Mitral Valve Prolapse and Cerebral Ischemic Events
A Comparison Between a Neurology Population with Stroke and a Cardiology Population with Mitral Valve Prolapse Observed for Five Years

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SUMMARY
Two populations of patients with mitral valve prolapse were analyzed to identify factors predisposing to the development of cerebral emboli. Of 760 patients followed for up to five years by our cardiologists with echocardiographically demonstrated mitral valve prolapse (MVP), only one, aged 82 years, has had a stroke. In contrast, of 43 patients admitted to our neurology service with a cerebral embolus and no evidence of carotid or other cardiac lesion and in whom echocardiography was performed, MVP was present in 9. No contributing etiologic mechanisms were uncovered to account for the disparity between the cardiology and neurology populations. However, with the apparent increased incidence of MVP in young patients with cerebral ischemia, both groups require longitudinal follow-up to understand better the factors that predispose a small percentage of patients with mitral valve prolapse to the development of cerebral ischemia.

Results
Our cardiologists identified 760 patients with MVP (Group A). This was a selected population as the patients were seen specifically because of some question of cardiac disease and were then referred for echocardiography. All had a complete history, physical exam, and standard electrocardiography. Particular attention was carefully directed toward any history of cerebral or ocular ischemia. These patients have been observed for up to five years, with an average of 24.3 months, and are currently being re-evaluated at the Lahey Clinic Medical Center at least every two years in our Cardiology Section. The 59% of patients found to have MVP as the only possible pathophysiologic mechanism (see Discussion).

Methods
We reviewed the records of all patients (Group A) with echocardiographically proven mitral valve prolapse seen at the Lahey Clinic Medical Center between July 1974 and July 1979. The diagnosis of MVP was made according to established criteria. All patients have continued to be followed prospectively once MVP was identified. These are compared with an entirely separate population of patients not previously known to have MVP who were initially seen in the Department of Neurology for an acute cerebrovascular event (Group B). Thorough investigation identified MVP as the only possible pathophysiologic mechanism (see Discussion).
ages 40 and 60. These patients were selected from a total of 401 patients seen with cerebrovascular disease. It should be noted, however, that echocardiography was performed in only 43 of the 401 patients. Identifiable common causes for stroke, such as carotid lesions or more obvious cardiac problems, obviated the need for echocardiography in many of these; however, among those with no identifiable cause in whom echocardiography was not performed, we would suspect from our findings that there are possibly further numbers who have unsuspected MVP. Thus, 9 of 43 patients who had echocardiography at the time of a cerebrovascular event were found to have evidence of MVP. No other possible mechanism for their stroke could be found. Eight of the 9 patients were less than 60 years of age, and 4 were less than age 40.

Analysis of Group B identified the presence of a completed cerebral infarction (CI) in 7 of the 9 patients. Clinical analysis of the 7 patients with CI demonstrated 2 with pure motor stroke, 2 with homonymous hemianopsia, and one each with a pure sensory stroke, aphasia, and left central facial weakness. The lesion appeared clinically to mainly affect medium-sized or small vessels in each of the 7 patients with CI; 3 lesions were of lacunar nature, and 4 were a branch occlusion. No patient sustained an occlusion large enough to produce any sign of obtundation to suggest cerebral edema, such as might be seen with a proximal massive occlusion. Although no fatalities occurred, 6 of the 7 with CI had a mild to moderate residual deficit. Two patients had a transient ischemic attack (TIA), both involving the carotid territory. One patient sustained a hemimotor sensory deficit and the other a muscular sensory deficit. (No retinal emboli were seen in this patient or any of the others with carotid system disease on careful undilated fundus examination by the primary neurologist.)

Computed tomography of the brain was carried out in 7 of 9 patients, including 5 with CI and 2 with TIA. These demonstrated a specific focal area of cortical abnormality in the 5 patients with CI and were normal in the 2 patients with TIA. Cerebral angiography was abnormal in 2 of 6 patients demonstrating embolic lesions, one each in the right middle and left posterior cerebral arteries. None of the 6 patients had evidence of primary carotid artery atherosclerotic disease.

