The Significance of Mitral Valve Prolapse

A. K. BROWN, MB, FRCP, Physician
VALERIE ANDERSON, MB, Medical Assistant
Cardiac Department, Royal Lancaster Infirmary, Lancaster

Until the recognition by Reid in 1961[1] that systolic clicks and murmurs originated in the mitral valve apparatus, it was widely believed that the clicks came from an extracardiac source. Many names were used to describe the syndrome—'the click-murmur syndrome', 'the billowing mitral valve', 'the floppy mitral valve', 'the redundant cusp syndrome' and 'Barlow's syndrome'—but when angiography and echocardiography showed mitral valve prolapse (MVP) to be the cardinal feature, that term superseded previous ones[2].

Although the condition may be associated with arrhythmias, chest pain, sudden death, systemic emboli, chordal rupture, progressive mitral regurgitation and infective endocarditis, it appears to be benign in most cases. Since the advent of echocardiography, the diagnosis of MVP has become increasingly popular and one report using phono- and echocardiography found suggestive evidence of prolapse in 28 per cent of a group of 100 females[3]. Is this condition therefore a benign anatomical variant or a true pathological entity progressing to serious clinical disease, and should all patients with systolic clicks and otherwise unexplained systolic murmurs be investigated and reviewed regularly?

Anatomy

The anterior and posterior leaflets of the normal mitral valve have approximately similar areas, but the anterior is twice the length of the posterior leaflet, which has a wider rectangular base. The posterior leaflet is divided into three scallops or segments, lateral, central and medial. Insertion of the leaflets is into the mitral ring or annulus which is incomplete anteriorly, and the leaflets are divided into proximal zones composed of dense collagen, and distal zones of looser collagen, separated usually by a ridge of demarcation. The distal or 'rough' zones of the anterior and posterior leaflets oppose during closure of the normal mitral valve. The mitral valve apparatus consists of the posterior left atrial wall, the annulus, chordae tendinae, papillary muscles and the left ventricular wall as well as the leaflets. The detailed anatomy has been well reviewed[4-7].

Pathology of Prolapsed Mitral Valve

Abnormalities of the mitral valve leaflets and chordal apparatus are usually regarded as the cause of MVP. The essential pathological feature is weakening of the central fibrous core of the leaflets, which allows cusp separation and chordal lengthening[8] and the redundant leaflets show myxomatous infiltration. Altered coaptation of the leaflets results in prolapse, and mitral regurgitation is caused by loss of coaptation. Chordal deficiency in 6 of 100 normal hearts and 36 of 40 hearts with valve deformity has been demonstrated in an anatomical study[9], and the authors suggest that minor variations in the mitral valve apparatus may render unsupported parts of the leaflets vulnerable to high pressures and cause prolapse in some cases. Others[10-13] have described abnormalities of left ventricular contraction, and it is suggested that some patients with MVP have a cardiomyopathy[14]. A recent study by Malcolm et al.[15] found enzyme and histochemical changes in left ventricular biopsy specimens in which left ventricular function was apparently normal. Abrams[2] takes the view that mitral valve prolapse is the final common pathway responsible for the clinical picture; most authors concur with this concept.

Aetiology

Most cases of MVP are idiopathic, and familial incidence with an autosomal dominant mode of transmission is described[16-18]. It is associated with connective tissue disorders such as Marfan's syndrome, osteogenesis imperfecta and Ehlers-Danlos syndrome, and the rising prevalence with age may reflect degeneration of connective tissue in the mitral apparatus[19]. Mitral prolapse has also been associated with atrial septal defect, rheumatic carditis, neuromuscular and minor skeletal abnormalities, including the straight back syndrome[20-24]. Although MVP is frequently associated with coronary artery disease, the nature of the relationship is unclear and it may be a chance association[25-27]. Prolapse occurs in children but is commoner with advancing years. It was originally thought to show a female preponderance[28] but it is probably equally common in males[29].

Clinical Features

Symptoms

Most patients are asymptomatic[30], although some authors report symptoms in 75-80 per cent of
patients[28,31], possibly owing to the referral of complicated patients to special centres. Some patients are aware of the systolic noise originally described by Osler as the systolic whoop[32].

