without MVP. 1, 15, 16 A linked mesenchymal dysplasia involving platelets and collagen of the mitral valve has been postulated. 17

An embolic mechanism for the cause of MVP-associated stroke is supported by angiographic evidence. 13 Valvular thrombi forming on the abnormal valves presumably constitute the typical example. Two-dimensional echocardiography in patients with MVP-associated cerebral ischemia has visualized valvular lesions that suggest small thrombi and histologically verified thrombus has been found attached to the valve. 18 However, MVP-associated atrial fibrillation could cause left atrial clot as a source of larger emboli. Further, it is possible that MVP is only a marker of, and not the cause of, hyperaggregate platelets. 13, 15, 16

The treatment of patients with MVP-associated cerebral ischemia has been largely empiric. Recurrent events have been reported, often separated by years, but the natural history is uncertain. 2, 7, 10, 13 The strategy of initial therapy with platelet antiaggregation agents as outlined by Barnett^13 and Sandok and Giuliani^8 seems reasonable pending further information.
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