Discussion

Our data lend support to Barnett's findings that there is an increased percentage of MVP in patients less than age 60 who present with a stroke. Unfortunately, only 10% of our patients with CI or TIA actually had echocardiography, and we are unable to make a statement comparing our findings with Barnett's thorough analysis of the incidence of MVP in all patients with CI or TIA. None of our patients had concomitant evidence of hypertension, coronary disease, rheumatic heart disease, atrial fibrillation, claudication of the legs, diabetes, abnormal hematologic function, significant elevation in erythrocyte sedimentation rate, abnormal antinuclear antibodies, or positive serologic test for syphilis. Two patients, including the only one using estrogens, had a history of uncomplicated migraine, but in both a cerebral embolus was documented by cerebral angiography. Although patients with MVP have an increased incidence of bacterial endocarditis, none of our patients had clinical suggestion or laboratory data to support such a diagnosis. Nevertheless, this possibility should always be considered in any patient in whom an acute cerebral event develops and in whom MVP is documented by echocardiography. Thus, analysis of the many factors known to predispose to cerebrovascular disease has not been particularly helpful to us in explaining the apparent disparity present when primary cardiac patients with MVP are separated from the primary neurologic groups with CI or TIA and later found to have MVP.

Initial treatment in Group B presenting with CI or TIA and found to have MVP has consisted of either antiplatelet (acetylsalicylic acid in 6 and dipyrimidole in one) or antithrombotic therapy (warfarin sodium) in one. None of these 8 patients has had recurrent episodes during a three-year average follow-up. The one patient who did not receive therapy after her first CI returned with four episodes of left carotid system TIA after an asymptomatic period of 23 months. Our results with antithrombotic therapy are similar to those reported by others. It is interesting to note a disproportionately large number of men with TIA or CI associated with MVP compared to patients found to have uncomplicated MVP, which is many times more common in women. This pattern has also been recognized in other studies. Whether this may have therapeutic implications because of the possible inherent differences in sex responses to antiplatelet therapy will also have to be determined by long-term follow-up studies.

The results of our studies place us in a therapeutic dilemma. On the one hand we have also found an increased incidence of MVP among younger patients with CI or TIA, yet have been unable to identify any subset at risk for CI or TIA among our cardiologic patients with MVP.

One primarily cardiologic study of 53 patients diagnosed as having MVP on the basis of a clinically detectable click or late systolic murmur was followed a mean of 13.7 years. None was reported to have a cerebral ischemic event. However, 9 patients died and in only 2 were the causes defined as due to primary cardiac lesions related to MVP. In the other 7 fatalities, one was related to aortic dissection and Marfan's syndrome. The other 6 deaths were not specified as to etiology. As Barnett had already published his initial data on the association of MVP and cerebral ischemic events, one would assume these were not found as the cause of death in this population study. From the cardiologist's point of view, our prospective data concerning the population initially found to have MVP and presenting primarily with cardiac complaints would not identify a significant enough risk to justify consideration of long-term prophylactic therapy for the asymptomatic patient found to have MVP. This is in agreement with other cardiologic opinions. However, since our initial report of these data,
Cleveland Clinic studies\textsuperscript{12} have reviewed 24 patients with MVP and either CI or TIA found among analyses of populations from both the cardiologic and neurologic services. In 20, MVP was first recognized after CI or TIA; 4 of their 24 patients with CI or TIA were among 225 patients initially seen in the cardiology section prior to having a cerebral ischemic event. They did not identify any factors that predisposed these 4 patients with previously recognized MVP to later development of TIA or CI.

Therefore, continued long-term analysis of the patients primarily seen by cardiologists and identified as having MVP seems indicated because of the increased incidence of MVP among younger patients with cerebral ischemic events. Such studies should attempt to find contributory mechanisms separating those who eventually have either a TIA or CI from the larger group in whom MVP is a much more benign lesion, at least as far as neurologic problems are concerned.

In summary, the risk of CVA among patients with MVP has shown a significant discrepancy, depending on whether the patients were initially seen because of a cardiologic problem or initially seen in the neurologic section because of a cerebral ischemic event. Prospective follow-up of patients initially seen in our cardiologic section and found to have MVP has not identified a subset with increased risk of future development of TIA or CI. In contrast, there appears to be a definite increased incidence of previously undetected MVP among patients less than 60 presenting primarily to our neurology department with either a TIA or CI. This disparity suggests need for a continued analysis of factors that may predispose a few of the many patients with MVP to the risk of cerebral ischemic event.

References
Mitral valve prolapse and cerebral ischemic events. A comparison between a neurology population with stroke and a cardiology population with mitral valve prolapse observed for five years.

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