Chest pain is the commonest symptom and it has been postulated that an imbalance between myocardial oxygen supply and demand, with relative ischaemia of the papillary muscles caused by excessive stretching, is responsible[31,33]. Congenital papillary may occur[28,31], possibly owing to angina pectoris may occur, most cases have atypical pain unrelated to exertion; episodes may persist for hours and are unrelieved by glyceryl trinitrate. It is claimed that propranolol relieves the pain[31,35]. It is tempting to attribute a causal relationship when chest pain occurs in patients with MVP, but it is our experience that the pain is frequently identical with pain otherwise diagnosed as \textit{innocent left sub-mammary pain} or \textit{oesophageal spasm}, and treatment with mild tranquilisers or antispasmodics is successful if reassurance fails. If there are no ECG abnormalities, the patient with MVP and atypical pain is at risk of becoming a cardiac invalid.

Fatigue, dyspnoea and lightheadedness are frequent complaints, but again their relevance to the associated prolapsed valve is questionable. Palpitations are also common[33,36-38] and may be associated with the rare cases of sudden death[39-42]. Exercise tests may be terminated by arrhythmias[11,43] but 24-hour ECG monitoring often shows a poor correlation between symptoms and recorded arrhythmias.

**Signs**

The hallmark of the auscultatory signs is the systolic click; it may be midway, late, or even early, in systole and may vary in timing in the same individual at different examinations. The typical late systolic murmur extends to or slightly beyond the aortic component of the second sound. A pansystolic murmur occurs in under 10 per cent of cases[31], and occasional patients demonstrate a striking \textit{‘whoop’} or \textit{‘honk’} which may be intermittent. Variation in auscultatory signs occurs with physical and pharmacological manoeuvres[44,45]. The standing position, the straining phase of the Valsalva manoeuvre and amyl nitrite inhalation cause the click to come earlier in systole and the murmur lengthens, probably because left ventricular end-diastolic volume decreases and the leaflets prolapse earlier into the left atrium. Squatting has the reverse effect: left ventricular end-diastolic volume is increased, the click comes later and the murmur shortens or may disappear, although it may become louder. Despite these interventions, up to 10 per cent of patients considered to have MVP on echocardiographic or angiographic evidence are silent to auscultation, although Barlow and Pocock[46] dispute this and believe that repeated examinations reveal a click or late systolic murmur.

The cardiac impulse is normal except in some of the cases with sufficient initial regurgitation to cause left ventricular enlargement; in these cases the impulse is double, being shown on apex cardiography as a mid-systolic retraction[44,47].

**Investigation**

Electrocardiographic abnormalities are common, with T wave flattening or inversion in leads II, III and AVF, and sometimes in V4-6. Prolonged ambulatory ECG monitoring may reveal arrhythmias such as ventricular extrasystoles, and ventricular and supraventricular tachycardia[36,45], and significant bradycardia may occur[48]. Exercise-testing may provoke arrhythmias in up to 75 per cent of patients and significant ST depression may be demonstrated[49].

Standard X-rays may reveal skeletal abnormalities such as a straight back, scoliosis or pes excavatum, but the cardiac outline is normal unless left atrial or left ventricular enlargement has taken place, owing to mitral regurgitation.

Angiography has made the recognition of MVP much easier and the introduction of echocardiography has given added impetus to its investigation.

**Angiography**

Many reports[49-53] have confirmed the original demonstration[54] that angiography can show mitral valve prolapse in patients with the systolic click-murmur syndrome, but the limitations of the technique are still a matter of debate. Two articles in the \textit{American Journal of Cardiology} exemplify the problems. Although only six patients had a click and murmur with echocardiographic evidence of prolapse in the series reported by Smith \textit{et al.}[55], 43 per cent of 336 consecutive left ventricular angiograms were thought to show MVP. This led the authors to question the specificity of posterior bulging of the mitral valve on left ventricular angiography. Rutherford \textit{et al.}[56] reported that 12 patients with angiographic evidence of posterior systolic bulging of one or both mitral leaflets nevertheless had no systolic click (9 patients) and negative echocardiograms (8 patients); they concluded that angiograms were more specific than echocardiograms in the diagnosis of MVP. Morphological studies using normal left ventriculograms[57] suggested that anatomical variations in the position of leaflet attachment to the mitral ring, and the configuration of the adjacent left ventricular wall in diastole, could produce false appearances suggestive of prolapse on the right anterior oblique view during ejection. These authors suggest that this normal variant should be described as pseudo-prolapse. Although cine-angiography in the right anterior oblique position provides good views of the posterior leaflet, demonstration of anterior leaflet prolapse requires left anterior oblique ventriculography. The overall impression is that angiographic criteria for the diagnosis of MVP remain a matter for debate, and posterior leaflet prolapse is probably over-diagnosed, whereas anterior leaflet prolapse may be missed.

