Editorial: Thromboembolic Studies in the Patient with the Prolapsed Mitral Valve
Has Salome Dropped Another Veil?

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THE PROLAPSED MITRAL VALVE, or click-murmur syndrome, continues to evoke interest, concern and controversy. Although the midsystolic click and late systolic murmur were well described in the late 19th century,\(^1\) it was not until 1961 that Reid\(^2\) suggested the mitral valve as the cause of the click and mitral insufficiency as the cause of the murmur. This was confirmed by angiocardiography and phonocardiography. Subsequently, noninvasive identification of the presence of mitral valve prolapse became possible by echocardiography. When population studies were done, the prevalence of mitral valve prolapse by physical or echocardiographic findings varied from 5–20%.\(^3\) If both echocardiographic and auscultatory evidence is required before mitral valve prolapse is diagnosed, the prevalence in the population is 5–10%.

Although Barlow\(^7\) described a subgroup of these patients who were symptomatic with chest pain (usually atypical for angina), palpitations, dizziness, and T-wave ECG changes, the finding of click-late systolic murmur had been assumed to be benign, even a normal variant. Anecdotal evidence that this apparently common problem was not entirely benign began to accumulate in the form of case reports describing the development of sudden severe mitral insufficiency, often associated with rupture of the chordae tendineae, occasional cases of infective endocarditis, atrial and ventricular arrhythmias (including runs of ventricular tachycardia) and, most distressingly, occasional reports of sudden death.

Out of this Pandora’s box called prolapsed mitral valve, an increasing number of serious and frightening complications continue to emerge. The latest problem reportedly associated with the prolapsed mitral valve is stroke, presumably thromboembolic. In 1976, in a prospective study of patients with transient cerebral ischemic attacks and partial, nonprogressing strokes, Barnett et al.\(^8\) reported finding 12 patients with angiocardiographically proved mitral valve prolapse out of 166 patients, and suggested an etiologic relationship.

In this issue of Circulation, Steele and colleagues report evidence that patients with mitral valve prolapse and stroke have a decreased platelet survival compared with normal. In five patients with mitral valve prolapse and stroke, the platelet survival time as measured by the chromium-51-tagged platelet technique was significantly shortened compared with 17 patients with mitral valve prolapse and no history of stroke. In the 17 patients with mitral valve prolapse without stroke, the platelet survival time was considered shorter than normal in seven (33%).

The study raises some interesting questions. Although Steele et al. used the most accepted method of estimating platelet survival time, there is some question about what the results indicate. A shortened platelet survival time is found in many diseases with an increased incidence of thromboembolism, such as mitral stenosis, coronary artery disease and recurrent venous thrombosis, as well as in patients with prosthetic heart valves.\(^8\) Unfortunately, the incidence of decreased platelet survival time in all these diseases is high, much higher than the incidence of clinical thromboembolism. For instance, Ritchie and Harper\(^9\) observed that more than half the patients with documented coronary atherosclerosis had shortened platelet survival time. In Steele's paper, 138 patients with rheumatic mitral stenosis were studied. Of 41 with a history of thromboembolism, 40 (98%) had a shortened platelet survival time, compared with 76 of 97 patients (78%) without a previous thromboembolic event. In all these diseases, patients who are prone to thromboembolism cannot be readily differentiated by the shortened platelet survival time.

Since this is a retrospective study, the shortened platelet survival time may be related to the previous embolic episode rather than to the prolapsed mitral valve. The evidence in this paper that patients with prolapsed mitral valve without a history of stroke have a decreased platelet survival time is not convincing. Since both stroke and prolapsing mitral valve are common problems in the population, we may be seeing the chance association of these relatively frequent problems in the same patient.

Other problems, such as the definition of mitral valve prolapse by echocardiography and even angiocardiography, further confuse the issue. In one study,\(^4\) a reported incidence of mitral valve prolapse by echocardiography in 100 apparently normal women was 21%. The angiocardiographic definition of mitral valve prolapse is by no means agreed upon. Angiocardiography has never been done on a group of normal people, but in one report,\(^11\) the incidence of mitral valve prolapse in 336 consecutive left ventriculograms of patients unselected for their cardiac diagnosis was 40% in patients with coronary artery disease, 32% in

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patients with rheumatic valvular disease, and 60% in patients with chest pain and normal coronary arteriography. It appears that angiocardiography very commonly identifies what some investigators call mitral valve prolapse.

With all the objections, the risk of thromboembolic stroke remains possible. At the last American Heart Association Scientific Sessions in Dallas, the same physicians who made the initial observations, Boughner et al., reported a retrospective study in patients who had had clinical studies. There were 141 patients 45 years and older, and 57 younger than age 45. A control group was age-matched and echocardiography was done on all patients. The incidence of mitral valve prolapse in the older patients was 5% and their controls showed a 7% incidence of prolapse. In the stroke patients younger than age 45 years, the incidence of mitral valve prolapse was 40%, compared with a 7% incidence in their control group.

The critical question is whether a shortened platelet survival time will predict the patients who are at risk for thromboembolism and the magnitude of that risk. In the reports of long-term follow-up studies of patients with mitral valve prolapse, stroke is not mentioned. In a recent extensive review of mitral valve prolapse, stroke is not indicated as a possible complication. In fact, in another review of the literature of mitral valve prolapse, Barlow and Bosman reported only one patient, a 23-year-old woman with mitral valve prolapse and a convincing, otherwise unexplained stroke. The incidence of stroke in patients with prolapsed mitral valve must be vanishingly small.

On identifying even rare complications associated with common clinical problems, the physician must decide what to tell the patient. It serves no useful purpose to inform the patient with a mid-systolic click or late systolic murmur that he or she is at risk from a long series of possible complications, no matter how rare, unless the physician is prepared to recommend a therapeutic intervention. For example, many physicians will recommend prophylactic antibiotics at the time of dental manipulation to decrease the incidence of endocarditis.

Until the suggestion that these patients may be subject to thromboembolism is verified by studies, and until we have better identified the subgroup of patients with prolapsed mitral valve who are at risk from this complication, informing patients of this risk is not indicated, nor is it reasonable to recommend "prophylactic" platelet-active drugs.

When first widely recognized as a distinct problem in cardiology, the prolapsed mitral valve was found to be very common and thought to be quite benign, with an excellent prognosis over many years of follow-up. In most patients with this auscultatory finding, this assessment is still accurate. Yet, as we live longer with the benign and friendly Dr. Jekyll of click-murmur syndrome, we are catching more frequent glimpses of the sinister Mr. Hyde.

References

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