**Echocardiography**

Interest in mitral prolapse dramatically increased after the initial descriptions of M mode echocardiographic
changes in 1970-71[58-60]; mid-systolic buckling, which has been likened to a question mark turned approximately 90° clockwise[61] (Fig. 1), is usually accepted as diagnostic of MVP, but the other characteristic finding, pansystolic bowing, is less specific, and Sahn and his co-workers[62] have shown that false positive diagnoses are easily made. Nevertheless, M mode criteria have been used in prevalence studies of mitral prolapse and a prevalence of 6-10 per cent in healthy young females[3,63], healthy young males[29], and newborn baby girls[64] is suggested. Although there have been suggestions that phonocardiographic findings have correlated with the two main types of echocardiographic features, our experience has been similar to the general view that there is no clear correlation between phonocardiographic findings.

The anatomical detail and spatial orientation provided by cross-sectional (2D) echocardiography (CSE) has led to reports of the value of this technique in the diagnosis of MVP[65-68]. However, there is no agreement about the true diagnostic value of either M mode or 2D echocardiography in mitral valve prolapse. Jeresaty[69] believes that it is too early to speculate on the value of cross-sectional echocardiography in the diagnosis of MVP, and Kisslo[70], in a recent comparison of M mode and two-dimensional cross-sectional echocardiography, concludes that both methods are of uncertain value in the diagnosis of mitral prolapse. Our experience of echocardiography in the diagnosis of MVP in 36 patients attests to the value of cross-sectional (2D) recordings. We have used the four-chamber apical view to supplement the long axis parasternal view (Fig. 2a, b) used by earlier investigators, and have shown clear separation of normals from patients with prolapse if superior arcing of one or both leaflets above the atrio-ventricular ring in systole is taken as the diagnostic criterion. With echocardiography, particularly CSE, anterior and posterior leaflets can be seen, and it appears that prolapse of both leaflets is most common. Earlier reports based on angiography had suggested that isolated posterior leaflet prolapse was the most frequent abnormality.

We believe that with cross-sectional (2D) echocardiography, systolic arcing of the mitral leaflets into the left atrium beyond the mitral ring can be shown clearly in most patients with mitral valve prolapse, and that this provides the best diagnostic technique for MVP. Difficulty can arise if one or other leaflet fails to record but, in most cases, individual leaflet prolapse can be assessed, and it is possible that technical improvements will make

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**Fig. 1.** Phono-echocardiogram of a patient with mitral valve prolapse. The late systolic murmur is recorded at the apex, and corresponds with the mid-systolic bowing (broad arrow) of the mitral valve leaflets. LFI—low frequency recording gain 1 (Cambridge Fibre-Optic Recorder); IVS—interventricular septum; AMVL, PMVL—anterior and posterior mitral valve leaflets; P—pericardium. (Echocardiograms taken with a Smith Kline 20A Echograph.)

**Fig. 2 (a).** Still frame polaroid photograph from a cross-sectional echocardiogram of a volunteer with a normal mitral valve. A line is drawn from the posterior aortic root to the atrio-ventricular junction to represent the atrio-ventricular ring, and neither leaflet projects beyond this line during systole.
Fig. 2 (b). A patient with anterior mitral valve prolapse: the anterior leaflet can be seen to move beyond the arbitrary line into the left atrium, and forms an acute angle with the posterior aortic root.

Cross-sectional echoes are displayed as real time moving images and recorded on video-cassettes. Still frame photographs suitable for publication result in degradation of the image and provide less information than the moving image.

AAR, PAR—anterior and posterior aortic root; LA—left atrium; IVS—interventricular septum; LV—left ventricle; AMVL, PMVL—anterer and posterior mitral valve leaflets; Ch—chordae; AV Junction—atrio-ventricular junction.

(Cross-sectional echocardiograms taken with a Smith Kline Ekosector I.)

cross-sectional echocardiographic criteria the ‘gold standard’ that is sadly lacking in all methods for the diagnosis of mitral prolapse.

Discussion

Should mitral valve prolapse (MVP) be regarded as a benign anatomical variant or a potentially lethal disorder warranting major investigation and constant surveillance? As it is a common problem in clinical practice, a coherent policy of management, based on the clinical features, diagnostic measures and prognosis, is essential. There is no doubt that patients with a systolic click and murmur, ECG changes and left atrial and left ventricular enlargement warrant investigation using echocardiography, exercise stress testing, ambulatory ECG monitoring and, possibly, left ventricular cine-angiography. Patients with MVP and associated disease such as Marfan’s syndrome, other connective tissue disorders and coronary artery disease need investigation and careful management. The problem is how to manage symptomatic and asymptomatic patients who have signs of MVP but no evidence of associated disease or cardiac embarrassment. Although serious complications of MVP are rare, it is because they exist that the decisions about long-term management are vitally important. Barlow and Pocock[71] recommend prophylaxis for infective endocarditis in all patients with constant, early, late or pansystolic murmurs. Progressive mitral regurgitation is more common in males than females, and patients with demonstrable arrhythmias are likely to be at greater risk of sudden death. Chest pain associated with unequivocal clinical and echocardiographic evidence of MVP warrants further investigation, and non-cardiac causes of the pain should be considered if resting and exercise ECGs are normal.

We put forward our current policy as a suggestion for the rational care of patients with mitral valve prolapse. Diagnosis is considered in all patients with systolic click and/or murmur, and these signs are specifically sought in patients with atypical chest pain, palpitations, light-headedness or syncope. Patients are routinely examined lying, in the left lateral position, standing and squatting, and amyl nitrite inhalation is occasionally used. A resting ECG and chest X-ray are performed and M mode and 2D echocardiography are used to demonstrate prolapse of mitral valve leaflets. A combined approach using the clinical signs of systolic click and murmur, together with positive echocardiographic findings, probably provides the clearest definition of MVP at present.

Patients with mitral valve prolapse associated with significant mitral regurgitation or disorders such as Marfan’s syndrome, other connective tissue disorders and coronary artery disease, receive full investigation, regular surveillance and appropriate treatment. Equally, patients with MVP who have chest pain, lightheadedness, palpitations or syncope require further investigation, such as exercise stress testing and prolonged ambulatory ECG monitoring, particularly if the resting ECG is abnormal.

This still leaves a large number of asymptomatic cases with a click and/or murmur, and recent evidence suggests that these comprise a large percentage of the apparently normal population. A click associated with a persistent long systolic murmur is widely believed to be more significant than a click alone, but this begs the question whether the latter may be just an early feature of a progressive condition that could end as haemodynamically significant mitral regurgitation with all the attendant clinical hazards. At present there is no clear answer to this problem and only general guidelines can be discussed.

Patients with a click but no abnormalities on the tests are reassured and discharged. If the click is associated with unequivocal signs of prolapse on the echocardiogram, penicillin prophylaxis for major dental work is
advised and the patient is assured that no serious cardiac disease has been found. Again, no follow-up is advised.

All patients with a murmur as well as a click and echocardiographic evidence of prolapse proceed to 24-hour ambulatory ECG monitoring and exercise stress testing. Only those patients with short, inconsistent systolic murmurs and minor or equivocal echo findings are discharged from the clinic. Patients with a systolic click, constant murmur and echocardiographic confirmation of MVP are seen at annual or longer intervals. If resting or exercise ECG abnormalities are found, the patients are seen at more frequent intervals and the rare cases with a family history of sudden death are specially observed. All these patients are advised to have penicillin prophylaxis against bacterial endocarditis. Active treatment is restricted to patients with important arrhythmias or disabling chest pain: beta-blockers are the drugs most often employed but other anti-arrhythmic agents, particularly verapamil, may be useful. Mitral valve replacement is considered if there is evidence of progressive regurgitation, and one of our patients with Marfan's syndrome had a successful replacement.

From this discussion of management policy it may seem that many patients require repeated examinations and treatment, but it is emphasised that most of our patients present with mild or absent symptoms, a systolic click and a short, often inconsistent, systolic murmur, and echocardiographic features show only minor degrees of prolapse. These patients are reassured and discharged from medical supervision. Most of the remainder, although seen at intervals, require no treatment and are also assured of the benign nature of their condition. Our belief that the majority of patients require no treatment and have a benign cardiac condition is reinforced by Leatham and Bigden[72], who stress that the risks of mitral valve prolapse have been grossly over-emphasised in some publications.

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